Page numbers followed by b indicate boxes; f, figures; t, tables.

GLOSSARY **B C D E F G H I J K L M N O P Q R S T U V W X Y Z**

A

Abducens nerve. Cranial nerve VI, **the nerve,** that innervates the lateral rectus, the extraocular eye muscle that moves the globe laterally. 260f, 559, 614b

Abductor. That which draws a body part away from the median line; typically associated with a muscle.* 241–242, 242t

Abembryonic pole. The side of a blastocyst opposite the embryonic pole, that is, the side opposite the inner cell mass. 43

Abnormal spindle-like microcephaly associated microcephaly (ASPM). A gene that plays an essential role in embryonic neuroblasts in normal mitotic spindle function, and is expressed in proliferating regions of the cerebral cortex during neurogenesis. 290b–291b

Abortifacient. That which causes an embryo or fetus to abort. 45b

Accutane. A drug taken orally for the treatment of acne. 161–162

Acetazolamide. A carbonic anhydrase inhibitor with a wide variety of uses, including the treatment of glaucoma. 638b

Acheiropodia. A disorder resulting in the absence of hands and feet. 634t, 636t

Achondroplasia. The most common and most recognizable form of dwarfism. It is caused by mutations in Fibroblast growth factor receptor 3 (Fgfr3). 219b, 220f, 239b, 602b

Achondroplasia/hypochondroplasia syndrome. Skeletal dysplasia caused by the Fgfr3 mutation, which results in brachydactyly (abnormal shortness of the fingers) and rhizomelia (shortening of the proximal limbs). 635t

Acoustic meatus, external. The ear canal. 572

Acro-dermato-ungual-lacrimal-tooth (ADULT) syndrome. A syndrome that affects ectodermally derived structures, caused by mutations in the transcription factor Tumor protein P73-like (Tp73l; also known as P63). 203b

Acromegaly. A condition in which growth hormone production is increased. 241b

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* Selected definitions adapted from *Dorland's Illustrated Medical Dictionary,* 31st ed, 2007. Philadelphia: Elsevier.

Acrosome. The apical vesicle, filled with hydrolytic enzymes (e.g., acrosin, hyaluronidase, and neuraminidase), that caps the head of the spermatozoon. It plays an essential role in fertilization. 25

Actin-binding protein. Any of a number of proteins that binds to actin, which is a protein of the cytoskeleton. Acting along with myosin, it is responsible for changing and maintaining cell shape.* 111b

Activin. A member of the Tgf-β family. 157

Acvr2b. An activin receptor. 383b

Adactyly. A disorder resulting in the absence of all the digits on the hand or foot. 634t

ADAM. A superfamily of proteins in which all 30 or so family members contain a disintegrin and a metalloprotease domain. 39

ADAM2. Also known as Fertilinβ. A protein present on male germ cells and/or mature sperm, it is a member of the ADAM superfamily. 39

Adductor. That which draws a body part toward the median line; typically associated with a muscle.* 242, 242t

Adenohypophysis. The anterior lobe of the hypophysis (pituitary gland).* 282

Adenoids. The tonsils. 576

Adherens junction. An intercellular junction associated with the deposition of E-Caderin, a calcium-dependent cell adhesion molecule, on lateral cell surfaces. 43

Adrenal cortex. The outer, firm, yellowish layer that comprises the larger part of the adrenal gland, consisting of the zona glomerulosa, the zona fasciculata, and the zona reticularis. It secretes, in response to release of corticotropin by the pituitary gland, many steroid hormones.* 499–500

Adrenal gland. A flattened organ found in the retroperitoneal tissues at the cranial pole of the kidney.* 499f, 499–500

Adrenocorticotropic hormone (ACTH). A polypeptide hormone that stimulates the adrenal cortex.* 500b

Afadin. An actin filament-binding protein. 81b

Agyria. Lack of gyri, a malformation in which the convolutions of the cerebral cortex are not fully formed, so that the brain surface is smooth (lissencephaly).* 287b

Ala orbitalis. Also called orbitosphenoid. Cartilage that, along with the ala temporalis, or alisphenoid, develops around the eye. They will ultimately contribute to the greater and lesser wings of the sphenoid. 547

Alagille syndrome. Also called arteriohepatic dysplasia. A disorder, caused by mutation of the Jagged1 or Notch2 genes, that affects the skeletal, cardiovascular, and gastrointestinal systems. 92b, 159, 230b, 231b, 233b, 383b, 416b, 449b

Alar (dorsal) plates. Combined with the pair of ventral (basal) plates, these structures make up the mantle zone of the spinal cord and brain stem. 247b, 257, 257f

Albinism. A general term for pigmentation defects. 128b

Albumin. A hepatic marker within the endoderm. 449b

Alpha-Fetoprotein (AFP). A protein produced by the fetal liver, whose level steadily increases during pregnancy. 114b, 180, 182, 184

Alisphenoid. A cartilage of the fetal chondrocranium on either side of the basisphenoid bone. Later in development it forms most of the greater wing of the sphenoid bone.* 547, 553, 554f

Allantois. One of four extraembryonic membranes. The umbilical arteries and veins form in the mesoderm of the allantois. 104f, 105, 472, 474f

Alpha cells. One of the cell types in the periphery of the pancreatic islets that secrete somatostatin (α_1 cells) and glucagon (α_2 cells).* 453b
Alpha-actinin. A cytoskeletal linker protein. 160

Alveolus(i). The bony socket that holds a tooth. 214, 319b, 323, 327b–328b,
Amacrine cells. One of five types of retinal neurons that lack large axons, having only processes that resemble dendrites.* 607

Ambisexual phase. Also called the "biopotential phase of genital development." The period near the end of the 6th week of gestation when the male and female genital systems appear indistinguishable, although subtle cellular differences may already be present. In both sexes, germ cells and somatic support cells are present in the presumptive gonads, and complete mesonephric and Müllerian ducts lie side by side. From the 7th week on, the male and female systems pursue diverging pathways. 502

Amegakaryocytic thrombocytopenia syndrome. A disorder resulting from HoxA11 mutation. 637b

Amelia. A disorder resulting in the absence of one or more limb. 632b, 633f, 634t

Ameloblasts. Cylindrical epithelial cells in the innermost layer of the enamel organ that take part in the elaboration of the enamel prism. The ameloblasts cover the dental papilla.* 195b, 210, 212f

Amelogenesis imperfecta. The defective development of enamel or dentin resulting from a mutation in Dlx3. 214b

Amhr-I receptors. A type of anti-Müllerian hormone receptor, with Amh being a Tgfβ/Bmp family member. Studies have found Alk2, Alk3 (or Bmpr1α), and Alk6 also serve as Amhr-I receptors. When these receptors are knocked out in mice or if their signaling is blocked within the Müllerian duct mesenchyme, Amh-induced Müllerian duct regression is lost. 509, 510

Aminoglycoside antibiotics. Any of a group of antibiotics (e.g., amikacin, gentamicin, streptomycin) derived from various species of *Streptomyces* or produced synthetically. Aminoglycosides inhibit bacterial protein synthesis by binding with the 30S ribosomal subunit and are bactericidal. Irreversible hearing loss is possible if too high a dose is administered.* 596b, 597b

Amniocentesis. The process by which embryonic cells obtained from the amniotic fluid are analyzed to detect many genetic disorders early in pregnancy. 35b, 114b, 169b, 184–185, 185f

Amnion. One of four extraembryonic membranes. It completely encloses the fetus and surrounds it with amniotic fluid. 51b, 55f, 57

Amniotic band syndrome. A disorder that involves a complex etiology that in some cases may result from rupture of the amnion and constriction of limbs by fibrous amniotic bands. It is related to limb-body wall complex (LBWC). 107b

Amniotic cavity. The first cavity to appear, typically on day 8 of embryonic development. It forms within the amnion at the embryonic pole of the blastocyst between the epiblast and overlying trophoblast. 51b, 57

Amniotic fluid. The fluid that surrounds and cushions the fetus, very similar to blood plasma in composition. It is initially produced by transport of fluid across the amniotic membrane. 179

Ampulla. The second portion of the oviduct (fallopian tube) where a sperm cell undergoes a process of functional maturation that prepares it to fertilize an oocyte. 28, 486

Ampulla of Vater. Also called hepatopancreatica ampulla. A structure created by the junction of the pancreatic and common bile ducts.* 451

Anagen. One of four phases (growth phase) of embryonic hair growth. 204

Anal agenesis. Failure of the anal orifice to form properly. 538b, 540f

Anal atresia. Congenital absence or pathologic closure of the anal orifice. 538b

Anal pit. The distal one-third of the anorectal canal formed from an ectodermal invagination. 474, 474f

Anal stenosis. Abnormal narrowing or constriction of the anal passage. 538b

Anaphase. That stage in meiosis and mitosis, following metaphase, in which the centromeres divide and the chromatids lined up on the spindle begin to move apart toward the poles of the spindle to form the daughter chromosomes.* 22f, 23t, 24

Androgen insensitivity syndrome (AIS). Also called testicular feminization syndrome. A disorder in which, if androgen receptors are disabled or absent, the male fetus may have normal or high levels of male steroid hormones, but the target tissues do not respond and development proceeds as though androgens are absent. 482b, 518, 535b, 535f

Anencephaly. Total dysraphism of the brain, with normal formation of the spinal cord. 113b

Angelman syndrome. A disorder involving deletions in a region of human chromosome 15 (15q11.2–q13) inherited from the mother. It is called Prader-Willi syndrome when the same defect is inherited from the father. Symptoms include developmental delay, speech and balance disorders, and a unique happy demeanor. 53b, 67b–68b

Angioblasts. The mesenchymal tissues of the embryo from which the blood cells and vessels differentiate.* 392

Angiogenesis. The development of embryonic blood vessels that "sprout" from preexisting blood vessels. 377, 385b, 392, 395b–399f

Angiogenic factors. Stimulation of blood and lymph vessels to grow into developing organs. If vessel growth is not inhibited at the appropriate time or if it is stimulated again later in life, blood or lymph vessels may proliferate until they form a tangled mass that may have clinical consequences. 399b

Angioma. A port-wine colored birthmark of the skin. It may also present as a tumor made up of blood vessels or lymph vessels.* 399b, 401b

Angiopoietin-1 (Ang-1). Protein growth factor involved in angiogenesis. 396b

Aniridia. The absence of the iris of the eye. In those with this syndrome, aniridia is caused by a hemizygous deletion of the *Pax6* transcription factor. 495b, 614b

Ankyloblepharon-ectodermal dysplasia clefting syndrome (AEC). Also called Hay-Wells syndrome. A disorder in which ankyloblepharon refers to the fusion of the eyelids. 203b

Ankyloglossia. Restricted movement of the tongue, resulting in speech difficulty.* 574

Ankyrin. A membrane protein of erythrocytes and brain that anchors spectrin to the plasma membrane at the sites of anion channels. 158

Annulus fibrosus. A ringlike structure developed from sclerotomal cells that are left in the region of the resegmentating sclerotome as its cranial and caudal halves split apart. 227, 227f

Anocutaneous occlusion. Excessive dorsal fusion of urogenital folds that completely cover the anus. This condition usually occurs in males because the genital folds do not normally fuse at all in females. 539b

Anophthalmia. A developmental defect characterized by the complete absence of the eyes (rare) or by the presence of vestigial eyes.* 602b, 613b

Anosmia. Loss of the sense of smell. 287b

Anotia. Suppressed growth of all the auditory hillocks; particularly, absence of the auricle. 601b, 601f, 602b

Antennapedia. In Drosophila, the gene that causes cells to form into antennae. 152–154

Anterior commissure. The first axon tract to develop (week 7) in the commissural plate, which interconnects the olfactory bulbs and olfactory centers of the two cerebral hemispheres. 288, 289f

Anterior segment ocular dysgenesis (ASOD). Defective development of the anterior part of the eye involving the cornea, iris, lens, and ciliary body. 614b

Anterior visceral endoderm (AVE). A specialized region of extraembryonic endoderm. 97b

Anterior-posterior patterning. Cranial-caudal patterning of the embryo, so-named because the cranial-caudal axis of human embryos is equivalent to the anterior-posterior axis of vertebrate embryo models. 97b

Antihelix. The prominent semicircular ridge seen on the lateral aspect of the auricle of the external ear, anteroinferior to the helix.* 601

Anti-Müllerian hormone (Amh). Also termed Müllerian-inhibiting substance (Mis). A hormone produced by pre-Sertoli cells following expression of the sex-determining region of the Y chromosome, which causes regression of the paramesonephric ducts. It is a member of the TGF-β family. 509, 509b, 510b, 510f

Antitragus. One of the six auricular hillocks (number 4) that arise in the 5th week and eventually form each part of the pinna. 601

Antrum. A fluid-filled cavity that forms within a growing ovarian follicle. 29

Aortic arches. The paired arteries derived from arteries surrounding the pharynx of piscine progenitors that correspond to arches 1, 2, 3, 4, and 6 of the ancestral fish, which have become highly modified to form the great vessels of the neck and thorax. 354, 354f, 385b, 402f, 402–408, 413b, 415b, 415f–417f, 545b

Aortic arch artery. The continuation of the ascending aorta that gives rise to the brachiocephalic trunk and the left common carotid and left subclavian arteries. It continues as the thoracic aorta.* 402

Aortic coarctation. A localized malformation characterized by deformity of the aortic media, and causing narrowing, usually severe, of the lumen of the vessel.* 415b–416b, 418f–419f

Aortic, gonad, and mesonephros (AGM) region. The dorsal aorta in the region of the genital/mesonephric ridge of the embryo where hematopoietic stem cells cluster in dense packs on the ventral endothelium. 390b, 391f

Aortic sac. A dilated expansion connected to the cranial end of the truncus arteriosus. 346

Aortic valve. A valve composed of three semilunar cusps or segments (semilunar cusps of aortic valve), which guards the aortic orifice in the left ventricle of the heart and prevents backflow into the left ventricle.* 346, 403, 556

Aortic valvular stenosis. Abnormal narrowing of the aortic valve. 380b

Aorticopulmonary septum. Also called conotruncal septum. A partition that completely separates the heart's right and left ventricular outflow pathways. 370–371, 374f
Aorticorenal ganglia. A knot-like body of nerves that innervate the kidney and suprarenal gland. 310

Apert syndrome. A disorder involving Fgfr2 mutation that results in craniosynostosis and severe fusion of digits. See also syndactyly. 158, 550b, 551f, 630b, 635t, 638b

Aphakia. The absence of the lens of the eye. 607b

Apical constriction. Alteration in the distribution of F-actin to the apical side of epithelial cells, which regulates the formation of a contractile actomyosin network associated with apical intercellular junctions. Typically it is caused by the actin-binding protein *Shroom.* 111b

Apical ectodermal ridge (AER). Thickened ectoderm on the distal margin of the limb bud that maintains outgrowth of the limb bud along the proximal-distal axis. 619, 621b

Apocrine glands. Highly coiled, unbranched organs that develop in association with hair follicles, which secrete a complex mix of substances that are modified by bacterial activity into odorous compounds. They initially form over most of the body, but in the later months of fetal development they are lost except in certain areas, such as the axillae, mons pubis, prepuce, scrotum, and labia minora. 193b, 207–208

Apoptosis. Also called programmed cell death. A change (decrease) in cell number; cell death. 20b, 81b, 137, 196, 303b, 617b, 626

Appendicular bone. Bone found in the limbs. 219

Appendicular skeleton. Bones of the limbs and girdles formed by endochondral ossification. 234

Appendix epididymis. The small remnant of the degenerate cranial end of the mesonephric duct in males. 511

Appendix testis. The small remnant of the proximal end of the paramesonephric duct in males. 504f, 509

Arachnodactyly. The disorder resulting in the abnormal elongation of the fingers and toes. 634t

Arachnoid mater. The spider-like membrane between the dura mater and pia mater surrounding the neural tube. 113b

Aristalesslike 4. A paired-type homeodomain protein. 630b

Arnold-Chiari malformation. An abnormality at the base of the brain that disrupts the normal drainage of cerebrospinal fluid (CSF) from the brain ventricles to the subarachnoid space surrounding the spinal cord. 115b

Aromatase. An enzyme activity occurring in the endoplasmic reticulum and catalyzing the conversion of testosterone to the aromatic compound estradiol. It proceeds via three successive hydroxylations, loss of a carbon atom, and rearrangement.* 517b

Arrector pili muscle. The tissue that erects hair follicles on the skin's surface (the cause of "goose bumps"). 201f, 204

Arteriohepatic dysplasia. Also known as Alagille syndrome. A human disorder that results from defects in Jagged1 or Notch2 signaling. 92b, 159, 230b, 231b, 233b, 383b, 416b, 449b

Articular cartilage. The layer of cartilage at either end of a future limb joint. 237

Artificial insemination. The deposition of semen within the vagina with a catheter. 17b

Arytenoid cartilage. One of the paired, pitcher-shaped cartilages of the back of the larynx at the upper border of the cricoid cartilage.* 553

Assisted hatching. A medical procedure performed before the embryo is inserted into the uterine cavity in cases where the zona pellucida is tougher than normal, thus making it more difficult for embryos to hatch. The zona pellucida ("shell") can be tougher in women older than 40 or in younger women who have a paucity of eggs. Assisted hatching involves making a small tear in the zona pellucida using acid tyrode solution, laser ablation, or mechanical means. 46b

Assisted reproductive technology (ART). A series of in vitro techniques, used to assist couples with conception, that consists of embryo transfer and in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), gamete intrafallopian transfer (GIFT), and zygote intrafallopian transfer (ZIFT). 46b–49b, 47f, 48f

Association neurons. Cells that form in the alar plates. 304

Astrocyte. A neuroglial cell of ectodermal origin, characterized by fibrous, protoplasmic, or plasmatofibrous processes. Collectively, such cells are called astroglia.* 257

Ataxia. Those cerebellar disorders identified by disruptions of coordination. 269b

Ataxia-telangiectasia. An autosomal recessive cerebellar ataxia syndrome. 269b, 613b

Atria. The chambers of the heart. 346, 354b–355b, 356b, 362–363, 363f–366f, 365, 423f, 424

Atrial septal defects. Human congenital diseases of the heart. The septum secundum is too short to cover the foramen secundum completely (or the foramen secundum is too large), so that an atrial septal defect persists after the septum primum and septum secundum are pressed together at birth. The defects are mostly detected by echocardiography in childhood, and they may warrant closure either surgically or by an occluding device to prevent the onset of cardiac hypertrophy and pulmonary hypertension. An atrial septal defect is associated with almost all documented autosomal and sex chromosome aberrations, and is a common accompaniment of several partial and complete trisomies, including trisomy 21 (Down syndrome). 378b–379b, 379f

Atrial spine. Also called spina vestibule. A projection of cells sent into the atrium from the dorsal mesocardium that joins the septum primum and contributes to this atrial septum. 362–363

Atrichia. An anomaly that results in the congenital absence of hair. 206b

Atrioventricular canal. The passage formed in the atrioventricular and outflow tract regions of the embryonic heart from the eventual fusion of the opposing endocardial-derived cushion tissues. 362–363, 363f–366f, 365

Atrioventricular (AV) node. The heart's secondary pacemaker center, which connects to the sinoatrial node (primary pacemaker region) via impulse-carrying fibers within the crista terminalis. 357, 377

Atrioventricular septum. Also called septum intermedium. The structure that divides the common atrioventricular canal into right and left atrioventricular canals. It is formed at the end of the 6th week when the endocardial-derived dorsal and ventral cushions meet and fuse. 364f–366f, 365

Atrioventricular sulcus. A groove on the external surface of the heart, that separates the atria from the ventricles. Portions of it are occupied by the major arteries and veins of the heart.* 346

Atrioventricular valves. The bicuspid (mitral) and tricuspid structures that develop from atrioventricular cushion tissue during the 5th and 6th weeks of gestation. 369–370, 370f–372f, 379b–380b

Auricle, atrial. A small functionally contractile appendage that develops from the atrium and around the upper portions of the right and left ventricles. 357-358, 359f

Auricle, of ear. The portion of the external ear not contained within the head; the flap of the ear. 357–358, 359f

Autonomic nervous system. The portion of the nervous system concerned with regulation of the activity of cardiac muscle, smooth muscle, and glands. It is usually restricted to the two visceral efferent peripheral components, the sympathetic nervous system and the parasympathetic nervous system.* 124–126, 251, 257, 297b, 299, 316

Autosomal dominant polycystic kidney disease (ADPKD). A common genetic disease associated with formation of cysts in the kidneys as well as in the ductal epithelia in the liver, pancreas, testis, and ovary. 495b

Autosomal recessive polycystic kidney disease (ARPKD). A disease associated with genes involved in mediating ciliary function. It is caused by mutations in the Pkhd1 gene, which mutates slowly to develop renal, hepatic, and biliary cysts. 495b

Autosomes. Twenty-two pairs of matched homologous chromosomes. 21, 503

Axenfeld-Rieger anomaly. A developmental anomaly consisting of defects including hypoplasia of iris stroma and usually glaucoma.* 614b

Axial bones. The bones of the cranium, vertebral column, ribs, and sternum, formed from the paraxial mesoderm. 219

Axon. That process of a neuron by which impulses travel away from the cell body. At the terminal arborization of the axon, the impulses are transmitted to other nerve cells or to effector organs. The larger axons are surrounded by a myelin sheath.* 277b–279b, 277f–279f, 308b

Azoospermia. The lack of spermatogenesis. 512b, 536b

Azygous vein. An intercepting trunk for the right intercostal veins as well as a connecting branch between the superior and inferior venae cavae. It arises from the ascending lumbar vein, passes up in the posterior mediastinum to the level of the fourth thoracic vertebra, where it arches over the root of the right lung, and empties into the superior vena cava.* 423f, 424

B

β-Catenin. A component of the cadherin/catenin adhesion complex. 81b, 238b, 291b, 465b, 466f, 467b

Bardet-Biedl syndrome. An autosomal recessive disorder characterized by mental retardation, pigmentary retinopathy, obesity, polydactyly, and hypogonadism.* 635t

Barr bodies. Structures condensed from the inactivated X chromosome in each cell of a female. 67b

Barrier contraceptives. A device or substance that physically blocks sperm from entering the vagina. 44b–45b

Basal ganglia. A knot-like mass crucial to executing commands from the cerebral hemispheres. It is formed from the ventral subpallium, which includes the corpus striatum and globus pallidus. 250b, 272, 282

Basal layer. The inner proliferating layer of cells of the developing skin. 193b, 195–196, 196f

Basal plate. (1) The portion of the decidua basalis that becomes an integral part (the maternal face) of the placenta. (2) Either of the pair of longitudinal zones of the embryonic neural tube ventral to the sulcus limitans, from which are developed the ventral gray columns of the spinal cord and the motor centers of the brain.* 171, 247b, 257, 257f

Basic helix-loop-helix (BHLH) transcription factors. A type of transcription factor. 610b

Basket cell. A cell of the cerebellar cortex whose axon gives off brushes of fibrils, forming a basket-like nest in which the body of each Purkinje cell rests.* 264

Brain-derived growth factor (Bdnf). A small-growth factor called a neurotrophin, which is secreted by the neural tube and the dermomyotome subdivision of the somite. 128b

Becker-type muscular dystrophy. A disorder involving a mutation in Dystrophin, a large protein (encoded by the largest gene in the human genome), which links intracellular cytoskeletal proteins with the sarcolemma, the plasma membrane of the muscle fiber. 244b

Beckwith-Wiedemann syndrome. A congenital autosomal dominant syndrome with variable expressivity characterized by exomphalos, macroglossia, and gigantism, often associated with visceromegaly, adrenocortical cytomegaly, and dysplasia of the renal medulla. 68b, 461b

Bell stage. The point occurring in the 14th week at which the dental papilla deeply invaginates the dental lamina and constitutes the core of the developing tooth. 195b, 210, 213f

Bergmann glia. Also known as radial glia. Develops in the cerebellum from glioblasts. 267, 268f

Beta cell. One of the cells that compose the bulk of the islets of Langerhans and secrete insulin.* 453b

Bf1. Also known as FoxG1, a forkhead gene. A transcription factor that establishes the telencephalon as a distinct region of the forebrain. 253b, 274b

Bicommissural aortic valve. A defective valve having two rather than three leaves that is asymptomatic or stenotic from infancy or may become stenotic over time, often due to calcification. 380b

Bicuspid valve. Also called mitral valve. The left atrioventricular valve, which has only anterior and posterior leaflets. 337b, 370

Bilaminar blastoderm. The stage of development in which the embryo is represented by two primary layers, the epiblast and the endoderm.* 51b, 56

Bile canaliculi. Fine tubular canals running between liver cells throughout the parenchyma. They usually occur singly between each adjacent pair of cells, and form a three-dimensional network of polyhedral meshes, with a single cell in each mesh.* 446

Binocular vision. The sight resulting when the visual fields of the left and right eyes overlap and the information from the visual fields from both eyes is relayed to one side of the brain. 278b

Bipolar cell. A nerve cell with two processes.* 607

Birthmark. Any congenital blemish or spot on the skin, usually visible at birth or shortly after.* 399b

Bladder. A membranous sac, such as one serving as receptacle for urine. 475b, 495, 496f, 497

Blastema. A group of cells that gives rise to an organ or part in either normal development or regeneration.* 493b

Blastocoel. A large cavity that forms within the morula, during the second week, and receives two waves of migratory endodermal cells sent by the hypoblast. The first of these waves forms the primary yolk sac (or the exocoelomic membrane or Heuser's membrane); the second transforms the primary yolk sac into the secondary yolk sac. 43

Blastocyst. The embryo at day 5 when it hatches from the zona pellucida by enzymatically boring a hole in it and squeezing out, then begins migrating to the uterus where it becomes tightly adhered to the uterine lining. 15b, 43–44, 44f, 53b, 55b–56b

Blastomeres. The cells that make up the morula and blastula. 41, 42f, 43, 43b, 47b, 48f

Blepharophimosis. An abnormality of the eye whereby the eyelids are partially fused. 613b

Blood-nerve barrier. The barrier formed by the endothelial cells and their tight junctions that blocks circulating macromolecules from entering the endoneurium. 307b

Bloomstrand chondrodysplasia. A disorder caused by loss-of-function mutations in Pthrp receptor (R1). Those affected have endochondral bone defects and absence of the breasts, and hence absence of the nipples. 210b, 237b

Bmp. A bone morphogenetic protein, a secreted signaling molecule of the Tgf-beta family. 19b, 72b, 81b, 83b, 95b, 97b, 112b, 119b, 129b–130b, 157, 157f, 214b, 237b, 240b, 253b, 255b, 276b, 312b, 328b, 340b–342b, 362b, 393b, 449b, 467, 468f, 490b–491b, 492f, 493b, 514f, 515b, 524b, 524f, 564b, 566b, 630b, 632b

Bmpr. Transmembrane Bmp receptor. 157

Body axes. The major planes of the body, defined for the first time by formation of the primitive streak: the **cranial-caudal (or head-tail) axis, dorsal-ventral (or back-belly) axis, medial-lateral axis,** and **left-right axis**. Before the flat embryonic disc folds up into a three-dimensional tube-within-a-tube body plan, these axes remain incompletely delimited. During gastrulation, three cardinal body axes are established. In the embryo and fetus, these three axes are called the **dorsal-ventral, cranial-caudal,** and **medial-lateral** axes, and are equivalent, respectively, to the **anterior-posterior, superior-inferior,** and **medial-lateral axes** of the adult. 69b, 71

Body cavity. A hollow place or space, or a potential space, within the body.* 320

Body folding. The process by which the forming embryo separates from its extraembryonic membranes. Body folds are caudal, cranial, lateral, and establish the tube-within-a-tube body plan. 103, 319b, 329, 331f, 437, 438f, 439, 439t

Bowman's capsule. A cup-shaped sac at the end of the metanephric tubules that wraps around a knot of capillaries (glomerulus) to form a renal corpuscle. 484f, 485

Brachial artery. A major artery of the arm. 411, 413f

Brachial plexus. A network of nerves originating from the ventral branches of the last four cervical spinal nerves and most of the ventral branch of the first thoracic spinal nerves. Situated partly in the neck and partly in the axilla, it is composed successively of ventral branches and trunks (supraclavicular part), which are related to the subclavian artery and

which give off the dorsal scapular, long thoracic, subclavius, and suprascapular nerves. The infraclavicular part consists of divisions that lie approximately behind the clavicle and cords and branches in the axilla in relation to the axillary artery. Its branches are medial and lateral pectoral, medial brachial cutaneous, medial antebrachial cutaneous, median, ulnar radial, subscapular, thoracodorsal, and axillary nerves.* 640

Brachiocephalic artery. The region of the aortic sac connected to the right fourth aortic artery. 403, 405f

Brachiocephalic vein. Either of the two veins that drain blood from the head, neck, and upper limbs, and unite to form the superior vena cava.* 423f, 424

Brachydactyly. A disorder resulting in the abnormal shortness of the fingers and toes. 239f, 240b, 240f, 634t, 635t, 636t, 637b

Brachyury. A T-box–containing transcription factor expressed throughout the primitive streak during gastrulation. 72b, 94b, 94f

Brain stem. The stalklike portion of the brain connecting the cerebral hemispheres with the spinal cord and consisting of the mesencephalon, pons, and medulla oblongata. Some also consider the diencephalon to be part of the brain stem.* 258–270, 259f, 260f, 262f, 264f–268f, 271f, 272f

Branchial arches. The five pairs of pharyngeal, or branchial, arches, that form on either side of the pharyngeal foregut, starting on day 22. Because of their evolutionary history from ancestors with six arches, these arches correspond to numbers 1, 2, 3, 4, and 6. Each arch has an outer covering of ectoderm, an inner covering of endoderm, and a core of mesenchyme derived from paraxial and lateral plate mesoderm, and neural crest cell–derived ectomesenchyme. 402, 543b

Branchial efferent neurons. The cells that serve the striated muscles, derived from the pharyngeal arches and ensheathed by connective tissue derived from cranial neural crest cells (V, VII, IX, X). The motor nucleus of the accessory nerve (XI) is branchial efferent because it forms part of this column. 259–260, 260f, 261

Branching morphogenesis. A process by which glandular organ rudiments form by a series of branches. Errors in patterns of pulmonary branching during the embryonic and early fetal periods result in defects ranging from an abnormal number of pulmonary lobes or bronchial segments to the complete absence of a lung. 324b, 327b–328b

Branchio-oto-renal (BOR) syndrome. A single-gene disorder recognizable by cup-shaped ears, preauricular pits, and small cysts over the sternocleidomastoid muscle. 494b, 586b, 587f, 602, 602b

Branchless. An Fgf-like ligand; one of three components identified during development of the tracheal system in Drosophila (the other two being Breathless, an Fgf receptor; and

Sprouty, an endogenous Fgf inhibitor). Branchless and Breathless are used repeatedly to control branch budding and outgrowth. 136, 328b

Broad ligament of the uterus. The peritoneal fold that receives the ovaries in the third month of gestation. 530, 531f–532f

Bronchial buds. Branches of the respiratory diverticulum that form the primary, secondary, and tertiary bronchial buds. The latter undergo further branching to form the terminal bronchioles, respiratory bronchioles , and terminal sacs (primitive alveoli). 319b, 321

Bronchioles. Branches of the tertiary bronchial buds within the lungs. There are two types: respiratory and terminal. 319b, 321, 323, 324f

Bronchopulmonary dysplasia. Chronic lung injury associated with preterm infants. 326b

Bronchopulmonary segments. Bronchi and associated tissue in the mature lung. 321

Bruch's membrane. The basal lamina of the pigmented epithelium of the eye that develops on day 33. 607

Buccinator muscles. Muscles in the face that compress the cheeks and retract the angle of the mouth.* 559

Buccopharyngeal membrane. A transient embryonic septum at the cranial limit of the foregut, in the depths of the stomodeum.* 563, 564f

Bulbourethral glands. One of three accessory glands—the seminal vesicle and prostate being the other two—of the male genital system, all of which develop near the junction between the mesonephric ducts and pelvic urethra. All three glands contribute to the seminal fluid protecting and nourishing the spermatozoa after ejaculation. 28, 482b, 511, 511f

Bulboventricular sulcus. The structure that separates the primitive ventricle from the bulbus cordis. 346

Bulbus cordis. The structure that forms much of the right ventricle. 337b, 346

Bulge. A structure in hair follicle development that, studies show, is a source of progenitor cells or stem cells. 204, 205f, 206b

Bullous congenital ichthyosiform erythroderma. An inherited skin disease involving mutations in genes encoding Krt1 or Krt10, which causes blistering in the suprabasal layers and also reddening of the skin. 198b

Bundle of His. A bundle of specialized conducting cells that accompanies development of the atrioventricular (AV) node, and that sends one branch into the left ventricle and the other into the right ventricle within the moderator band. 377

C

C cells. Calcitonin-producing cells that arise from a controversial fifth pouch and descend to populate the thyroid. 578

Cadherins. Any of a family of calcium-dependent cell adhesion molecules.* 160, 493b

Cajal-Retzius cells. Transient neurons found within the marginal zone, lamina I, the majority of which originate in a dorsal midline structure of the telencephalon (the cortical hem) and migrate tangentially into lamina I. Through their secretion of the large glycoprotein Reelin, Cajal-Retzius cells are believed to orchestrate the inside-to-outside migration of neurons into the cortical plate. 285

Calcitonin gene-related peptide (Cgrp). The principal neurotransmitter released by the genitofemoral nerve. 530b

Calmodulin kinase II. A candidate gene that may determine facial morphology; an intracellular signaling factor that promotes distal outgrowth. 566b

Calvaria. The flat bones of the cranial vault. 547

Calyx. Anatomic nomenclature for a cup-shaped organ or cavity.* 487–488, 488f

Calcium-independent adhesion molecules (Cams). Any of a group of cell adhesion molecules, e.g., N-Cam (neural-cell adhesion molecule); V-Cam (vascular-cell adhesion molecule); and Pe-Cam (platelet-endothelial–cell adhesion molecule). 160, 361b

Camptodactyly. The disorder resulting in flexion contracture of a finger (often the fourth or fifth), which cannot be fully extended. 634t

Camptomelic dysplasia. A condition involving mutations in Sox9, which is typified by bowing of the long bones and defects in all the endochondral bones. Camptomelic dysplasia is also associated with XY sex reversal in males. 221b, 505b, 636t

Canalicular stage. The phase of lung development prior to week 26 of gestation. Infants born at this stage require intensive respiratory assistance to survive. 322t

Cancer. A neoplastic disease the natural course of which is fatal. Cancer cells, unlike benign tumor cells, exhibit the properties of invasion and metastasis and are highly anaplastic.* 68b, 465b, 466f, 467b

Canonical Wnt pathway. A development course whereby, in the absence of Wnts, cytoplasmic β-Catenin (a component of the Cadherin/Catenin adhesion complex) interacts with a complex of proteins, including Axin (product of the mouse gene Fused that regulates axis development), Apc (Adenomatous polyposis coli), and Gsk3 (a serine threonine kinase). This interaction results in the proteolysis of β-Catenin and no Wnt signaling. 155, 155f

Cap stage. The stage of dental development when the mesenchymal component forms a hillock-like dental papilla (a "cap") that indents the epithelial enamel organ formed from the bud. 195b, 210

Capacitation. Action that takes place within the female genital tract and is thought to require contact with secretions of the oviduct. Spermatozoa used in vitro fertilization (IVF) procedures are artificially capacitated. 27–28

Cardia bifida. A condition in which failure of the cardiac crescent limbs to fuse results in the formation of two tube-like structures instead of one. 342

Cardiac arrhythmia. Abnormal heart rhythm that is the result of genetic heart malformations; responsible for most incidents of sudden death in the US. One malformation involves mutation in Kcnq1: long QT syndrome characterized by prolongation of the depolarization (Q) and repolarization (T) intervals. 383b

Cardiac crescent. Also known as primary heart field. A cardiac primordium within the splanchnic mesoderm at the cranial end of the embryonic disc, formed from cardiogenic precursors in response to inductive and permissive signals emanating from the endoderm, ectoderm, and midline mesoderm. 337b, 339, 340f

Cardiac incisure. A structure that develops at the end of the 7th week as a result of the continual differential expansion of the superior part of the greater curvature of the stomach. 445

Cardiac ion channels. A diverse group of pore-forming proteins that traverse the cardiac cell membrane and allow the selective passage of ions across a lipid barrier. Ion channels are the major transducers of intercellular physiologic signals and are particularly important in the heart, where they play a vital role in every heartbeat.† 383b

Cardiac jelly. A thick layer of extracellular matrix deposited mainly by the developing myocardium, thereby separating it from the fused endocardial tubes. 342, 346f

Cardiac progenitor cells. Cells derived from intraembryonic mesoderm emerging from the cranial third of the primitive streak during early gastrulation. 339, 340f, 340b–342b, 341f, 343f

Cardinal system. A primitive venous network that drains the head, neck, body wall, and limbs into the right and left sinus horns. It initially consists of paired anterior (cranial) and posterior (caudal) cardinal veins that meet to form short common cardinal veins. 385b, 419, 420f–423f

† Adapted from Cesario DA, Brar R, Shivkumar K. 2006.Alterations in ion channel physiology in diabetic cardiomyopathy. Endocrinol Metab Clin N Am 35:602.

Cardiogenic area. The horseshoe-shaped structure cranial to the oropharyngeal membrane that appears in the 3rd week of gestation, eventually becoming the heart. 103

Cardiomegaly. Abnormal enlargement of the heart. 339b

Carotid arteries. Sets of arteries that supply blood to the head, brain, and face. 403, 405f, 406f, 556f, 557

Carpal region. The area in the hand plate of the upper limb that is surrounded by a thinner crescentic rim, the digital plate, which will form the fingers. 626

Carriers. Either or both of the parents responsible for passing a congenital disease to an offspring. 67b

Catagen. One of the four phases (the regression phase) of hair growth. 204

Cataract. A partial or complete opacity of the lens caused by genetic or environmental factors. 614b

Cathepsin K. A secreted osteoclast enzyme that works at low pH to degrade exposed organic residues. 241b

Caudal. Also called inferior. A term often associated with the cauda, or tail, or individual structures within that region. 442b

Caudal dysplasia. Also called caudal agenesis, caudal regression syndrome, and sacral agenesis. A condition characterized, to varying degrees, by (1) flexion, inversion, and lateral rotation of the lower extremities; (2) anomalies of the lumbar and sacral vertebrae; (3) an imperforate anus; (4) agenesis of the kidneys and urinary tract; and (5) agenesis of the internal genital organs except for the gonads. 92b, 93f, 94b, 94f

Caudal eminence. Also called tail bud. The remnants of the primitive streak that, on about day 20, swell to produce a caudal midline mass of mesoderm, which will give rise to the most caudal structures of the body. 97–98

Caudal genito-inguinal ligament. Also called gubernaculum. One of the two ligaments (the other being the cranial suspensory ligament) that anchors the mesonephric-gonadal complex as it becomes more segregated from the adjacent intermediate mesoderm. 525, 526f

Caudalization. Abnormal formation of vertebral segments that is the result of the ectopic application of excess retinoic acid. 229b, 232f

Cdx1. A caudal homolog in vertebrates. 442b

Cdx2. A homeobox-containing transcription factor. 43b, 442b

Cdx3. A caudal homolog in vertebrates. 442b

C/EBPα. CAAT-enhancer binding protein, a transcription factor that activates several liver genes and is involved in the functional change to mature liver function. 449b

Cecum. A blind pouch or cul-de-sac.* 435b

Celiac artery. The most superior of the three abdominal vitelline arteries. 408, 409f, 435b

Celiac ganglia. Those groups of nerve cells that innervate the distal foregut region vascularized by the celiac artery. 310

Celiac trunk. The artery that supplies the abdominal foregut (i.e., the abdominal esophagus, stomach, and cranial half of the duodenum and its derivatives). 442

Cell biology. The study of cell physiology and structure. 133b

Cell intercalation. Also called cell rearrangement. The process whereby cells move from lateral to medial within the neural plate, thereby narrowing the neural plate and stacking up in the cranial-caudal plane, increasing the length of the neural plate. 110b

Cell lineage studies. Investigations in which individual cells, rather than groups of cells, are marked (often genetically with reporter genes), and their descendants then followed over time. 83, 137

Cell rearrangement. Also called cell intercalation. A process whereby cells move from lateral to medial within the neural plate, thereby narrowing the neural plate and stacking up in the cranial-caudal plane, increasing the length of the neural plate. 110b

Cell type-specific antibody markers. Antibodies that mark specific types of cells. 393b, 394f

Cell-cell interaction. A form of intercellular communication mediated by the secretion of soluble signaling molecules that diffuse within the extracellular environment to reach adjacent cells. 87b

Cell-to-cell adhesion. The process by which certain cell-surface molecules create a bonding element between cells. 80b, 81b

Cell-to-cell intercalation. The medial-lateral interdigitation of cells. 87b

Cell-to-extracellular matrix adhesion. The process by which certain cell-surface and extracellular molecules create a bonding element between cells and the extracellular matrix. 80b

Cellular retinoic acid-binding protein (Crabp). A binding protein in the cytoplasm for retinoic acid. 161, 161f

Cellular retinol-binding protein (Crbp). A binding protein in the cytoplasm for retinol. 161, 161f

Celsr1. A mutation in the ortholog of the Drosophila protocadherin Flamingo gene. 111b

Cementoblasts. Cells differentiated from the inner cells of the mesenchymal dental sac, which secrete a layer of cementum to cover the dentin of the root. 214

Cementoenamel junction. The point at the neck of the tooth root where the cementum meets the tooth's enamel. 214

Cementum. The bonelike rigid connective tissue covering the root of a tooth from the cementoenamel junction to the apex and lining the apex of the root canal. It also serves as an attachment structure for the periodontal ligament, thus assisting in tooth support.* 214

Central nervous system (CNS). The portion of the nervous system consisting of the brain and spinal cord.* 247–291, 251, 257, 299

Central sulcus. The cerebral sulci that forms in the 6th month and serves to separate the frontal and parietal lobes. 284

Central tendon of diaphragm. The cloverleaf-shaped aponeurosis, immediately below the pericardium, onto which the diaphragmatic fibers converge to insert.* 333, 334f

Centromere. The constricted portion of the chromosome at which the chromatids are joined and by which the chromosome is attached to the spindle during cell division. According to its location, a centromere is said to be metacentric (central), submetacentric (off center), acrocentric (near one end), or telocentric (at one end). The last type does not occur in human chromosomes.* 21

Cephalic flexure. The sharp flexure separating the prosencephalon and mesencephalon. 255

Cerberus. An inhibitor of Bmp signaling. 81b, 95b, 157

Cerebellar cortex. Exterior gray matter of the cerebellum. 247b, 263

Cerebellar hemispheres. The large cranial portions that become the dominant component of the mature cerebellum. 263

Cerebellar nuclei. The interior gray matter of the cerebellum. 247b, 263, 264, 267f

Cerebellar plates. Also called cerebellar primordia. The rudimentary structures of the cerebellum. 263, 265f–266f

Cerebellum. Part of the higher centers of the brain, a center for balance and postural control. 247b, 263–264, 265f–268f, 267, 267b, 269b

Cerebral aqueduct. The primitive ventricle of the mesencephalon that carries the cerebrospinal fluid produced by the choroid plexuses of the forebrain to the fourth ventricle. 251, 253, 270, 271f

Cerebral cortex. The thin (about 3 mm) layer or mantle of gray substance covering the surface of each cerebral hemisphere, folded into gyri that are separated by sulci. It is responsible for higher mental functions; general movement; visceral functions, perception, and behavioral reactions; and association and integration of these functions.* 282, 284f, 285b, 287b

Cerebral hemispheres. Either of the pair of structures formed by evagination of the embryonic telencephalon, which lie on either side of the midline, partly separated by the longitudinal cerebral fissure. They contain a central cavity, the lateral ventricle, and are covered by a layer of gray substance, the cerebral cortex; together they constitute the largest part of the brain in humans.* 250b, 272

Cerebral sulci. The furrows on the surface of the brain between the gyri. 284

Cerebrospinal fluid (CSF). A specialized dialysate of blood plasma that fills the brain ventricles, central canal of the spinal cord, and subarachnoid space, which surrounds the central nervous system. The CSF is under pressure and thus provides a fluid jacket that protects and supports the brain. 253, 257

Cerberus-like (Cerl). A gene expressed by the anterior visceral endoderm. 72b

Cervical aortic arch (CAA). The result of abnormal development of the aortic arches, with regression of the left fourth aortic arch and enlargement of the left third aortic arch. 545b

Cervical arteries. A group of arteries (ascending, descending, deep descending, superficial, and transverse) that supply the neck. 411

Cervical cap. A form of birth control using a device inserted into the vagina to cover the cervix and is usually used in conjunction with a spermicide. 45b

Cervical carcinoma. A malignant growth made up of epithelial cells that tend to infiltrate the surrounding tissues, giving rise to metastases. 68b

Cervical cyst. An abnormal closed cavity in the neck, lined by epithelium and containing a liquid or semisolid material. 573, 574f

Cervical fistula. An abnormal passage or communication on the side of the neck and leading into the pharynx, resulting from failure of closure of the second pharyngeal (branchial) groove and second pharyngeal pouch.* 573, 574f

Cervical flexure. One of the brain tube folds that appear between the 4th and 8th weeks, which is located near the juncture between the myelencephalon and spinal cord. 247b, 255

Cervical ganglia. Any of three ganglia in the neck. (1) The inferior cervical ganglion is an inconstant ganglion formed in place of the usual cervicothoracic ganglion by fusion of the lower two cervical ganglia in instances where the first thoracic ganglion remains separate. (2) The middle cervical ganglion, a variable ganglion, often fused with the vertebral ganglion, on the sympathetic trunk at about the level of the cricoid cartilage, whose postganglionic fibers are distributed mainly to the heart, cervical region, and upper limb. (3) The superior cervical ganglion is the uppermost ganglion on the sympathetic trunk, lying behind the internal carotid artery and in front of the second and third cervical vertebrae; it gives rise to postganglionic fibers to the heart via the cervical cardiac nerves, to the pharyngeal plexus and then to the larynx and pharynx, and to the head via the external and internal carotid plexuses.* 310, 310f

Cervical loop. The junction of the inner and outer enamel epithelia of the developing tooth where the cells proliferate and elongate to form the epithelial root sheath during late fetal and early postnatal life. 214

Cervical sinus. A transient space formed from caudal pharyngeal clefts, which normally disappears rapidly and completely. 573, 573f

Chain ganglia. Ganglia of the sympathetic trunk, sympathetic ganglia that are arranged in a chainlike fashion along each sympathetic trunk, about 20 to 23 on either side.* 124–125

Charcot-Marie-Tooth (CMT) disease. A chronic demyelinating disease of peripheral nerves, especially the peroneal nerve. 128b, 307b–308b

CHARGE syndrome. A birth defect in humans, involving both the outflow tract and pharyngeal arches, that results in **c**oloboma of the eye, **h**eart defects, **a**tresia of the choanae, **r**etarded growth and development, **g**enital and urinary anomalies, and **e**ar anomalies and hearing loss. 128b, 375b, 383b, 597b, 602b

Chemoaffinity hypothesis. A conditional statement to explain topographic mapping of the eye, which holds that each position in the optic tectum has a unique address dictated by the gradient distribution of molecular labels along orthogonal axes, matched by an equivalent distribution of labels in the retina. This hypothesis, long neglected in favor of more mechanical mechanisms for axon guidance, has been substantially vindicated by the discovery of Eph/Ephrin gradients and their central role in retinotectal mapping. 280b

Chemotactic molecules. Molecules involved in the migration of certain cells such as neural crest cells. Chemotactic molecules attract the neural crest cells, while *negative* chemotactic molecules repulse the crest from a distance. 121b

Chemotaxis. Directed cell movement according to the presence of so-called chemotactic factors in the cellular environment. 328b

Chemotropic signal. A kind of chemical stimulation, for example, the attractive signals produced by the developing gonads that regulate primordial germ cell honing. 20b

Chiasma. A joint structure whose formation makes it possible for the two homologous chromosomes to exchange large segments of DNA. It is composed of four chromatids, two centromeres, and two chromosomes that form during prophase (i.e., chromosomes condense into compact, double-stranded structures) when the double-stranded chromosomes of each homologous pair match up, centromere to centromere. 24

Chimeras. Organisms composed of cells from two or more different sources. 148

Choana. A normal opening that forms in the nasal cavity. The *primitive* choana develops during the 7th week as a result of the bursting of the thin oronasal membrane. Later, the *definitive* choana forms as an opening behind the secondary palate, thereby linking the two nasal passages to the pharynx. 568–569

Choice points. Distinct anatomic areas where the growth cone (the specialized structure at the tip of the axon) "chooses" a pathway during wiring of the nervous system. 277b

Chondrocranium. The bones of the skull, formed by endochondral ossification, that enclose the brain and help to form the sensory capsules that support and protect the olfactory organs, eyes, and inner ears. 543b, 545, 547

Chondrocytes. Cartilage cells that, along with osteoblasts and osteoclasts, form endochondral bones. Chondrocytes have three tissue origins: (1) the paraxial mesoderm forms the axial skeleton, including the occipital portion of the cranial base; (2) the lateral plate mesoderm forms the appendicular skeleton and sternum; and (3) neural crest cells (i.e., ectodermal cells) give rise to the cartilaginous elements in the face and neck. 217b, 219, 234, 236f

Chondrodysplasia. A general term referring to several disorders (particularly, Bloomstrand and Grebe-type chondrodysplasias) that occur during development of bone and cartilage. 210b, 237b, 239b, 239f, 240b

Chondrogenesis. The formation of cartilage. 237b–238b, 238f

Chondroitin sulfate. One of the large, complex proteoglycans that are part of the rich extracellular matrix that fills spaces between tissue layers and between cells within tissue layers. 160

Chorda tympani. A special branch of the facial nerve (cranial nerve VII) that innervates the submandibular, sublingual, and lingual glands, and taste buds on the anterior two-thirds of the tongue. 575

Chordae tendineae. The tendinous cords that connect each cusp of the two atrioventricular valves to appropriate papillary muscles in the heart ventricles. The cords are of varying lengths and thicknesses and are frequently branched.* 370, 370f, 371f

Chordins. Proteins that are secreted by the developing notochord and that antagonize Bmp signaling. 157

Choriocarcinomas. Malignant tumors arising from complete hydatidiform moles. 64b

Chorion. One of four extraembryonic membranes, composed of trophoblast lined with mesoderm. It develops villi about 2 weeks after fertilization, is vascularized by branches of the allantoic vessels and contributes to the placenta, and persists until birth.* 51b, 57, 388

Chorion frondosum. The area of the chorion that, during the 3rd month, bears villi and becomes the site of the mature placenta. 167b, 171

Chorion laeve. The remaining smooth portion of the chorion that lacks villi. 167b, 171

Chorionic cavity. The new hollow space that develops in the 2nd week as the extraembryonic mesoderm splits into two layers. 51b

Chorionic gonadotropin (hCG). A hormone that supports the corpus luteum and thus maintains the supply of progesterone (maternal recognition of pregnancy). 510

Chorionic plate. The part of the inner chorionic wall in the area of its uterine attachment, which gives rise to chorionic villi.* 171

Chorionic stem villi. Protrusions on the chorion that develop in three stages between the 9th day and the end of the 3rd week. Primary stage: extensions of cytotrophoblast grow out into the blood-filled lacunae, carrying with them a covering of syncytiotrophoblast. Secondary stage: primary stem villi are transformed when the extraembryonic mesoderm associated with the cytotrophoblast penetrates the core. Tertiary stage: villi contain differentiated blood vessels following the establishment of a working uteroplacental circulation. 60, 62f

Chorionic villi. Outgrowths of the fetal tissue that form during early development of the placenta to extend into maternal blood sinusoids. 51b

Chorionic villus sampling (CVS). A technique used to detect many disorders early in pregnancy whereby a sample of embryonic cells (10 to 40 mg) is obtained from the chorionic villi and checked for heritable chromosome anomalies. 35b, 185, 186f

Choroid. The thin, pigmented, vascular coat of the eye, extending from the ora serrata to the optic nerve, which furnishes blood supply to the retina and conducts arteries and nerves to the anterior structures.* 586b, 611

Choroid fissure. A longitudinal groove that forms by the 6th month in the lateral ventricle along the line between the floor and the medial wall of the cerebral hemisphere. 275f, 284, 285f

Choroid plexuses. Zones of minute, finger-like structures specialized to secrete cerebrospinal fluid projecting from the choroid fissure into the third, fourth, and lateral ventricles. 250b, 263, 272, 274, 275f

Choroidal fissure. A groove in the optic vesicle that allows a terminal branch of the ophthalmic artery, the hyaloid artery, to supply blood to the developing lens and retina. 586b, 602, 604f

Chromaffin cells. Specialized postganglionic sympathetic neurons innervated by preganglionic sympathetic fibers that release epinephrine and norepinephrine on sympathetic stimulation. 500

Chromatids. The two parallel strands of each chromosome that develop once the DNA replicates. 21

Chromodomain helicase DNA-binding protein 7 (CHD7). A gene, mutation which (on chromosome 8) is found in 60% of patients with CHARGE syndrome and in 75% of patients exhibiting heart defects. 383b

Chromosomal abnormalities. Defects that are the cause of about 40% to 50% of spontaneous abortions. In fetuses that survive to term, the resulting infants display nonrandom patterns of developmental abnormalities (i.e., syndromes). 32b–35b

Chromosome. In animal cells, a structure in the nucleus that contains a linear thread of DNA, which transmits genetic information and is associated with RNA and histones. During cell division, the material (chromatin) composing the chromosome is compactly coiled, making it visible with appropriate staining and permitting its movement in the cell with minimal entanglement. Each organism of a species normally has a characteristic number of chromosomes in its somatic cells, normally 46 in humans, including the 2 (XX or XY) that determine the sex of the organism.* 21, 34b, 64b–65b

Chromosome analyses. Techniques used for both diagnosis and genetic counseling. Blood cells of a prospective parent can be checked for heritable chromosome anomalies, and embryonic cells obtained either from the amniotic fluid (amniocentesis) or from the chorionic villi (chorionic villous sampling) can be used to detect many disorders early in pregnancy. 34b–35b, 36f, 37f

Chx10. A homeobox gene with the role of transcription factor responsible for regulating progenitor cell differentiation. Loss of function causes microphthalmia and congenital cataract in humans and ocular retardation in mice. 605t, 609f, 610b

Cilia. Minute vibratile hairlike processes that project from the free surface of a cell, which are composed of nine pairs of microtubules arrayed around a central pair. They are extensions of basal bodies and move in rhythmical beats that serve to move the cell around in its environment or to move fluid or mucous films over the cell surface. Genetic mutations in Dynein axonemal heavy chain 5 (Dnah5) can result in cilia being *immotile*, whereby fluids do not move. In lungs this defect leads to poor mucus transport and chronic infection; affected males with this defect in sperm transport are sterile. 321b

Ciliary body. The thickened part of the vascular tunic of the eye anterior to the ora serrata, which connects the choroid with the iris. It is composed of the corona ciliaris (ciliary crown), ciliary processes and folds, ciliary orbiculus, and ciliary muscle.* 586b, 613

Ciliary ganglion. A ganglion of the oculomotor nerve (III), formed by neural crest cells arising in the caudal part of the diencephalon and the cranial part of the mesencephalon. 314

Ciliary muscle. Part of the ciliary body, the muscle that effects the shape of the lens of the eye. 613

Circletail. One of four mouse mutants that exhibit convergent extension defects. 111b–112b

Circulatory system. The primitive circulatory system that forms by day 22 and is bilaterally symmetric. The right and left cardinal veins (common, anterior, and posterior) drain the two sides of the body, and blood from the heart is pumped into the right and left aortic arches and dorsal aortae. 355, 357–358, 357f–359f

Circumventricular organs. Specialized ependymal secretory structures in the third ventricle of the developing brain. 250b, 272, 274

c-Kit ligand. The ligand for the c-Kit Tyrosine kinase receptor, which is encoded by the mouse mutant steel. This mutation results in failure of the primordial germ cells to populate the gonads, causing sterility and failure of the hematopoietic stem cells to migrate from the yolk sac into the liver, causing severe deficiencies in blood formation. 20b, 122b, 390b

Clavicle. Also called the collar bone. A bone, curved like the letter *f*, that articulates with the sternum and scapula. It forms the anterior portion of the shoulder girdle on either side. 545

Clear cell adenocarcinoma of vagina. A very rare form of cancer usually found in women 50 years and older who are daughters of women given diethylstilbestrol (DES), the first synthetic estrogenic compound orally administered to pregnant women between 1947 and 1971 to prevent miscarriage. 520b

Cleavage. The third phase of human embryogenesis comprising a series of rapid cell divisions that result first in the formation of the morula, a solid ball of cells, and then in the formation of the blastocyst, a hollow ball of cells containing a central cavity. 15b, 41–43, 42f

Cleidocranial dysplasia. A disorder caused by mutations in Runx2, characterized by clavicular hypoplasia (that allows the juxtaposition of the shoulders), large open sutures in the skull, a wide pubic symphysis, and dental abnormalities such as delayed erupting or supernumerary teeth. 215b, 221b

Clinodactyly. A disorder resulting in curving of the fifth finger toward the fourth. 634t

Clitoris. Part of the external female genitalia, homologous with the penis in the male.* 521, 523f

Cloaca. An expansion formed from the portion of the primitive hindgut tube lying just deep to the cloacal membrane. 472, 474f

Cloacal folds. Also called the urogenital folds. A pair of swellings that develop early in the 5th week of development of the hindgut on either side of the urethral plate through an expansion of mesoderm underlying the ectoderm. Inferiorly, these folds meet and join the genital tubercle. 474, 523f, 533f

Cloacal membrane. The caudal bilaminar membrane that develops as part of the formation of the intraembryonic mesoderm. Later the membrane forms one of the blind ends of the gut tube (the other end being formed by the cranial membrane called the oropharyngeal membrane) before disintegrating in the 7th week to form the openings of the anus and the urinary and genital tracts. 70f, 72f, 78, 439

Clock and wavefront model of somitogenesis. A model proposed to explain the origin of somites. According to this model, the formation of somites involves an oscillator, the so-called segmentation clock, whose periodic signal is used to specify somite boundaries at progressively more caudal levels where the signal coincides in both time and space with a traveling threshold level of expression of another signaling molecule. 91f, 91b–92b

Club foot deformity. A limb defect resulting from physical factors, such as a constricted uterine environment caused by oligohydramnios (insufficient amniotic fluid) or reduced fetal movement. 639b, 639f

c-Met. A proto-oncogene; a normal gene that when mutated can become an oncogene, resulting in the development of cancer. 242b

Coagulation plug. Acellular material that develops around day 9, which seals the small hole where the blastocyst implanted in the uterine wall, temporarily marking this point in the endometrial epithelium. 53, 55f

Cocaine. A recreational drug that is teratogenic (tends to produce congenital anomalies). It crosses the placenta, causing fetal cocaine addiction, which for newborns often results in permanent effects requiring intensive emotional and educational support through the first years of life. Cocaine use by pregnant mothers is associated with low birthweight; premature birth; some specific developmental anomalies, including infarction of the cerebral cortex and a variety of cardiovascular malformations; and higher frequencies of preterm labor and fetal morbidity (disease) and mortality (death). 177–178, 638b

Cochlea. The structure within the inner ear that perceives sound waves. 588, 590f

Cochlear duct. The earliest form of the cochlea that begins to appear during the 5th week, once the ventral tip of the pars inferior begins to elongate and coil. 583b, 584f, 588, 590f

Cochlear ganglion. The sensory ganglion located within the spiral canal of the modiolus. It consists of bipolar cells that send fibers peripherally through the foramina nervosa to the spiral organ and centrally through the internal acoustic meatus to the cochlear nuclei of the brain stem.* Combined with the vestibular ganglion, it forms the vestibulocochlear ganglion of the vestibulocochlear nerve (cranial nerve VIII). 314

Cochlear hypoplasia. The partial absence or underdevelopment of the cochlea of the inner ear. 597b

Coelom. The body cavity. In higher invertebrates, it persists throughout life. In the embryo, it is situated between the somatopleure and the splanchnopleure; it is both extraembryonic and intraembryonic. The principal cavities of the trunk arise from the intraembryonic portion.* 51b, 57, 104f, 106, 329, 330f, 331f

Collagen. A basement membrane molecule found in the cranial somite. 160

Collecting ducts and tubules. Outgrowths of the ureteric bud in the fetal kidney that develop via inducement from the metanephric mesenchyme. When fully developed, these will serve as part of the collecting system for passing urine produced by the nephron. 487, 487f

Colliculi. Round protuberances on the dorsal surface of the midbrain that rise from the alar plates. The superior colliculi control ocular reflexes; the inferior colliculi serve as relays in the auditory pathway. 247b, 270, 271f, 280b

Collodion babies. Newborns that did not shed the periderm in the 21st week, but retained the "shell" or "cocoon" to birth. It is removed by the physician or shed spontaneously during the first weeks of life. 196

Coloboma. An abnormality in which the optic fissure fails to fuse, leaving a gap in one of the structures of the eye. 613b, 614f

Colon. The part of the large intestine extending from the cecum to the rectum.* The various portions (transverse, sigmoid, ascending, and descending) develop within the midgut and hindgut during the 6th and 7th weeks. 68b, 435b, 465b, 466f, 467b

Color blindness. A vision deformity, involving the photoreceptors, which is due to the absence of one or more S-cones (responding to short wavelengths—blue light), M-cones (responding to a medium wavelength—green), and L-cones (responding to longer wavelengths—red). The genes encoding the photoreceptors are located on the X chromosome; thus, color blindness frequently occurs in males (>2%). 608

Columns of Bertin. Inward extensions of the cortical structure of the kidney between the renal pyramids.* 489, 489f

Combinatorial code. The expression of combinations of paralogs of Hox genes in the hindbrain establishes a unique code that defines each segment (rhombomere). 229b

Combinatorial signaling. The interaction of multiple signaling pathways in different combinations. For example, during formation of head, trunk, and tail levels of the body, the amounts expressed of each of the three signaling molecules (Wnts, Bmps, and Nodal) vary at different levels. 97b

Common bile duct. The duct formed by a union of the common hepatic and cystic ducts, which empties into the duodenum at the major duodenal papilla, along with the pancreatic duct.* 448, 448f

Commissural plate. The dorsal portion of the zone of final neuropore closure, where axon tracts, called commissures, connecting the right and left cerebral hemispheres, form from a thickening at the cranial end of the telencephalon. 250b, 288

Compact layer of myocardium. The rapidly proliferating layer of heart muscle tissue that forms from the primitive epicardium adjacent to the outer cardiomyocytes. 368, 368f, 369b, 369f

Compaction. Reorganization of the blastomeres, starting at the eight-cell stage of development, when the originally round and loosely adherent blastomeres begin to flatten, developing an inside-outside polarity that maximizes cell-to-cell contact among adjacent blastomeres. As differential adhesion develops, the outer surfaces of the cells become convex and their inner surfaces become concave. This reorganization also involves changes in the blastomere cytoskeleton. 41–42, 42f, 43

Comparative genomic hybridization. One of three molecular approaches routinely used for chromosomal analysis. 35b, 36f–37f

Compensation. A situation in which, in the absence of expression of one gene, the expression of another gene is upregulated. 149

Competence. The situation in tissue development in which one tissue acts on another to change its fate. In particular, the responding tissue must be capable of responding (that is, must be competent to respond) to the inducing tissue by changing its fate. 145, 255b, 610b

Conceptus. The product of conception or fertilization. 4, 45b, 55b–56b

Conduction system. A system of specialized muscle fibers, comprising the sinoatrial node, atrioventricular node, bundle of His and its right and left bundle branches, and the subendocardial branches (rami subendocardiales) of Purkinje fibers, which generates and rapidly transmits cardiac impulses and serves to coordinate contractions,.* 188, 342b, 376–377, 382b

Cone photoreceptors. One of six major classes of neurons of the mature neural retina that arises from the inner and outer neuroblastic layers. With rods, cones are derived from the outer neuroblastic layer to eventually form the outermost layer of the mature neural retina. 586b, 607, 608, 608f

Congenital adrenal hyperplasia (CAH). The condition caused by a genetically determined deficiency of the suprarenal cortical enzymes necessary for the synthesis of glucocorticoids. This deficiency leads to adrenocorticotropic hormone–driven hyperplasia of the suprarenal cortex. 500b

Congenital aganglionic megacolon. Also known as Hirschsprung disease. A defect that results when lumbosacral neural crest cells fail to innervate the terminal portion of the colon, resulting in impaired gut motility. 470b, 471f

Congenital bilateral aplasia of the vas deferens (CBAVD). A disorder of mesonephric duct development that is characterized by an absence of the body and tail of the epididymis, vas deferens, and seminal vesicle. CBAVD is responsible for 1% to 2% of male infertility and almost 10% of obstructive azoospermia (absence of spermatozoa in semen due to duct blockage, rather than to absence of spermatozoa production, which is called nonobstructive azoospermia). 512b

Congenital cystic adenomatoid malformation. A multicystic mass of pulmonary tissue that causes lung compression and resulting hypoplasia. 186–187

Congenital insensitivity to pain with anhidrosis (CIPA). A hereditary neurologic disorder that manifests as a paucity of small nerve fibers in the skin, lack of pain sensations, and an absence of innervation of the sweat glands (producing *anhidrosis,* or lack of sweating). 299b

Conjunctival sac. A part of the formation of the eyelids in the 8th week; the space between the fused eyelids and the cornea. 613

Connecting stalk. A thick stalk of extraembryonic mesoderm in the chorionic cavity that suspends the embryonic disc with its dorsal amnion and ventral yolk sac. 57, 60f, 104f, 105, 105f, 388

Connexin proteins. Cx26, Cx30, Cx31, components of gap junctions that, if mutated, are linked to deafness. 597b

Conotruncal segment. Also called outflow tract. The cranial-most segment of the primitive heart tube that forms the distal outflow region for both the left and right ventricles. 337b, 346, 370–371, 373f, 374f, 375b–376b, 376f, 380f, 381f

Conotruncal septum. The structure that completely separates the right and left ventricular outflow pathways in the primitive heart tube. 370–371, 374f

Conotruncal swellings. A pair of endocardial-covered ridges that grow inward along the length of the conotruncal segment and eventually develop into the conotruncal septum. 370, 374f

Conotruncus. The outflow channel in the upper end of the right ventricle of the primitive heart tube. 337b

Constrictors. Muscles originating in the fourth and sixth pharyngeal arches comprising the superior, middle, and inferior constrictors of the pharynx, the cricothyroid, and the levator veli palatini, which function in vocalization and swallowing. 559

Contiguous gene syndrome. A gene-deletion syndrome that requires deletion of multiple, contiguous genes to manifest the phenotype. 581b

Contraception. The prevention of conception or impregnation.* 44b–46b

Conus arteriosus. Also called conus cordis. The subdivided conotruncus that eventually becomes incorporated into the left and right ventricles. 346

Convergence. (1) During gastrulation, one of four types of coordinated cellular group movements, called morphogenetic movements, where cells move toward the midline. Convergence occurs in conjunction with extension (i.e., lengthening in the cranial-caudal plane) as a coordinated movement called convergent extension. 80b (2) The process by which the craniocaudal flexure facilitates cardiac looping by helping to bring the venous (sinus venosus) and arterial (truncus arteriosus and aortic sac) poles closer to one another. 354

Convergent extension. Coordinated cell movement involving cell rearrangement to narrow the medial-lateral extent of a population of cells, and concomitantly increase its cranial-caudal extent. 80b

Copula. A midline swelling that appears on the second pharyngeal arch in the 4th week, then is rapidly overgrown during the 5th and 6th weeks by a midline swelling of the third and fourth pharyngeal arches, called the hypopharyngeal eminence. 574, 575f

Cord blood. Blood from the fetal umbilical cord that may be drawn from a normal fetus and transferred to a fetus in need of gene therapy. Cord blood is an excellent source of hematopoietic stem cells. The collection and storage of fetal cells from umbilical cords is called cord blood banking. 189

Corium. Also called dermis. The layer of skin that underlies the epidermis, which contains blood vessels, hair follicles, nerve endings, sensory receptors, as well as other structures. 201, 201f

Cornea. The transparent structure forming the anterior part of the sclera of the eye* that becomes apparent in the 8th week. It originates from three tissues: mesodermal and neural crest cells form the mesothelium and the substantia propria, whereas the outer layer of the cornea (anterior epithelium) is derived from the overlying surface ectoderm. 611

Corneal dystrophy. A disorder characterized by cell fragility and the formation of cysts and resulting from mutations in Krt3 and Krt12, the corneal-specific Keratins. 198b

Corneal endothelium. A thin inner membranous tissue overlying the cornea that differentiates from the mesenchyme late in the 6th and into the 7th weeks. 611

Cornelia de Lange syndrome (CdLS). A multiple malformation syndrome associated with limb anomalies. The majority of those affected have upper limb anomalies ranging from small hands to severe limb reduction defects. 636t, 638b, 639f

Corniculate cartilage. Small horn-like structure within the larynx. 553

Cornification. The process in skin development by which lytic enzymes are released within the cell, metabolic activity ceases, and enucleation occurs, resulting in the loss of cell contents including the nucleus. Consequently, the keratinocytes that enter the stratum corneum are flattened, scalelike, and terminally differentiated keratinocytes, or squames. 200

Cornified layer of skin. Also called stratum corneum. The layer that forms as the third definitive (outer) layer of keratinocytes. 193b, 196, 197f

Coronary arteries. The arteries that arise from the ascending aorta to supply the muscle of the heart. 377, 403

Coronary ligament. The peritoneum covering the inferior surface of the peripheral diaphragm that encircles the bare area of the liver like a crown. 455, 455f

Coronary sinus. The left sinus horn that drains the myocardium. It receives most of the blood draining from the coronary circulation of the heart muscle. 337b, 338f, 355, 357, 357f–359f

Coronary vasculature. The system of channels through which blood circulates from and to the heart. 377

Corpora bigemina. Two bodies in the brain of the human fetus that later split to become the corpora quadrigemina (the rostral and caudal colliculi of the tectum of the mesencephalon considered together).* 270, 271f

Corpus callosum. The large commissure that joins the cerebral hemispheres of the cranial telencephalon. 250b, 287f, 288, 289f, 290, 547b

Corpus luteum. An endocrine structure that secretes steroid hormones to maintain the uterine endometrium in a condition ready to receive an embryo. If an embryo does not implant in the uterus, the corpus luteum degenerates after about 14 days and is converted to a scarlike structure called the corpus albicans. 4f, 29f 37, 38f

Corpus striatum. Along with the globus pallidus, a structure that forms the large neuronal nuclei of the basal ganglia that are crucial to executing commands from the cerebral hemispheres. 27f, 250b, 282

Cortical bone. Bone formed from the primary bone collar (the ossified region surrounding the diaphysis) that thickens as osteoblasts differentiate in progressively more peripheral layers of the perichondrium. 235

Cortical granules. Special structures found in the cortex of the ovum of many animals, which break up during fertilization and supply the material for the development of the fertilization membrane. This strong membrane is formed around the fertilized ovum in some species of animals by adhesion of part of the contents of the cortical granules to the inner surface of the vitelline membrane; it prevents the entry of additional spermatozoa. 39, 40f

Costal cartilages. Those structures that connect the first seven ribs ventrally to the sternum by day 45, thereby creating what are called the true ribs. 227

Costal processes. The small lateral mesenchymal condensations that develop in association with the vertebral arches of all the developing neck and trunk vertebrae. 218f, 227, 228f

Cotyledons. The 15 to 25 partially separated compartments that comprise each intervillous space of the placenta. 167b, 171, 173f, 174f

Coup-TFII (Chicken ovalalbumin upstream promoter transcription factor II). An important human protein located on human chromosome 15q26.2, a genomic region that is found to be deleted in some patients with congenital diaphragmatic herniations. 335b

Cowper's gland. Also called bulbourethral gland. A structure that contributes to the seminal fluid protecting and nourishing the spermatozoa after ejaculation. 481f, 511, 511f

CpG islands. The sites of DNA methylation during imprinting that are often stretches of alternating cytosine and guanosine bases. 65b

Cranial flexure. Also known as mesencephalic flexure. One of the three points of flexion in the primordial brain portion of the neural tube. 247b

Cranial nerves. Twelve pairs of nerves connected with the brain to control specific functions: Three pairs are exclusively sensory (I, II, and VIII); four are exclusively motor (IV, VI, XI, and XII); one is mixed sensory and motor (i.e., mixed; V); one is motor and parasympathetic (III); and three include sensory, motor, and parasympathetic fibers (VII, IX, and X). 258, 259t, 313–315

Cranial suspensory ligament. One of the two ligaments (the other being the caudal genito-inguinal ligament) that anchors the mesonephric-gonadal complex as it becomes more segregated from the adjacent intermediate mesoderm. 525, 526f

Cranial vault. Also called the calvarium. A subdivision of the neurocranium, the bones covering the brain. The bones of the cranial vault do not complete their growth during fetal life. The soft, fibrous sutures that join them at birth permit the skull vault to deform as it passes through the birth canal and also allow it to continue growing throughout infancy and childhood. 543b, 547

Cranial-caudal axis. One of the three major axes of the embryo that becomes identifiable during gastrulation. 69b, 91, 621b

Cranial-caudal patterning. Typically called anterior-posterior patterning, that is patterning of the head-tail axis of the embryo. 97b, 629f

Cranialization of vertebral segments. The result of genetic loss of function of two or more members of the family of Retinoic acid receptors in which more caudal segments become converted to more cranial segments. 229b, 232f

Craniofacial anomalies. Any of a number of congenital defects, including malformations of the frontonasal process, clefting defects, calvarial malformations, and anomalies of the pharyngeal arch derivatives of the face and head. Most craniofacial anomalies have a multifactorial etiology, such as inherited autosomal traits (e.g., Treacher Collins syndrome), maternal ingestion of teratogens (e.g., alcohol, the anticonvulsant hydantoin), or smoking. 240b, 579b, 580f

Craniofrontonasal dysplasia. A disorder that results from defects in Ephrin signaling. This syndrome involves a mutation in Efnb1. Although this mutation affects the development of bones in the skull and face (characterized in part by the early fusion of the coronal suture), multiple other defects occur, such as umbilical hernia; genitourinary anomalies; skin, nail, and hair anomalies; and developmental delay. 158, 550b

Craniorachischisis. A neural tube defect appearing during week 3 or 4 that results when neurulation fails to occur normally. In this case, the entire length of the neural tube opens onto the surface of the head and back. 113b

Cranioschisis. Also called anencephaly. A neural tube defect involving total dysraphism of the brain, with normal formation of the spinal cord. Infants with anencephaly lack a functional forebrain (cerebrum) and fail to gain consciousness; most do not survive more than a few hours after birth. 113b

Craniosynostosis. The premature closure of sutures (sagittal and coronal sutures are the most commonly affected) affecting approximately 1 in 2500 children and occurring in many syndromes, including Crouzon, Apert, Pfeiffer, Muenke, and Saethre-Chotzen. Sutures, which occur where two membrane bones meet, contain the progenitor cells that will give rise to new bone cells, the osteoblasts, which are the sites of membrane bone growth. Closure at one suture causes increased growth at other sutures, thereby deforming the brain and skull. 158, 239b, 240f, 550b, 551f, 638b

Crash. A mouse mutant that exhibits convergent extension defects. Crash mice have a mutation in the ortholog of the Drosophila protocadherin Flamingo gene, called Celsr1. 111b

***Cre* recombinase**. A site-specific recombinase derived from phage that acts on the loxP sites flanking the gene of interest, which is then excised, preventing its expression only in the tissue of interest (i.e., there is precise spatial control of gene inactivation). 149–150

***Cre-lox* system**. A method used to study mutations whereby genes are deleted (knocked out) in specific organ-forming regions. 149–150

Cri du chat. A chromosome deletion syndrome involving 5p, which may cause cerebellar anomalies. 269b

Cricoarytenoid muscles. One of three muscles that comprise the intrinsic laryngeal musculature; mainly associated with vocalization. 559

Cricoid cartilage. One of six cartilages that make up the larynx. 549f, 553, 554f

Cricothyroid muscles. Muscles originating in the fourth and sixth pharyngeal arches that function in swallowing and vocalization. 555t, 559

Cripto. An essential cofactor required for Nodal signaling. Loss-of-functions mutations result in failure to form a primitive streak. 57b, 72b

Cristae. A projection or projecting structure; the prosensory region formed in the semicircular canals that detects angular acceleration. 357, 592

Crista terminalis. A ridge of tissue that delimits the trabeculated right atrium from the smooth-walled sinus venarum. It contains the fibers that carry impulses from the sinoatrial node to the atrioventricular node. This fiber tract is part of the conducting system that channels the spread of depolarizing electrical currents through the heart and organizes the contraction of the myocardium. 357, 359f

Critical sensitive periods. Those specific periods of active differentiation and morphogenesis when an embryonic structure is usually susceptible to teratogens. 177

Crkl. A ubiquitously expressed gene encoding a receptor adaptor protein. Its loss has been linked to increased Retinoic acid signaling in the cranial pharyngeal arches. 581b

Crossing over. The process by which two homologous chromosomes exchange large segments of DNA across chiasmas. 22f, 23t, 24

Crouzon syndrome. The Fgfr2 mutation that results in craniosynostosis without limb defects. 158

Crura of diaphragm. A pair (right crus, left crus) of fibromuscular bands arising from the superior two or three lumbar vertebrae and ascending to insert into the central tendon of the diaphragm.* 333, 334f

Cryopreservation. A method for preserving gametes and embryos, especially useful for its high rate of stem cell recovery. 189

Cryptic. A human gene that if malformed can cause randomized laterality and visceroatrial heterotaxy. 383b

Cryptophthalmos. An abnormality of the most anterior eye structures, the eyelids and sclera, occurring when the fissure that separates the upper and lower eyelids (i.e., the palpebral fissure) fails to form properly, resulting in complete fusion of the eyelids. 613b

Cryptorchidism. Undescended testes. 509, 521b, 526, 527f, 530b

Crystallin. A gene in the structural component of the lens, a mutation of which leads to congenital cataracts. 614b

Cubitus interruptus (Ci). Part of Hedgehog signaling, one of three proteins (called Gli proteins) that function as either transcriptional activators or repressors. 157

Cumulus oophorus. A small mass of follicle cells surrounding the oocyte. 29, 30f, 31f

Cuneiform cartilage. Wedge-shaped cartilage within the larynx. 553

Cupula. An acellular matrix in the cristae. 593

Cushion tissue. Mesodermally-derived mesenchymal cells (endocardial-derived cushion tissue) and ectodermally-derived mesenchymal cells (neural crest cell–derived cushion tissue) that lines the cushion tissue of the outflow tract of the heart. 338f, 360f, 361

Cusps. The atrioventricular valves that begin to form between the 5th and 8th weeks. These valve leaflets are firmly rooted in the rim of the right and left atrioventricular canals and are

thought to arise from proliferation and differentiation of the adjacent endocardial cushion tissues. 214b, 369, 371f

Cut-and-paste experimental embryology. A technique in which tissue is removed from one area of an embryo and grafted to another area of the embryo. 133b, 147, 147f

Cyanosis. Inadequate oxygenation of the blood; a symptom of double-outlet right ventricle malformation. With this defect, both the aortic and pulmonary outflow tracts connect to the right ventricle; this malformation is almost always accompanied by a ventricular septal defect. All arterial blood flow leaves from the right ventricle, and there is mixing of oxygenated blood with unoxygenated blood within the right ventricle.

Cyclopia. A developmental defect where only a single, mid-line eye forms. It results from a mutation in transcription factor Otx2 or secreted protein Shh. 602b

Cymba concha. The dorsal-most hillock of the ear to appear on the first pharyngeal arch in the 5th week. It will eventually develop as part of the auricle. 600f, 601

Cyst. An abnormal closed cavity in the body, lined by epithelium and containing a liquid or semisolid material.* 186, 207b, 461b, 475b, 476f, 495b, 518, 519f, 573, 574f, 576, 583b, 588, 588b, 589f, 592b, 592f

Cystein-rich protein with EGF-like domains (Creld1). A cell adhesion molecule that, when mutated, has been found in individuals with atrioventricular septal defects. 382b

Cystic duct. The temporary structure that develops on day 26 from the cystic diverticulum before joining with the hepatic duct to form the common bile duct. Afterward, it is carried away from the duodenum. 435b, 448, 448f

Cystic fibrosis (CF). An autosomal recessive disease that affects breathing and digestion. It is caused by mutations in both alleles of the Cystic fibrosis transmembrane conductance regulator (CFTR). 48b, 327b, 512b

Cytokine. A regulatory protein released by cells of the immune system that acts as an intercellular mediator in the generation of an immune response. 20b, 197b, 198b

Cytokinesis. The final stage in each metaphase of cell division (mitosis, meiosis, and meiosis II) in the germ line in which the cell actually divides. 23t, 24, 27, 39, 63b, 111b

Cytomegalovirus. A viral genus of the Herpesvirus group that is the cause of one of the most common viral infections of the fetus. If this virus infects the embryo early in development, it may induce abortion; infection occurring later may cause a wide range of congenital abnormalities, including blindness, microcephaly (small head), hearing loss, and mental retardation. 176, 596b

Cytoskeleton. The skeleton of the cell. 81b, 160f, 287b, 313b, 401b, 493b, 494b

Cytotrophoblast. The cellular layer of the trophoblast that develops during transplantation and contributes to the extraembryonic membranes, but not to the embryo proper. 51b, 53, 54f

D

De Morsier syndrome. Also called septo-optic dysplasia. A disorder involving hypoplasia of the optic nerve and caused by mutations in the Hesx1 gene. It occurs in conjunction with pituitary hypoplasia and midline brain abnormalities. Children with this syndrome are short in stature due to growth hormone deficiency. 614b–615b

Deafness. Partial or total loss of hearing. Genetic causes may be nonsyndromic (occurring as an isolated defect) or syndromic (occurring in conjunction with other anomalies). 308b, 472b, 593, 596b, 597b

Decapentaplegic. A protein, the best-known Drosophila member of the *Tgfβ* superfamily, a family of proteins that signals through receptors having a cytoplasmic serine/threonine kinase domain. Many members of this family play important roles in vertebrate development, such as the Bone morphogenetic proteins (Bmps), Activin, Vg1, and Nodal. 157

Decidua. A nutrient-packed, highly vascular tissue that develops when the implanting blastocyst induces the decidual reaction in the maternal endometrium. 167b, 171, 172f

Decidua basalis. The tissue that underlies the embedded embryonic pole of the embryo (the pole at which the embryonic disc and connecting stalk are attached), which forms the maternal face of the developing placenta. 167b, 171, 172f

Decidua capsularis. A thin capsule of uterine lining that covers the protruding side of the embryo. It bulges into the uterine lumen in the second month, and later disintegrates as the fetus fills the womb. 167b, 171, 172f

Decidua parietalis. The remainder of the maternal uterine lining following the development of the decidua capularis and growth of the fetus as it fills the womb. 167b, 171, 172f

Decidual cells. Metabolically active secretory cells that reside in the endometrial stroma. 44, 170

Decidual reaction. The response by the adjacent cells of the endometrial stroma to the presence of the blastocyst becoming tightly adhered to the uterine lining and to the progesterone secreted by the corpus luteum differentiating into decidual cells. 44, 167b, 170

Decidual septa. Also called placental septa. Wedge-like walls of decidual tissue that grow during the 4th and 5th months into the intervillous space from the maternal side of the placenta, separating the villi into 15 to 25 groups (cotyledons). Because the placental septa do not fuse with the chorionic plate, maternal blood can flow freely from one cotyledon to another. 171, 174f

Decision-making region. The place where motor axons accumulate and mix before migrating into a developmental region. 640

Decussation. Anatomic nomenclature for the intercrossing of fellow parts or structures in the form of an X.* 274, 276f, 278

Definitive oocyte. The result of gametogenesis, the process that converts primordial germ cells into female gametes. 15b, 20–21, 24f, 25, 30f, 39

Deformation. A structural birth defect involving perturbation of a developing structure indirectly owing to mechanical forces. 133b, 134, 135

7-Dehydrocholesterol reductase. An enzyme produced by the Dhcr7 gene and involved in the penultimate step of cholesterol synthesis. Mutation of the gene leads to Smith-Lemli-Opitz syndrome, reduced or complete elimination of enzyme activity that prevents cells from producing enough cholesterol. 550b

Dehydroepiandrosterone (DHEA). A hormone secreted by the fetal corticoid layer, then converted by the placenta into estradiol, which is essential for maintaining pregnancy. 500

Delta. A Notch ligand that binds a neuronal precursor cell to another, thereby inhibiting the neighboring cells from differentiating as neurons. 159f

Delta 1. A ligand for the Notch signaling pathway linked to sclerotome resegmentation, 222b

Delta 3. A ligand for the Notch signaling pathway linked to spondylocostal dysostosis. 231b

Dental lamina. A U-shaped epidermal ridge that is the first sign of the tooth development that forms along the crest of the upper and lower jaws. Twenty dental lamina downgrowths, which induce condensation of the underlying neural crest cell-derived mesenchyme, together form the tooth buds of the primary (deciduous) teeth. 193b, 210, 212f, 213f

Dental papilla. The hillock-like structure that forms from its mesenchymal component soon after each tooth bud forms and indents the epithelial enamel organ formed from the bud. 193b–195b, 210, 212f, 213f

Dental sac. An enclosure formed from the mesenchyme surrounding the papilla and its condensed dental lamina cap. 210, 212f

Dentate nucleus. One of the four deep nuclei that form on each side of the cerebellum, relaying all input to the cerebellar cortex. 263

Dentin. The hard portion of the tooth surrounding the pulp that is harder and denser than bone but softer than enamel. It is covered by enamel on the crown and cementum on the root.* 195, 210, 212f, 214, 214b

Dentinogenesis imperfecta. The defective development of enamel or dentin, caused by Dentin sialophosphoprotein mutations involving faulty differentiation. 214b

Denys-Drash syndrome. A syndrome in which heterozygous mutations in Wt1 result in genitourinary malformations including sexual ambiguity as well as podocytic underdevelopment and glomerular nephropathy caused by diffuse mesangial sclerosis leading to end-stage renal failure. 494b

Deoxyribonucleic acid (DNA). The essential element of chromosomes that encodes information required for the development and functioning of the organism. 21, 23t, 24, 24f

Depot preparation. A substance such as a medication that can be accumulated, deposited, or stored in a body area and from which it can be distributed.* 45b

Dermal bone. Bone that develops from neural crest cells (facial bones and the frontal bone of the skull) or unsegmented paraxial (head) mesoderm (e.g., parietal bone of the skull). In dermal bones, the osteoblasts directly differentiate within the mesenchyme. 127f, 219, 234, 543b, 545, 546f

Dermal papillae. Projections that develop from the superficial layer of the dermis, which interdigitate with the downward projections of the epidermis called epidermal ridges. 193b, 201, 201f, 203, 204f

Dermatomes. The mesodermal primordia that contribute to the dermis of the neck and trunk. 101b, 128

Dermis. Also called corium. The layer of skin that underlies the epidermis and contains blood vessels, hair follicles, nerve endings, sensory receptors, and so forth. 128, 193b, 201, 201f

Dermomyotome. One of the distinct zones that forms from somites, a series of segmental blocklike mesodermal condensations. The dermomyotome gives rise to the dermatome, which forms the dermis of the back skin of the trunk and neck (with the remainder of the dermis of these regions forming from lateral plate mesoderm), and the myotome, which forms the muscles of the trunk. 121f, 128, 129f, 130b, 130f, 217b, 222, 223f

Descriptive embryology. The study of how normal and abnormal development occurs. Descriptive embryology provides a catalog of developmental events, which when carefully studied and reflected on, can lead to the formulation of hypotheses about how developmental events occur. 142–143

Desert hedgehog (Dhh). One of three orthologs of the Drosophila Hedgehog gene expressed in mammals. Once Leydig progenitors immigrate into the developing gonad, paracrine interactions between Leydig progenitors and Sertoli cells play a central role in fetal and adult Leydig cell differentiation. Desert hedgehog (Dhh) and PdgfA are released by fetal Sertoli cells; their receptors, Patched1(Ptch1) and Pdgfrα, are expressed by fetal Leydig cells. 156, 157, 506f, 510b–511b.

Desmogleins 1 and 4. The protein associated with Desmoplakin, a component of the desmosome cell adhesion complex. Mutations result in skin fragility defects. 198b

Desmoplakin. A component of the desmosome cell adhesion complex. 198b

Desmoplakin 1. A desmosomal protein, mutations of which cause skin fragility and wooly hair. 207b

Desmosomes. Cell-to-cell membrane junctions, which provide a tight, impervious structure resistant to water uptake or loss and infection and which help to distribute force evenly over the epidermis. 43, 199

Desquamation. The process of cell shedding that canalizes the vaginal plate, thereby forming the vaginal lumen. 518

Determination wavefront. The distinct caudal boundary of a new pair of somites that develop as a result of the expression of cycling genes crossing the threshold level of Fgf8 signaling in the presomitic mesoderm. 91b, 91f

Deuteranope. An individual presenting a type of color blindness identified by a lack of M-cones called deuteranopia, a dichromasy characterized by retention of the sensory mechanism for two hues only (blue and yellow) of the normal four-primary quota, and lacking that for red and green and their derivatives, without loss of luminance or shift or shortening of the spectrum. It is an X-linked trait occurring in about 1% of males, but only rarely in females.* 608

Dextrocardia. A malformation in which the looping of the heart tube is reversed from its normal sinistral looping, producing a heart that is a mirror image of the normal heart. 74b, 353f, 353b

Diaphragm (contraceptive). A device inserted into the vagina to cover the cervix and usually used in conjunction with a spermicide. 332-333, 334f

Diaphragm, **musculotendinous.** The musculomembranous partition separating the abdominal and thoracic cavities, which serves as a major thoracic muscle.* The definitive musculotendinous diaphragm incorporates derivatives of four embryonic structures: the septum transversum, pleuroperitoneal membranes, mesoderm of the body wall, and esophageal mesenchyme. 332–333, 334f

Diaphragmatic hernia. A congenital defect in which the developing abdominal viscera bulge into the pleural cavity. 324b, 334b, 335b, 335f, 336f, 461b

Diaphyses. Ossified shafts of the limb bones consisting of a bone collar and trabecular core. 236

Diencephalon. The posterior of the two brain vesicles formed by subdivision of the prosencephalon in the developing embryo.* 247b, 249f, 250b, 251, 252f, 272, 273f, 274, 322f, 585f

Diethylstilbestrol (DES). The first synthetic estrogenic compound orally administered to pregnant women (1947–1971) to prevent miscarriage. It was discontinued because of increased risks of developing clear cell adenocarcinoma of the vagina in young women born of DES-treated mothers; increased risk of reproductive tract anomalies due to in utero exposure to DES; and because males exposed to DES in utero exhibited such anomalies as cryptorchidism, hypospadias (condition where penile urethra opens on the ventral surface of the penis), and testicular hypoplasia. 520b–521b

Digastric muscle. The muscle that develops from paraxial mesoderm in the first (anterior belly of the digastric) and second (posterior belly of the digastric) pharyngeal arches. 555t, 557f, 559

DiGeorge anomaly. The complex of congenital malformations characterized by a triad of malformations: (1) minor craniofacial defects, including micrognathia (small jaw), low-set ears, auricular abnormalities, cleft palate, and hypertelorism; (2) total or partial agenesis of the derivatives of the third and fourth pharyngeal pouches (the thymus and parathyroid glands); and (3) cardiovascular anomalies, including persistent truncus arteriosus and interrupted aortic arch. DiGeorge anomaly is also seen in 22q11.2 deletion syndrome, which is phenocopied by loss of neural crest cells. 581b

DiGeorge syndrome. The chromosome 22q11.2 deletion syndrome that is responsible for some vascular anomalies, especially when accompanied by craniofacial defects and velopharyngeal insufficiency (dysfunction of the palate and pharynx; “velo” refers to palate). 128b, 375b–376b, 383b, 545b, 581b

Digital plate. A thin crescentic rim surrounding the central carpal region in the hand plate of the upper limb on the 37th day. It will eventually form the fingers. 626

Digital rays. Radial thickenings in the digital plate of the upper limb that become visible on day 38. 617b, 626

Digoxigenin (DIG). Part of in situ hybridization, a technique used to show patterns of RNA expression. When the riboprobe is prepared, it is labeled with digoxigenin, a small antigenic molecule obtained from the digitalis plant. After hybridization and washing to remove unbound riboprobe, DIG can be detected essentially by using an anti-DIG antibody. 146

Dihydrotestosterone. A powerful androgenic hormone generated by Leydig cell 5α-Reductase, which is needed to induce the male urethra, prostate, penis, and scrotum, and for testicular descent into the scrotum. In the absence of dihydrotestosterone in female embryos, the primitive perineum does not lengthen, and the labioscrotal and urethral folds do not fuse across the midline. 503f, 510, 512b,

Dihydrotestosterone receptor. The Androgen receptor expressed by the mesenchyme adjacent to the mesonephric duct during development of the epididymus, vas deferens, and seminal vesicles. 512b

Diploid cells. Somatic and primordial germ cells that have two copies of each kind of chromosome. 15b, 21, 22f

Dishevelled 1 and 2. Two mouse orthologs of the cytoplasmic protein Dishevelled (Dsh) in Xenopus. Loss-of-function mutations block convergent extension during gastrulation and neurulation. 111b

Disproportionate growth. A dysplasia in which a part of the limb is abnormally larger, smaller, longer, or shorter. 632b, 633f

Distichiasis. The appearance of an extra row of eyelashes along the eyelid margin as a result of mutations in the forkhead gene (FOXC2). 613b

Diverticulum. A circumscribed pouch or sac of variable size occurring normally or created by herniation of the lining of the mucous membrane through a defect in the muscular coat of a tubular organ.* 193b, 207, 435b, 448f, 461b

Dlx. Homeobox-containing genes (Dlx1-6) thought to be part of patterning control of the facial primordial, a combinatorial expression of these factors determining facial structures. Mutation in Dlx3 causes tricho-dento-osseous syndrome (or amelogenesis imperfecta), thus affecting the hair and teeth, whereas loss of Dlx5/6 results in transformations in facial structures. 566b, 568f

Dkk1. A Wnt inhibitor, misexpression of which arrests development at the placode stage of all the ectodermal derivatives analyzed (hair, tooth, and mammary gland). 202, 209b

Dolly. A sheep, the most famous clone (offspring genetically identical to the mother) to date, born in 1995. 162

Dominant negative receptors. Engineered growth factor receptors containing the ligand-binding extracellular domain, which bind the growth factor but lack the intracellular domain necessary for signaling (i.e., they are truncated). When present in excess in the extracellular space, or bound to cell surfaces in excess, dominant negative receptors bind to secreted growth factors, preventing them from binding to intact receptors, thus blocking signaling. Dominant negative receptors can be injected into blastomeres as an effective method to study growth factor signaling. 150, 151f

Dorsal plates. Also called alar plates. The dorsal half of the neural tube. 247b, 257, 257f

Dorsal rami (ramus). Spinal nerves that innervate axial muscles; the axons that direct their path toward the epimere. 231, 241, 306, 307f

Dorsal root. Spinal nerves containing neurons whose cell bodies reside in the dorsal root ganglion. 258, 304, 305f, 306f

Dorsal root ganglia. Spinal nerve clumps housing the sensory neurons that conduct impulses to the spinal cord from end organs in the viscera, body wall, and extremities. A pair of dorsal root ganglia develops at every segmental level except the first cervical and the second and third coccygeal levels. Thus, there are 7 pairs of cervical, 12 pairs of thoracic, 5 pairs of lumbar, 5 pairs of sacral, and 1 pair of coccygeal dorsal root ganglia. The most cranial pair of cervical dorsal root ganglia (adjacent to the second cervical somite) forms on day 28, with the others forming in craniocaudal succession over the next few days. 121f, 124, 125f, 127f, 128b, 141f, 217b, 223f, 248f, 257f, 297b, 303, 304, 304f, 305f, 306b, 499f

Dorsalizing factors. Mesodermal patterning that includes the protein products of the Noggin, Chordin, Nodal, Follistatin, and Cerberus genes (with Bmps and Wnts acting as ventralizing factors). These dorsalizing factors are secreted by the organizer and its derivatives (the notochord and floor plate of the neural tube), and act by antagonizing Bmp and/or Wnt signaling. 81b

Dorsal-ventral axis. The body axis extends from the back to the front. 11, 56, 69b, 621b

Dosage compensation. The process activated to compensate for the presence of only one X chromosome in the cells of males (46,XY). One of the two active X chromosomes in each cell of the female blastocyst (46,XX) is stably inactivated. 67b

Dosage sensitive sex reversal, adrenal hypoplasia congenita-critical region of the X chromosome (Dax1). An ovarian-promoting factor that can act as an ‘‘anti-testis’’ factor, rather than as an ovarian-determining gene. In humans, when the Dax1-containing portion of the X chromosome is duplicated in XY individuals, Dax1 leads to sex reversal. 506f, 516b

Dose-response curve. A principle of teratology that states that an embryonic structure is susceptible to a critical dose of a teratogen during its specific critical sensitive period. The dose-response curve constructed for a suspected teratogen may show the lowest dose has no effect and the highest dose is lethal to the embryo. 177

Double cortex syndrome. A syndrome with complex symptoms associated with subcortical band heterotopia, the result of aberrant migration of differentiating neuroepithelial cells. Those affected have bilateral circumferential and symmetric ribbons of gray matter located just beneath the cortex and separated from it by a thin band of white matter. Seizures, mild mental retardation, and some behavioral abnormalities are often present in infancy. However, intelligence can be normal and seizures may begin later in life. 287b

Doublecortin. A gene located on the X chromosome that is mutated in those with X-linked lissencephaly and Sbh. The protein product of Doublecortin is highly expressed in fetal neurons and their precursors during cortical development. Like Platelet-activating factor acetylhydrolase, the Doublecortin protein is associated with microtubules, which suggests that it is also involved in cell migration through interactions with the cytoskeleton. 287b

Double-outlet right ventricle malformation. A defect in which both the aortic and pulmonary outflow tracts connect to the right ventricle. This malformation is almost always accompanied by a ventricular septal defect. All arterial blood flow leaves from the right ventricle and there is mixing of oxygenated blood with unoxygenated blood within the right ventricle. 379b

Dowling-Meara EBS. The most severe form of epidermal bullosa simplex (EBS), a disorder caused by dominant-negative mutations in genes encoding Krt5 and Krt14, specifically expressed in the stratum germinativum. For neonates, Dowling-Meara EBS can be life threatening. 198b

Down syndrome. A disorder most frequently caused by an error during meiosis. If the two copies of chromosome 21 fail to separate during the first or second meiotic anaphase of gametogenesis in either parent (a phenomenon called nondisjunction), half the resulting gametes will lack chromosome 21 altogether and the other half will have two copies. In addition to recognizable facial characteristics, mental retardation, and short stature, individuals with Down syndrome may exhibit congenital heart defects (atrioventricular septal defect is most common, that is, a failure to form both the atrial and ventricular septae), hearing loss, duodenal obstruction, a propensity to develop leukemia, and immune system defects. 32b, 33f, 34b, 34f, 114b, 135, 182, 379b

Down syndrome candidate regions. By determining which specific phenotypes occur in those with Down syndrome having particular translocated regions of chromosome 21, regions have been identified on the chromosome that must be triplicated to produce specific aspects of Down syndrome, such as mental retardation, characteristic facial features, and cardiovascular defects. These regions on chromosome 21 are called Down syndrome candidate regions. 34b

Duane anomaly. An extrinsic component of muscle weakness resulting from defects in motor nerve innervation characterized by lateral gaze palsy (abnormal eye movements) and abnormalities in cranial nerve VI (abducens nerve), which innervates the lateral rectus, the extraocular eye muscle that moves the globe laterally. 244b, 614b

Duchenne muscular dystrophy. An X-linked recessive disease resulting from a mutation in the gene encoding Dystrophin. This mutation occurs in 1 in 3500 male infants and causes progressive dystrophy and degeneration of myofibers of skeletal or cardiac muscle, and mild mental retardation. 67b, 244b

Ductus arteriosus. A connection between the aorta and the pulmonary trunk that normally closes soon after birth. 380b, 403, 405, 416b, 429, 430f

Ductus reuniens. A narrow channel connecting the saccule of the pars inferior to the cochlea. 588, 590f, 595f

Ductus venosus. A channel that shunts blood from the umbilical vein directly to the inferior vena cava during gestation. 386f, 387b, 419, 420f, 421, 429, 430f, 431

Duodenal papillae. Duodenal projections in two forms: (major), small elevations at the point where the main pancreatic duct and the common bile duct meet and empty their secretions into the duodenum; and (minor), small elevations at the site of the opening of the accessory pancreatic duct into the lumen of the duodenum.* 448f, 451

Duodenum. The first or proximal portion of the small intestine, extending from the pylorus to the jejunum; so-called because it is about 12 fingerbreadths in length (from L. duodeni, 12 at a time).* 126f, 435b, 439T, 441, 443f, 445, 445b, 450f, 451, 452b, 458f, 459f, 460f

Duplication defects. The presence of supernumerary limb elements, such as polydactyly (the presence of entire extra digits) and triphalangeal thumb (three phalanges rather than just the normal two). 632b, 633f

Dura mater. The outermost layer of the three membranes covering the brain and spinal cord. 113b, 123, 611

Dwarfism. Also known as achondroplasia. One of the results of a defect in Fgf signaling: deformation of the skeletal system caused by a mutation in Fgfr3. 158, 219b, 237b, 239b

Dyneins. Molecular motors composed of heavy and intermediate polypeptide chains. Dyneins use energy from ATP hydrolysis to move cargo toward the minus end of microtubules or cause bending of cilia and flagella by creating a sliding force between microtubules. Thus, there are two kinds of dyneins, cytoplasmic and axonemal. 74b, 383b

Dyskeratosis. A condition characteristic of nevoid basal cell carcinoma syndrome (NBCCS), evident from the pathognomonic dyskeratotic pitting of the hands and feet. 207b

Dysmorphogenesis. Perturbation of differential growth owing to a genetic mutation, teratogen exposure, or a combination of the two processes. Malformations consist of primary morphologic defects in an organ or body part resulting from abnormal developmental events that are directly involved in the development of that organ or body part. 133b, 133–135

Dysphagia. A malformation caused by the ductus arteriosus passing in front or behind the esophagus and trachea, which results in constriction in these structures and difficulty in swallowing. 415b

Dysplasias. Abnormalities of development of the fetus.* (See also specific dysplasias.) 632b, 633f

Dyspnea. Difficulty breathing or shortness of breath. It may result from the abnormal disappearance of the right fourth aortic arch. If the right fourth arch regresses, the seventh intersegmental artery (the future right subclavian artery), which normally connects to the right fourth aortic arch, forms a connection with the descending aorta instead. 415b

Dysraphism. Any of the severest forms of open neural tube defects (NTDS), which range from total dysraphism, called craniorachischisis, in which the entire length of the neural tube opens onto the surface of the head and back, to localized dysraphism, such as lumbosacral myeloschisis, in which only the lowermost region of the spinal cord is open. 113b

Dystocia. Abnormal or difficult delivery. It is a condition found in the majority of pregnant women with Müllerian anomalies. 520b

Dystrophin. A protein found in skeletal and cardiac muscle, normally in a tightly bound complex with sarcolemmal glycoproteins but lacking in those with Duchenne muscular dystrophy.* 244b

E

Eagle-Barrett syndrome. Also known as prune belly syndrome. A condition in which the anterior body wall closes, the abdomen becomes distended by bladder outlet obstruction, and the abdominal muscles fail to develop. Consequently, there is a marked wrinkling of the anterior abdominal wall. This syndrome occurs almost exclusively in males and is also associated with undescended testicles, suggesting a complex etiology. 106b–107b

Eardrum. Also called tympanic membrane. The obliquely placed thin membranous partition between the external acoustic meatus and the tympanic cavity. 584f, 590f, 599

Early specification model. The process that explains proximal-distal patterning of the limb. Fgf signaling from the apical ectodermal ridge is required for the prespecified limb segments to develop and expand. 623b, 625f

Eccrine secretion. The secretion of fluid from eccrine sweat glands. 208, 211f, 299

Echocardiography. A method of graphically recording the position and motion of the heart walls or the internal structures of the heart and neighboring tissue by using the echo obtained from beams of ultrasonic waves directed through the chest wall.* Abnormalities of the fetal heart and heart beat can be analyzed using fetal echocardiography, a more detailed ultrasonography of the heart performed by a pediatric cardiologist. 184, 379b

Ectoderm. One of the three primary germ layers that develop during gastrulation. These germ layers give rise to tissues and organ rudiments during subsequent development. Once formation of the definitive endoderm and intraembryonic mesoderm is complete, epiblast cells no longer move toward and ingress through the primitive streak. The remaining epiblast now constitutes the ectoderm, which quickly differentiates into the central neural plate and peripheral surface ectoderm. 7–8, 8f, 51b, 69b, 78, 80f, 83, 85, 86f, 89f, 92, 94, 95b, 101b, 104f, 105–107, 109f, 110b–112b, 118f, 120f, 123, 126, 195, 196f, 202b, 388f

Ectodermal dysplasia. Any of several X-linked disorders of the skin. 198b, 202b–203b, 203f, 207b, 208, 634b.

Ectodermal placodes. Platelike structures, especially thickened plates of ectoderm in the early embryo, from which sense organs develop.* 205, 282, 297b, 299b, 313, 315f, 560

Ectodysplasin. A transmembrane protein (Eda) and its receptor (Edar). Mutations in either, or in components of the signaling pathway (Edaradd, Ikkγ/Nemo), result in hypohidrotic ectodermal dysplasia (HED): hair is absent or thin; nails, sweat, and sebaceous glands are hypoplastic; skin is dry; and teeth are absent, malformed, and/or small. 202, 202b, 205b, 207b, 328b

Ectopia cordis. An anterior body wall defect that results in isolated protrusion of the heart through the thoracic wall. 106b, 461b

Ectrodactyly. Also called split-hand or split-foot malformation. A disorder resulting in longitudinal divisions of the autopod into two parts, often with absence of central digits 634t, 636t

Ectrodactyly-ectodermal dysplasia-clefting (EEC) syndrome. A disorder involving mutations in transcription factor Tp73l (also known as P63), which in part is characterized by a split-hand and split-foot anomaly, a condition referred to as ectrodactyly. 203b, 634b, 637b

Ectromelia. A disorder resulting in the absence of one or more limbs. 634t

Edinger-Westphal nucleus. The nucleus from which the general visceral efferent nerve fibers arise that supply parasympathetic pathways to the pupillary constrictor and the ciliary muscles of the globe. 261, 270

EDTA soluble (ES) complex. A multicomponent aggregate expressed within the heart and restricted to the atrioventricular and outflow tract regions. Antibodies directed against this complex can block epithelial-to-mesenchymal transformation. 361b

Efferent ductules. Pathways from the seminiferous tubules and rete testis tubules to the epididymis, which develop in the 3rd month. 482b, 511

Eggs. Also called oocytes. The final cells produced by oogenesis. 7, 41f

Ehlers-Danlos syndrome (EDS). A hereditary connective tissue disorder. EDS is a group of disorders caused by mutations in several genes involved in the formation of the structural components of skin and joints. Classical EDS is caused by mutations in Collagen type VA1 or VA2. 195b

Ejaculation. The expulsion of sperm through the vas deferens and urethra and into the vagina during intercourse. As many as 300 million spermatozoa may be deposited in the vagina by a single ejaculation. 28

Ejaculatory duct. The portion of the vas deferens (mesonephric duct) between each seminal vesicle and the urethra. 511

Electromotility. The process by which the outer hair cells of the cochlea change their length exceptionally rapidly in response to sound. 593

Electroporation. The technique for introducing donor DNA sequences into cultured embryonic stem (ES) cells in which a suspension of ES cells is mixed with many copies of the donor DNA and subjected to an electric current. 148

Ellis-van Creveld syndrome. A condition involving human mutation in limb development recognizable by short limbs and post-axial polydactyly. 635t

Emboliform nucleus. A small cerebellar nucleus, between the dentate nucleus and globose nucleus, that contributes to the superior cerebellar peduncles* through which all input to the cerebellar cortex is relayed. 263

Embolism. The sudden blocking of an artery by a clot, foreign material, or air bubble, which has been brought to its site of lodgment by the blood current.* 180

Emboly. The "internalization" type of coordinated cell movement—one of the morphogenetic movements—that takes place during gastrulation. Emboly involves the movement of cells into the interior of an embryo and can involve the movement of individual cells or sheets of cells. 80b–81b, 87b

Embryo. The term for the developing organism from the 4th day after fertilization to the end of the 8th week. 51b, 169, 170f

Embryo transfer. A means of introducing an embryo into the uterus of women who otherwise may not be able to become pregnant through normal means. It is part of a technique called assisted reproductive technology (ART). 46b, 536b

Embryoblast. The central inner cell mass of the cleaving embryo that gives rise to the embryo proper and associated extraembryonic membranes. 15b, 43

Embryonic disc. The term for the embryo before the 4th week of gestation when it then becomes three-dimensional, and a typical tube-within-a-tube body plan is established. 5, 51b, 56, 58, 69b, 78

Embryonic period. The stage during which most of the major organ systems are formed, which concludes by the end of the 8th week of gestation. 167b, 169, 248f

Embryonic pole. The side of the blastocyst containing the inner cell mass. 43

Embryonic stage of lung development. The period between the 26th day and the 6th week when the respiratory diverticulum arises as a ventral outpouching of foregut endoderm. The diverticulum undergoes three initial rounds of branching, successively producing the primordia of the two lungs, lung lobes, and bronchopulmonary segments. The stem of the diverticulum forms the trachea and larynx. 322t

Embryonic stem (ES) cells. Cells derived from the inner cell mass of the human blastocyst. Such cells are potentially valuable for replacing tissues in people suffering from various diseases such as heart disease, juvenile diabetes, Alzheimer's, and Parkinson's disease, as well as from spinal cord injuries and resulting paralysis. Although proven to be at least partially effective in animal models, the potential value of human ES cells has not been determined. 162, 301b

Empty spiracles homolog-2 (Emx2). A transcription factor expressed in the ureteric bud that when knocked out fails to activate Wnt4 expression within metanephric mesenchymal condensations, resulting in renal agenesis. 505b

Enamel epithelium. Two structures of the dental lamina. The inner enamel epithelium is the layer that overlies the dental papilla, whereas the outer enamel epithelium encases both the inner enamel epithelium and the central layer, the enamel (otellate) reticulum. 210, 212f

Enamel organ. The structure that forms the enamel layer of the tooth. This stage of dental development is called the cap stage because the enamel organ sits on the papilla like a cap. 194b–195b, 210

Encephaloceles. In the brain, skin-covered neural tube defects (NTDs) with brain tissue protruding through the skull. Large encephaloceles can severely affect neurologic function and threaten survival. 113b, 114f

Endocardial cushions. The dorsal (or superior) and ventral (or inferior) cushions that develop around the periphery of the atrioventricular canal as the septum primum elongates by differential growth. 338f, 360f, 361f, 362b, 363, 363f

Endocardial tubes. A recognizable pair of vascular elements formed from a subpopulation of cells within the cardiac crescent in response to signals from the underlying endoderm through the process of vasculogenesis. These endocardial tubes coalesce into a single tube as the limbs of cardiac crescent join to make the primitive heart tube. 337b, 338f, 342, 345f

Endocarditis. Exudative and proliferative inflammatory alterations of the endocardium, usually characterized by the presence of vegetations on the surface of the endocardium or in the endocardium itself. Most commonly this involves a heart valve, but sometimes it affects the inner lining of the cardiac chambers or the endocardium elsewhere. It may occur as a primary disorder or as a complication of or in association with another disease. Bacterial endocarditis, for example, is caused by any of various bacteria, including streptococci, staphylococci, enterococci, gonococci, and gram-negative bacilli.* 432b

Endochondral bone. One of the two types of bone in the body, which develops via endochondral ossification from three cell types—chondrocytes (cartilage cells), osteoblasts (bone-forming cells), and osteoclasts (bone-resorbing cells). During bone development, a cartilaginous template forms preceding ossification. This pathway of differentiation is used by all the axial (vertebral column and ribs) and appendicular (limb) bones of the body, with the exception of part of the clavicle. 234, 235f–236f, 543b, 545

Endoderm. The innermost of the three primary germ layers of the embryo. The epithelia of the pharynx, respiratory tract, digestive tract, bladder, and urethra are derived from the endoderm.* 118f, 224f, 69b

Endodermal epithelium. Endoderm that makes up the epithelial lining of the gut. 462–464, 463f–466f, 464b–467b

Endoglin. A Tgfβ-binding protein that plays a critical role in vasculogenesis and angiogenesis. Along with Alk1, mutations in Endoglin have been linked to hereditary hemorrhagic telangiectasia (HHT). 157, 396b, 401b

Endolymphatic appendage. An elongated formation of the dorsomedial region of the otic vesicle that begins to appear by day 28. The appendage elongates over the following week, and its distal portion expands to form an endolymphatic sac that is connected to the pars superior by a slender endolymphatic duct. 588, 590f

Endolymphatic duct. The membranous tube connecting the utriculosaccular duct with the endolymphatic sac, which is located within the bony vestibular aqueduct. 583b, 588, 590f, 595f

Endolymphatic sac. The blind, flattened cerebral end of the endolymphatic duct. 584f, 588, 590f, 591f, 594f, 595f

Endometrial veins. Maternal blood enters the intervillous spaces of the placenta through about 100 spiral arteries, bathes the villi, and finally exits via the endometrial veins. 173

Endoneurium. The innermost layer of connective tissue in a peripheral nerve, which forms an interstitial layer around each individual fiber outside the neurilemma.* 307b

Endosonography. A procedure in which a miniature ultrasound probe is inserted into the vagina and brought close to the fetus, permitting a higher resolution image. 184

Endothelial cells. The first and earliest cell types to differentiate into a functional phenotype in the embryo. They form the vasculature. 388, 388f

Endothelial precursor cells (EPCs). One of the two cell lineages that arise (hematopoietic stem cells being the other) and develop from hemangioblastic aggregates. Together the two form what is often referred to as blood islands. EPCs differentiate into endothelial cells and organize into small vascular cords that coalesce to form a primitive embryonic vascular plexus. 385b, 388, 388f, 392f, 400f, 446

Endothelin. Any one of three 21–amino acid polypeptides that are potent vasoconstrictors. Endothelin-1, a small peptide, was originally found as a product of endothelial cells and later in the brain, kidney, and lung; it is a contractile factor that may play a role in controlling blood pressure and may also function as a neurotransmitter. Endothelin-2 and Endothelin-3 have been found in tissues such as the adrenal glands, kidneys, brain, and intestine. 407b–408b, 432b

Endothelin converting enzyme-1 (Ece1). The converting enzyme that proteolytically generates active Endothelins. Genetic inactivation of Ece1 (knocked out) results in severe hypoplasia of the lower jaw, together with cardiac and aortic arch remodeling abnormalities. 407b–408b

Engrailed. A homeobox gene believed to be involved in upstream regulatory control of the tectal gradients, which regulates the expression of Ephrin-A ligands in the caudal midbrain and which has a similarly graded expression pattern. The homeobox transcription factor Engrailed-1 is expressed in the ventral ectoderm and prevents the expression of Wnt7A. Engrailed-2 is a transcription factor produced in cells of the future midbrain/rostral hindbrain (the so-called isthmus region). 146f, 152f, 281b, 630b

Enhancer of split. An ortholog of Drosophila required for the development of supporting cells in hair growth. Mutation can cause excess hair cells. 159, 593b

Enteric ganglia. The group of nerve cell bodies derived from neural crest cells that are part of the enteric nervous system. 127f, 297b

Enteric nervous system. Part of the peripheral nervous system, the enteric nervous system is derived from neural crest cells originating from both the vagal and lumbosacral levels that migrate distally into the gut wall mesenchyme to form neurons that innervate all regions of the gut tube from the esophagus to the rectum. 121f, 126, 126f, 297b, 437b, 467–468, 469f, 470b

Envelope proteins. Proteins that line the inner surface of the plasma membrane. Such proteins, including Involucrin, Loricrin, and Envoplakin, are produced by cells of the stratum granulosum of the developing skin. 197f, 200

Envoplakin. A membrane-associated precursor of the outer stratum corneum of the skin. Envoplakin is homologous to Desmoplakin 1 and Desmoplakin 2 (Dp1/2) and is believed to link desmosomes and keratin filaments to the outer stratum corneum.[‡] 200

Eomes. A T-box transcription factor that performs essential functions in both trophoblast development and gastrulation. The name "Eomes" is short for "Eomesodermin." [§] 43b, 56b

Epaxial muscles. Muscles of the dorsal body wall that form from the somitic myotome, which is immediately subjacent to the dermatome, where it splits into a dorsal epimere and ventral hypomere. The dorsal epimere forms the deep epaxial muscles of the back, which are innervated by the dorsal ramus of the spinal nerve. 128, 217b, 223f, 231, 234b, 235f, 243f

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[‡]Adapted from Ruhrberg http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WG1-45MGX8D-36&_user=964951&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000000593&_version=1&_urlVersion=0&_userid=964951&md5=1b63e53ce2f464249f7fed6a6025d3e7-a1#a1 C, Williamson JA, Sheer D, Watt FM. 1996. Chromosomal localisation of the human envoplakin gene (*EVPL*) to the region of the tylosis oesophageal cancer gene (*TOCG*) on 17q25. Genomics 1 Nov 1996, 37(3):381-385.

[§] Russ AP, Wattler S, Colledge WH, et al. 2000.. Eomesodermin is required for mouse trophoblast development and mesoderm formation. Nature 2 Mar 2000;404(6773):95-99.

Ependymal cells. The type of cell that lines the central canal of the spinal cord and ventricles of the brain. They are the last cells produced by the ventricular layer of the differentiating neural tube. 247b, 255, 256f, 257

Ephrins. A family of proteins binding to the so-called Eph receptors, the cell line from which the first member of the family was isolated—the erythropoietin-producing human hepatocellular carcinoma line. The term, ‘‘Ephrins” is derived from the Eph family receptor interacting proteins. Both Ephrins and Eph receptors are classified into A and B subgroups consisting of Ephrins A1 to A5, B1 to B3, and Ephs A1 to A8, B1 to B6. Both the type A and B Eph receptors consist of an extracellular ligand-binding domain, a transmembrane domain, and an intracellular Tyrosine kinase domain. 157, 158, 222b, 225b, 278b–279b, 280b–281b, 464b–465b, 465f, 642b, 643b, 643f

Epiblast. A distinct external (or upper) layer of columnar cells comprising one of the layers of the bilaminar and trilaminar blastoderm stages that appears in the 2nd week when the embryoblast splits. A layer of epiblast cells expands on day 8 toward the embryonic pole and differentiates into a thin membrane separating the amniotic cavity from the cytotrophoblast. The first major event of the 3rd week, gastrulation, commences with the formation of a longitudinal midline structure, the primitive streak, in the epiblast near the caudal end of the bilaminar embryonic disc. 51b, 54f, 56, 57, 61f, 69b, 72f, 78, 79f, 80f

Epiboly. Also called internalization. Literally, spreading of an epithelial sheet; one of the morphogenetic movements of cells into the interior of an embryo, which takes place during gastrulation. Epiboly involves the spreading of a sheet of cells, generally on the surface of an embryo. Epiblast cells undergo epiboly to move toward and into the primitive streak. 80b, 81b

Epibranchial placodes. Also called epipharyngeal placodes. Small ectodermal structures that give rise to the neurons in the sensory ganglia of cranial nerves V, VII, IX, and X beginning roughly at the end of the 4th week of gestation. In contrast to neurons in the cranial nerve sensory ganglia, which can arise either from neural crest cells or ectodermal placodes, all glia in these ganglia are derived from neural crest cells. 123, 313

Epibulbar dermoids. Tumorous growths of the sclera, one of the cardinal findings in Goldenhar syndrome. 613b

Epicanthal folds. Folds of skin that cover the inner corner, the canthus, of the eye that are a characteristic feature of Down syndrome. They are also normally present in many ethnic groups. 135, 613b

Epicanthus inversus. An anomaly of the eyelids identified by folds curving down and laterally from the inner canthus. 613b

Epicardium. Also called visceral pericardium. A structure formed in the heart tube after day 21 by a population of mesodermal cells (the proepicardial organ) that are independently

derived from splanchnic mesoderm that migrates onto the outer surface of the myocardium. 338f, 342, 350, 367f, 369b, 372f, 377, 378f

Epidemiologic studies. Methods used to identify compounds as teratogens that attempt to relate antenatal exposure to a suspect compound with the occurrence of various congenital anomalies in humans (so-called retrospective studies). 177

Epidermal bullosa simplex (EBS). A disorder caused by dominant-negative mutations in genes encoding Krt5 and Krt14, specifically expressed in the stratum germinativum, in which the germinativum is exceptionally fragile and leads to blistering. The most severe form, Dowling-Meara EBS, can be life threatening for neonates. 198b

Epidermal growth factor (Egf). The factor that regulates the early growth and branching of the lung and the formation and maturation of terminal sacs during the saccular stage. Egf receptors are required for trabecular development (within the ventricles of the heart), as well as gestational survival. 55b, 157, 328b, 362b, 369b

Epidermal neural crest cell stem cells. Highly motile neural crest cell–derived stem cells that emigrate from the bulge of adult mammalian hair follicles. More than 88% of these migrating cells are pluripotent stem cells that can generate all cranial neural crest derivatives. Because of their existence in humans, accessibility, and high degree of physiologic plasticity, neural crest cell stem cells in the periphery of the adult organism are promising candidates for cell replacement therapy. 301b, 302f

Epidermal ridges. Downward projections of the epidermis that interdigitate with projections called dermal papillae that develop on the superficial layer of the dermis. U-shaped epidermal ridges on the oral epithelium are the first signs of tooth development. 193b, 201, 201f

Epidermal root sheaths. The epidermal cells lining the follicular canal, which constitute the inner and outer epidermal root sheaths. 204f, 205

Epidermis. The outermost and nonvascular layer of the skin, derived from embryonic ectoderm and varying in thickness from 0.07 to 0.12 mm, except on the palms and soles where it may be 0.8 and 1.4 mm, respectively.* 193b, 201f

Epidermolysis bullosa. Literally, blistering skin. A human disorder affecting the skin and connective tissue as a result of defects in Integrin signaling. Mutations in Laminin β3, a component of the basement membrane, cause blistering skin defects due to abnormal germinativum cell adherence. 161, 198b

Epididymis. A 40-foot-long highly coiled duct connected to the vas deferens near its origin in the testis. 28, 504f, 505, 511, 512b

Epigastric arteries. Superior and inferior epigastric arteries that develop from anastomoses of intersegmental arteries. 411

Epiglottal cartilage. The plate of cartilage that forms in the 5th month, long after the other pharyngeal arch cartilages have formed, and constitutes the central part of the epiglottis. 553–554

Epiglottis. The lidlike cartilaginous structure that overhangs the entrance to the larynx and serves to prevent food from entering the larynx and trachea while swallowing. It develops just posterior to the hypopharyngeal eminence,* 574, 575f

Epimere. The dorsal portion of a somite, from which muscles innervated by the dorsal ramus of a spinal nerve are formed.* 217b, 218f, 224f, 231, 233f

Epineurium. The outermost connective tissue sheath that surrounds the peripheral nerves and binds the perineurium-encased fasicles. This sheath contains collagen, fibroblasts, mast cells, and resident macrophages. 307b

Epipharyngeal placodes. Also called epibranchial placodes. Small ectodermal structures that give rise to neurons in the sensory ganglia of cranial nerves V, VII, IX, and X beginning roughly at the end of the 4th week of gestation. In contrast to neurons in the cranial nerve sensory ganglia, which can arise either from neural crest cells or ectodermal placodes, all glia in these ganglia are derived from neural crest cells. 123, 313

Epiphyseal cartilage plate. A layer of cartilage (the growth plate or physis) that persists between the epiphysis and the growing end of the diaphysis (metaphysis). 236

Epiphyses. The ends of limb bones. 234, 235, 236, 236f

Epiploic foramen of Winslow. The canal created by reduction in the communication between the greater and lesser sacs of the peritoneal cavity to a narrow canal lying just posterior to the lesser omentum. It is caused when the stomach rotates to the left, the liver shifts into the right side of the peritoneal cavity, and the lesser omentum rotates from a sagittal into a coronal (frontal) plane. 447f, 455

Epithalamus. The caudal part of the roof and the adjoining lateral walls of the third ventricle of the diencephalon, comprising the habenular nuclei and their commissure, pineal body, and commissure of the epithalamus.* 250b, 272, 273f, 274

Epithelial cadherin. Also called E-Cadherin. A calcium-dependent cell adhesion molecule. Cells adhere to one another using intercellular junctions, such as gap and tight junctions, and calcium-dependent and calcium-independent cell adhesion molecules. The calcium-dependent adhesion molecules consist of the Cadherins, such as E-Cadherin. 43, 81b, 160

Epithelial cap. The ectoderm that covers the mesenchymal core of mesoderm of each limb bud. 617b

Epithelial reticulum. A loosely organized network of cells of the developing thymus gland, which are thought to be of endodermal origin. 577

Epithelial root sheath. The roots of the teeth begin to form in late fetal and early postnatal life. At the junction of the inner and outer enamel epithelia, the cervical loop, the cells proliferate and elongate to form the epithelial root sheath. The mesenchyme just internal to the epithelial sheath differentiates into odontoblasts, which produce dentin. Each root contains a narrow canal of dental pulp by which nerves and blood vessels enter the tooth. 212f, 214

Epithelial-to-mesenchymal transformation (EMT). An event that begins on day 16 when epiblast cells elongate and become flask or bottle shaped, and detach from their neighbors as they extend footlike processes, which allow them to migrate through the primitive streak into the space between the epiblast and hypoblast (or into the hypoblast itself). 78, 81, 107, 119, 361

Epithelium. The covering of internal and external surfaces of the body, including the lining of vessels and other small cavities. It consists of cells joined by small amounts of cementing substances. Epithelium is classified into types based on the number of layers deep and the shape of the superficial cells.* 19, 27, 78, 79f, 94, 107, 109f, 210, 297b, 462–464, 463f–466f, 464b–467b, 586b, 607, 608f, 610b, 611

Eponychium. A thin layer of epidermis that initially covers the nail plate. This layer normally degenerates, except at the nail base. 210

Epoöphoron. One of the remaining vestiges of mesonephric ducts and mesonephric tubules that remains in females, It is found in the mesentery of the ovary. 502t, 504f, 515f, 518

Erα. An estrogen receptor that binds to diethylstilbestrol (DES). 517b, 521b

Erector spinae muscles. Deep epaxial muscles of the back innervated by the dorsal ramus of the spinal nerve. 231, 233f

Erythroblasts. Immature nucleated fetal red blood cells. These are destroyed in large numbers in erythroblastosis fetalis (also called hemolytic disease of the newborn), a disorder occurring when the mother's anti-Rh antibodies cross the placenta and destroy the fetal red blood cells of the Rh+ fetus, thus causing anemia in the fetus and newborn. 173, 175–176

Erythrocyte. One of the elements found in peripheral blood. In humans the normal mature form is a non-nucleated, yellowish, biconcave disk, adapted by virtue of its configuration and hemoglobin content to the transport of oxygen.* Primitive erythrocytes likely serve as a rapidly forming stopgap population of blood cells that fulfill the oxygen needs of the rapidly developing embryo. 388f, 389, 390b

Erythropoietic cells. Cells formed in the yolk sac from primitive hematopoietic stem cells (HSCs) through a process known as hematopoiesis or hemopoiesis (blood cell production). 388

Esophageal atresia. A malformation that makes it impossible for the fetus to drink. It results in an overabundance of amniotic fluid, a condition called hydramnios, or polyhydramnios. 324b–325b, 325f

Esophagotracheal fistula. Also called tracheoesophageal fistula. An abnormal connection between tracheal and esophageal lumina resulting from a failure of the foregut to separate completely into trachea and esophagus. This is quite dangerous to the newborn because it allows milk or other fluids to be aspirated into the lungs, so must be surgically corrected. 157, 324b–325b, 325f

Esophagus. The musculomembranous passage extending from the pharynx to the stomach and divided into two sections: thoracic (posterior to the trachea and pericardium and anterior to the vertebral column) and abdominal (the part of the esophagus below the diaphragm that joins the stomach).* 126f, 321, 322f, 325f, 334f, 335f, 415f, 417f, 435b, 439t, 444f, 444b, 458f, 552f, 573f, 577f,

Estriol (uE3). A serum component produced by the placenta and measured as part of maternal serum screening, a treatment method for diagnosing fetal malformations and genetic diseases. When carrying a fetus with Down syndrome, the mother's estriol levels are low. 182

Estrogen. One of the steroid hormones responsible for maintaining the pregnant state and preventing spontaneous abortion or preterm labor. It is produced in the 1st week by the corpus luteum, Also, individuals with Swyer syndrome (in which total gonadal dysgenesis occurs) are usually treated with estrogen and progesterone to facilitate development of secondary sexual characteristics and engender a menstrual cycle. 29f, 39, 179, 506f, 507f, 517b, 536b

Ethmoid sinus. Invaginations of the middle meatus of the nasal passages (the space underlying the middle nasal concha) that form during the 5th month and grow into the ethmoid bone. These sinuses do not complete their growth until puberty. 571

Eunuchoidism. A set of additional malformations of primary hypogonadism (a component of Klinefelter syndrome) identifiable by slender habitus, elongated extremities, and sparse hair. 536b

Eustachian tube. Also called auditory tube. A development of the first pharyngeal pouch, the channel connects the tympanic cavity to the pharynx. 545b, 573, 583b, 598

Eventration. Expansion or "ballooning" of the abdominal contents into the pulmonary cavity. Usually caused by deficient development of muscle tissue in the diaphragm, if the

herniation has resulted in severe pulmonary hypoplasia, the newborn may die of pulmonary insufficiency even if the hernia is repaired. 334b, 336f

Exocoelomic cavity. Referring to the cavity of the yolk sac, it forms from the first wave of migratory endodermal cells sent by the hypoblast. 51b, 57

Exocoelomic membrane. Also called Heuser's membrane. The lining of the exocoelomic cavity (yolk sac). 51b, 55f, 57, 58f

Exogen. The final, or shedding, phase of hair growth. 204

Experimental embryology. Science that involves conducting experiments on developing model embryos. Classically, experimental embryology has been used to define the tissue and cellular basis of development through a series of microsurgical manipulations. More recently, experimental embryology has merged with cell biology, molecular biology, and genetics, allowing investigators to define the molecular-genetic basis of development. 142–150, 143, 144f, 145

Exstrophy. The congenital eversion or turning inside out of an organ. 497, 497f

Extension. One of the coordinated group movements in gastrulation, involving lengthening in the cranial-caudal plane. 80b

Extensors. The muscles that extend a joint.* 241–242, 242t

Extracellular matrix. Any material produced by cells and excreted to the extracellular space within the tissues. It takes the form of both ground substance and fibers and is composed chiefly of fibrous elements, proteins involved in cell adhesion, and glycosaminoglycans and other space-filling molecules. It serves as a scaffolding holding tissues together, and its form and composition help determine tissue characteristics. In epithelia, it includes the basement membrane.* 328b

Extracellular matrix molecules. Cell molecules that can be permissive for migration, and hence determine the path, as well as inhibitory for migration, thereby determining the boundaries of the paths. For example, neural crest cells migrate only through the cranial half of the somite and fail to enter the caudal half; in so doing, they establish the segmental patterning of the peripheral nervous system. 121b

Extracellular signal–regulated kinase/Mitogen–activated protein kinase (Erk/Mapk) cascade. The binding-initiated phosphorylation cascade in which three kinases are sequentially phosphorylated: Mapk kinase (Mapkkk, also called Raf); Mapk kinase (Mapkk, also called Mek); and Map kinase (also called Erk). 158

Extraembryonic membranes. The amnion, chorion, yolk sac, and allantois. 51b, 171

Extraocular muscles. The six voluntary muscles that move the eyeball, including the superior, inferior, middle, and lateral recti, and the superior and inferior oblique muscles.* 559

Extrasphincteric outlets. A urinary tract anomaly in females identifiable by the connection of ectopic ureters to the vestibule, vagina, or uterus, which results in a constant dribbling of urine unless surgically corrected. 499b

Extravasation. The discharge or escape of blood or some other fluid (e.g., plasma proteins) normally found in a vessel or tube, into the surrounding tissues.* 397b

Extrinsic forces. Forces that are both sufficient and necessary for neurulation. Tissues lateral to the neural plate (surface ectoderm and mesoderm) generate extrinsic forces for bending of the neural plate. Like intrinsic forces acting during shaping, these extrinsic forces are generated by changes in cell behavior and also involve changes in cell shape, position, and number. 111b

Eya1. Eyes absent homolog 1, a transcription factor required for Gdnf expression and, hence, ureteric bud development. 494b

F

Facial clefting. A complete or partial failure of fusion between any of the five facial swellings, which results in a facial fissure that may be unilateral or bilateral. Facial clefting is a component of more than 300 syndromes. 569b–571b, 571f, 572f

Facial clefts. The spectrum of the congenital facial defects, including cleft lip and cleft palate, that result from the failure of some of these facial processes to grow and fuse correctly. 543b, 563

Facial nerve. Cranial nerve VII, one of the cranial nerves arising in the hindbrain that supply branches to the pharyngeal arches and their derivatives. It innervates the muscles of facial expression and one special branch, the chorda tympani, supplies the taste buds of the anterior two thirds of the tongue. 260f, 555t, 559

Facial prominences. The five protrusions, or projections, of the face: the frontonasal prominence, a pair of maxillary prominences, and a pair of mandibular prominences. The human face is formed between the 4th and 10th weeks by fusion of the facial prominences. 543b

Factor in germline alpha (Figα). The oocyte-released factor that activates the folliculogenesis program in the ovary. Without FIGα, primordial follicles never form and oocytes regress soon after birth. FIGα also stimulates formation of the zona pellucida in the primordial follicle. 506f, 507f, 516b

Failure to thrive. A condition diagnosed in an infant or child whose physical growth is significantly less than that of his or her peers, and is often associated with poor developmental and cognitive functioning. Although there is no clear consensus definition, the term usually refers to growth below the 3rd or 5th percentile or a change in growth that has crossed two major growth percentiles (i.e., from above the 75th percentile to below the 25th) in a short time.[**] 53b

Falciform ligament. A sickle-shaped sagittal fold of peritoneum that helps to attach the liver to the diaphragm, separates the right and left lobes of the liver, and extends from the coronary ligament of the liver behind to the umbilicus in front.* 447f, 448f, 455, 455f

Fallopian tube. A long slender channel, which forms from the proximal portion of the Müllerian ducts, and extends from the upper lateral cornu of the uterus to the region of the ovary of the same side. It is attached to the broad ligament by the mesosalpinx, and consists of an ampulla, infundibulum, isthmus, two ostia, and a pars uterina.* 482b, 502t, 518

Familial adenomatous polyposis. A condition involving multiple adenomatous polyps with high malignant potential that line the mucous membrane of the intestine, particularly the colon, beginning at about puberty. It occurs in several autosomal dominant conditions,

[**] Bauchner H. 2004. Failure to Thrive. In: Behrman RE, Kliegman RM, Jenson HB, eds. Nelson Textbook of Pediatrics, ed 17. Philadelphia, Saunders.

including Gardner's syndrome, Peutz-Jeghers syndrome, and Turcot's syndrome.* 155, 465b, 467b

Familial exudative vitreoretinopathy. The syndrome caused by mutations in the Wnt (and Norrin) receptor Frizzled4, and characterized in part by incomplete vascularization of the retina when the retinal blood vessels do not reach the periphery of the retina. 614b

Fanca. The gene that in its mutated form causes Fanconi anemia syndrome, which affects limb development and is identifiable by radial/thumb aplasia/hypoplasia and preaxial polydactyly. 635t

Fastigial nucleus. One of the four deep nuclei that form on each side of the cerebellum. All input to the cerebellar cortex is relayed through these nuclei. 263

Fate mapping. Studies in which groups of cells are marked in some manner (often with fluorescent dyes), and then followed over time. For example, fate mapping studies show that cardiac progenitor cells within the epiblast are topologically organized such that the cardiac inflow progenitors are located more lateral and the outflow progenitors are more medial. 83, 84f, 138, 144f

Fertile eunuch syndrome. A syndrome of hypogonadotropic hypogonadism, with variable development of secondary sex characters, that is associated with normal spermatogenesis, normal levels of follicle-stimulating hormone, and variably low levels of luteinizing hormone.* 536b

Fertilinβ. Also known as Adam2, A member of the Adam superfamily, a protein that is present on male germ cells and/or mature sperm. 39

Fertilization. The act of rendering gametes fertile or capable of further development. It is a sequence of events that begins with contact between a spermatozoon and an oocyte, leading to their fusion, which stimulates the completion of oocyte maturation with release of the second polar body. Male and female pronuclei then form and merge; synapsis follows, which restores the diploid number of chromosomes and results in biparental inheritance and the determination of sex. The process of fertilization leads to the formation of a zygote and ends with the initiation of its cleavage.* 15b, 39, 40f, 41, 41f

Fetal alcohol syndrome. Also known as fetal alcohol spectrum disorder. A syndrome of altered prenatal growth and morphogenesis seen in 2 in 1000 live-born infants born to mothers who were chronically alcoholic during pregnancy. It includes facial anomalies such as maxillary hypoplasia, prominent forehead and mandible, short palpebral fissures, microphthalmia, and epicanthal folds, as well as growth retardation, microcephaly, and mental retardation.* Consumption of amounts of alcohol as low as 80 g/day (i.e., between two and three shots of a grain liquor like rum) during the 1st month of pregnancy can cause significant defects, and it has been suggested that even a single binge may be teratogenic. 135, 135f, 638b

Fetal period. Following the 8th week of gestation, which signifies the end of the embryonic period, the remaining 30 weeks of gestation constitute the fetal period, which is devoted mainly to the maturation of organ systems and to growth. 167b, 169

Fetology. Also called prenatal pediatrics. The study and treatment of the fetus. 169b, 180

Fetus. The developing unborn child in the postembryonic period, from week 9 until birth. 1b, 5, 9, 16f, 167, 169, 170f, 172f

Fiber layer. The layer formed from axons of the ganglion cells that lines the inner surface of the retina and courses to the developing optic nerve. 607, 608f

Fibroblast growth factors. A group of peptide hormones secreted by the adenohypophysis, affecting many of the same cell types as Platelet-derived growth factor. It is a potent mitogen of vascular endothelial cells and is a regulator of tissue vascularization.* 157

Fibroblastic tissue. Undifferentiated connective tissue. 237, 237f

Fibronectin. Any of several related adhesive glycoproteins. One form circulates in plasma, acting as an Opsonin; another is a cell-surface protein that mediates cellular adhesive interactions. Fibronectins are important in connective tissue, where they cross-link to Collagen, and are also involved in aggregation of platelets.* 160, 160f, 161, 195

Fibrous stratum. The intervening layer, derived from infiltrating neural crest cells, is located between the outer lining of ectoderm and inner lining of endoderm of the tympanic membrane. 583b, 599

Filaggrin. A protein that aggregates with the Keratin filaments to form tight bundles helping to flatten the cells of the stratum germinativum. 200

Filopodia. Thin processes of epiblast cells that, along with foot-like processes called pseudopodia and flattened processes called lamellipodia, allow migration through the primitive streak into the space between the epiblast and hypoblast (or into the hypoblast itself). Filopodia, especially, have been implicated in the sensing and transducing of environmental signals that guide the growth cone to its target. 78, 277b, 277f

Finger rays. Radial thickenings in the digital plate of the upper limb that become visible on day 38. 10t, 626

First-cleft sinus. An ectoderm-lined cavity or cervical aural fistula located in the tissues anterior to the external acoustic meatus, which is formed as a result of duplication of the first pharyngeal cleft. 573

Fistula. An abnormal passage or communication, usually between two internal organs, or leading from an organ to the surface of the body.*

Flamingo. A gene involved in planar cell polarity (PCP) signaling in Drosophila. 111b

Flectin. A secreted protein having an asymmetric left-right distribution pattern within the cardiac jelly and dorsal mesocardium. 352b–353b

Flexors. Muscles that cross a joint and responsible for flexing the limbs. 242, 242t, 617b

Floor plate. The unpaired ventral longitudinal zone of the neural tube, forming the floor of that tube. * 247b

Flt4. A receptor for Vascular endothelial growth factors *C* and *D*. 428

5'-Fluoro-2-deoxyuridine. A chemotherapeutic agent that is an inhibitor of thymidylate synthetase. An agent that influences general cell metabolism or cell proliferation, it is also likely to cause limb defects if administered during the period of limb morphogenesis. 638b

Fog2. Friend of Gata2, a transcription factor. Fog2 is a critical gene for normal diaphragm formation. 335b

Folic acid. Also known as vitamin B_9. A supplement that can reduce the incidence of neural tube defects by up to 50%. 117b

Follicle. Any one of a number of sacs or pouch-like depressions or cavities.* 29, 30f, 31f, 35, 37, 38f, 482b, 515–561, 516b–517b, 517f

Follicle cells. Cells located in the epithelium of follicles, such as the cells of the thyroid follicles or ovarian follicles. In females, these are the result of differentiation of the somatic support cells in the 6th week. 479b, 515

Follicle-stimulating hormone (FSH). A gonadotropic hormone that, when secreted during the menstrual cycle, regulates later phases of folliculogenesis in the ovary and the proliferative phase in the uterine endometrium. 16f, 28, 29f, 30, 35,

Folliculogenesis. Maturation of the ovarian follicle. 16f, 516b

Follistatin. An inhibitor of Bmp signaling expressed in early development and involved in important events such as neural induction and establishment of left-right asymmetry. 157

Fontanelles. Four membrane-covered spaces remaining at the junction of the sutures in the incompletely ossified skull of the fetus or infant. They represent gaps in the bone structure that will be filled in by bone during the normal process of growth. Although these “soft spots” may appear very vulnerable, they may be touched gently without harm. There are normally two large fontanelles on the top of an infant's skull (the anterior and posterior fontanelles), and several smaller ones on the sides of the skull.* 547, 549f

Footplate. The distal end of the lower limb bud, becoming defined by day 38, that develops into the foot. 626

Foramen cecum. A visible depression, the site of origin of the thyroid gland, where the median sulcus intersects the terminal sulcus. 544f, 545b, 574–575, 575f

Foramen of Magendie. A single median aperture, or hole, in the roof plate of the fourth ventricle that allows fluid to gain access to the subarachnoid space. 263

Foramen of Monro. Also known as interventricular foramen. The persistent opening between each lateral ventricle and the third ventricle. 284

Foramen ovale. An opening left in the septum secundum near the floor of the right atrium. During embryonic and fetal life, blood passes from the right atrium to the left atrium through this opening, which closes at birth due to the change in pressure caused by the opening of pulmonary circulation and the cessation of umbilical flow. 365, 365f, 429, 430f

Foramen primum. The passage between the atria that diminishes during the 5th week as the septum primum and spina vestibuli grow toward the atrioventricular canal, thus gradually separating the nascent right and left atria. 363, 363f, 364f

Foramen secundum. Also called ostium secundum. A new passage that forms, before the foramen primum closes, from small perforations that coalesce following programmed cell death and cell rearrangement in an area near the dorsal edge of the septum primum. This processs allows a new channel for right-to-left shunting to open before the old one closes. 338f, 364f, 365

Foramina of Luschka. Two median apertures, or holes, in the roof plate of the fourth ventricle, that allow fluid to gain access to the subarachnoid space. 263

Foramina transversaria. Also called transverse foramen. The passage in either transverse process of a cervical vertebra that, in the upper six vertebrae, transmits the vertebral vessels.* 227

Forearm. The part of the upper limb between the elbow and wrist, which becomes distinguishable, along with the shoulder, arm, and hand plate, by day 33. 626

Forebrain. Also called prosencephalon. The portion of the brain developed from the anterior of the three primary brain vesicles before the end of the 4th week and comprising the diencephalon and telencephalon.* Even on day 19, before bending of the neural plate begins, the forebrain and the other two major divisions of the brain, the mesencephalon (midbrain) and rhombencephalon (hindbrain), are demarcated by indentations in the neural plate. 94, 95f, 101b, 251, 272–290, 273f, 274, 275f, 276–282, 284–288, 285f–286f, 288f, 289f, 290

Foregut. One of the subdivisions of the primitive gut. The endodermal canal of the embryo cephalic to the junction of the yolk stalk, which gives rise to the pharynx, lung, esophagus,

stomach, liver, and most of the small intestine.* 69b, 101b, 104f, 106, 435b, 439, 445–454, 450f, 450–451, 451f

Formative matrix. Also called formative root or zone. Stratum germinativum of the proximal nail fold that proliferates to become the matrix that produces the horny nail plate. 210

Forward genetic approach. The process of using random mutations in unknown genes to identify perturbed developmental events, thereby resulting in phenotypes, which is followed by identification and cloning of the mutated gene. 136, 137, 142

Fovea centralis. The region of the eye with the highest visual acuity, which postpartum contains only a dense population of cone photoreceptors. This region is also avascular, reducing light scattering within the eye. 608

FoxA1/FoxA2. Winged helix transcription factors required for the regulation of lung cell genes, including surfactant synthesis. The factors were previously known as Hepatic nuclear factor3α and β, or Hnf3α and Hnf3β). 57, 327b

FoxC2. A member of the Forkhead family of transcription factors linked to rare forms of lymphedema. 428b

FoxD3. A winged-helix transcription factor that when overexpressed promotes delamination of neural crest cells at all axial levels, showing it is sufficient by itself for delamination. 119b

FoxD1. A transcription factor expressed by stromal cells, necessary for balancing stromal and nephron progenitor specification and survival. 492f, 492b–493b

FoxJ1. One of the many Fox transcription factors, required for the development of differentiated ciliated cells and the formation of submucosal glands that are the major source of mucus production in the normal lung. 328b

Foxn1. A transcription factor mutated in the nude mouse, and in a rare human syndrome, required for keratinization. A consequence of this mutation is that hairs develop but do not penetrate through the epidermis. 206b

Fragile X syndrome. The most common cause of mental retardation in males. This syndrome is caused by trinucleotide repeat expansions in the Fmr1 (Fragile x mental retardation1) gene. Atresia or stenosis of the external auditory meatus can suggest deletion of the long arm of chromosome 18. 602b

Frameshift mutations. Small deletions or insertions involving the coding sequence that lead to alterations in the reading frame of the DNA strand.[††] 326b

[††] Kumar V, Fausto N, Abbas A. 2004. Robbins and Cotran Pathologic Basis of Disease, ed. 7. Philadelphia, Saunders.

Frasier syndrome. Also called cryptophthalmos syndrome. An autosomal recessive abnormality, characterized by absence of the palpebral apertures, disorganization of one or both ocular globes, malformed ears, cleft palate, laryngeal stenosis, syndactyly, meningoencephalocele, imperforate anus, cardiac defects, and maldeveloped kidneys.* 494b

Frenulum. A small fold of tissue that limits the movements of an organ or part.* 574

Friedreich ataxia. An autosomal recessive cerebellar ataxias that affects the dorsal root ganglia, spinal cord, and cerebellum. 269b

Frontal sinuses. One of the four pairs of paranasal sinuses that develop from invaginations of the nasal cavity extending into the bones. These cavities form during 5th or 6th postnatal year and expand throughout adolescence. 571, 572

Frontalis muscles. One of the muscles of facial expression. 555t, 557f, 559

Frontonasal ectodermal zone. A region in the frontonasal prominence characterized by the juxtaposition of Shh and Fgf8 expression. 566b

Frontonasal prominence (process). An expansive facial process in the embryo that develops into the forehead and bridge of the nose.* 543b, 563, 564f

FRT sequence. A sequence used for conditional gene targeting using Flp recombinase from yeast. 149

F-Spondin. A secreted protein produced by the floor plate of the neural tube that determines the pathways of neural crest cell migration, and one of the permissive extracellular matrix molecules in the cranial somite. 121b

G

GABA (Gamma-aminobutyric acid). An amino acid that is one of the principal inhibitory neurotransmitters in the central nervous system.* It may be required for motor axons to navigate correctly to their peripheral targets. 312b

Galactosemia. A defect in galactose metabolism known to cause cataracts. 614b

Gallbladder. A pear-shaped organ located below the liver that serves as a storage place for bile. It develops during the 5th week from the proximal duodenum. 435b, 448, 448f

Gallus homeobox 6 (Gh6). One of the two homeobox genes responsible for subdivision of optic vesicles in chicks. Each of these transcriptional control genes plays a part in patterning the craniocaudal axis, as both knockout and overexpression studies result in altered positional identity of retinal ganglion cells, revealed by their aberrant projections. However, it remains unclear how the patterned expression of these genes is directed by upstream signals. 276b

Gamete. One of two haploid reproductive cells, male (spermatozoon) and female (oocyte), whose union is necessary in sexual reproduction to initiate the development of a new individual.* 15b, 17.

Gamete intrafallopian transfer (GIFT). An in vitro technique used to help couples conceive in which the egg is fertilized in vitro and the blastocyst is transplanted into one of the woman's fallopian tubes. 46b, 49b

Gametogenesis. The formation of the gametes, egg, and sperm; the term for the process that converts primordial germ cells into female gametes (definitive oocytes) or male gametes (spermatozoa). 1b, 15b, 16f, 20–25

Ganglia. A group of nerve cell bodies located outside the central nervous system.

Ganglion cell layer. One of the layers of the neural retina that differentiates and develops between the 6th week and 8th month. It contains retinal ganglion cell bodies. 586b, 608f

Ganglionic eminences. Neuronal aggregations on the floor of the cerebral hemispheres that give rise to the basal ganglia, the corpus striatum and globus pallidus. 282

Gap genes. In Drosophila, zygotic genes that act in establishing the basic anterior-posterior body plan. The maternal effect genes regulate expression of the gap genes, which in turn regulate expression of the pair-rule genes. 151, 152f

Gap junctions. Narrowed portion of the intercellular space, containing channels linking adjacent cells and through which can pass ions, most sugars, amino acids, nucleotides, vitamins, hormones, and cAMP. In electrically excitable tissues the gap junctions serve to transmit electrical impulses via ionic currents and are known as electrotonic synapses; they are present in such tissues as the myocardium.* 43, 597b

Gartner's cyst. A closed rudimentary duct, lying parallel to the uterine tube, into which the transverse ducts of the epoöphoron open. It constitutes the remains of the part of the mesonephros that participates in formation of the reproductive organs.* 518, 519f

Gastroschisis. A failure of the anterior (ventral) body wall to form properly during body folding or subsequent development, resulting in a portion of the gastrointestinal system herniating beyond the anterior body wall. 103b, 106b, 106f, 114b, 461b

Gastrosplenic ligament. The portion of the dorsal mesentery between the spleen and stomach. 454

Gastrulation. The rearrangement of cells into three primary germ layer, ectoderm, mesoderm, and endoderm. 1b, 69b, 71–94

Gata. A zinc finger GATA-binding transcription factor, which serves as one of the downstream transcriptional regulators in endoderm formation. 56b

Gbx2. The transcriptional control gene expressed between the Otx2 and Hox expression domains, and important for neural plate and tube patterning. 253b

Gene. The biologic unit of heredity: self-reproducing, transmitted from parent to progeny, and located at a specific position in the genome. Genes make up segments of the complex DNA molecules that control cell reproduction and function. There are thousands of genes in the chromosomes of each cell nucleus; they play an important role in heredity because they control the individual physical, biochemical, and physiologic traits inherited by offspring from their parents. Through the genetic code of DNA, they also control day-to-day functions and reproduction of all cells in the body; for example, they control the synthesis of structural proteins, as well as the enzymes that regulate various chemical reactions that take place in a cell.*

Gene expression. (1) The flow of genetic information from gene to protein. (2) The process or regulation of the process by which effects of a gene are manifested. (3) The manifestation of a heritable trait in an individual carrying the gene or genes that determine it.* 65b, 140

Gene targeting. A technique that makes it possible to insert specific DNA sequences into their correct locations in the mouse genome. 147, 327b

Gene therapy. Manipulation of the genome of an individual to prevent, mask, or lessen the effects of a genetic disorder. The defective function may be replaced by introduction of genetic material into targeted cells, or the defective gene itself may be corrected by using recombination to replace all or part of the defective gene with a normal DNA sequence.* 189

Gene-environmental interaction. The susceptibility of an embryo for having a variety of birth defects can be genetically controlled. Thus, exposure to a teragen at a particular

concentration at a particular time in development in one embryo may result in a birth defect, but not in another with a difference genetic makeup. *See genetic constitution.* 177

Genetic anticipation. The worsening of a disease in successive generations. 269b

Genetic constitution. A principle of teratology that states that susceptibility to a teratogen depends on the genetic constitution of the developing embryo or fetus. For example, if two embryos of the same age are exposed to the same dose of teratogen, one may develop severe cardiac malformations whereas the other may remain unaffected. The molecular basis for this difference in susceptibility might be a genetic difference in the rate at which the enzyme systems of the two embryos detoxify the teratogen. 177

Genetic hierarchy. The order of genes in a genetic program, elucidated in part by examining gene expression patterns in mutants. 76b

Genetic mosaics. A consequence of random X inactivation in female cells where all females are genetic mosaics. Some cells express only the X-linked genes inherited from the mother, and some cells express only X-linked genes inherited from the father. Thus, in cases in which female offspring inherit a recessive X-linked mutation from one parent and a wild-type allele from the other, the offspring do not exhibit symptoms of the disease because of compensation by cells in their bodies that express the wild-type allele. 67b

Genetic-conflict hypothesis. The conditional statement that a conflict exists between males and females over allocation of maternal resources to offspring. During early development, the paternal genetic complement controls invasion and growth of the placenta, whereas the maternal genetic complement is responsible for early embryonic development. 64b, 65b

Genetics. The branch of biology concerned with the phenomena of heredity and the laws governing it.* 133b

Geniculate ganglion. The inferior ganglion of nerve VII (facial: general and special afferent) originating at the first epipharyngeal placode. 124f, 314, 315f

Geniculate nuclei. Areas within the thalamus that handle sense of sight (lateral) and sense of hearing (medial). 272, 274, 278b, 279b

Genital canal. Also called uterovaginal canal. A short tube with a single lumen formed when the Müllerian ducts begin to fuse from their caudal tips cranially just as the fused tips of the Müllerian ducts connect with the sinusal tubercle. 518, 519f

Genital ridges. The primitive gonads that develop as swellings created by proliferation of the somatic support cells, just medial to each mesonephros (embryonic kidney) on both the right and left sides of the gut mesentery. 19, 500, 501f, 502f

Genital system. Genitalia; the male and female reproductive organs, which begin to appear during the 5th week and become distinctive by the 6th week. 479

Genital tubercle. The expansion of the phallic segment of the urogenital sinus that eventually forms the phallus. 473f, 474, 474f, 482b, 495, 496f, 521, 522f

Genitofemoral nerve. The nerve that innervates the region that includes the spermatic cord in the male and the round ligament in the female. This nerve seems to have a role in mediating shortening of the gubernacula because, if this nerve is severed, cryptorchidism results. 530b

Genomic imprinting. The process by which genes are imprinted, that is, marked so that rather than being expressed biallelically (from both maternal and paternal alleles contributed to the zygote during fertilization), they are expressed from only one allele in a parent-specific manner. 64b–67b

Genotype-phenotype correlation. The relationship of differences in phenotypes (the appearance of an individual) with differences in specific mutations (the genotype of the individual). Drawing such correlations provides insight into mechanisms underlying birth defects. 240b, 505b

Gentamycin. An aminoglycoside antibiotic, neonatal exposure to which may lead to hearing loss. 596b

Germ cells. Specialized reproductive cells first identifiable in the wall of the yolk sac during the 4th to 6th weeks of gestation. By the 6th week, the germ cells migrating from the yolk sac begin to arrive in the mesenchyme of the dorsal body wall. The arrival of germ cells in the area just medial to the mesonephroi at the 10th thoracic segment induces cells of the mesonephros and adjacent coelomic epithelium to become somatic support cells that invest the germ cells. Somatic support cells will differentiate into Sertoli cells in the male and follicle cells (or granulosa cells) in the female. During the same period, a new pair of ducts, the Müllerian (paramesonephric) ducts, form in the dorsal body wall just lateral to the mesonephric ducts. 15b, 479b

Germ cell nuclear antigen 1 (Gcna1). One of three new germ cell-specific genes expressed shortly after primordial germ cells enter the genital ridge (after which they are usually called gonocytes). 20b

Germ cell-less (Gcl1). One of three new germ cell-specific genes expressed shortly after primordial germ cells enter the genital ridge (after which they are usually called gonocytes). Gcl1 is expressed in the Drosophila germ line shortly after it is established. It is named after the mutation in which the gene is inactivated and the germ line is lost. 20b

Germ layers. Primitive tissue layers established during gastrulation. 69b

Germ line. A series of cells that form the sex cells. 15b, 17

Germ plasm. Cytoplasm containing determinants of the germ line. 19b

Germinal epithelium. The original surface lining of the developing gonad. 19, 27

Germinal layer. A structure consisting of internal and external layers of proliferation and neurogenesis of the developing cortex and cerebellum. The external germinal layer also gives rise to primitive nuclear neurons, which migrate to form the deep cerebellar nuclei. 264, 267f

Germinal matrix. The layer of proliferating ectoderm responsible for producing the hair shaft, which overlies the dermal papilla in the base of the hair bulb. 193b, 204, 204f

Germinal vesicle. The large, watery nucleus of a dormant primary oocyte, which contain partially condensed prophase chromosomes. 28, 35, 38f, 47f

Germinative layer. Also called stratum germinativum. A new intermediate layer of tissue that develops from the basal layer of the developing skin in the 11th week just deep to the periderm. This layer is the forerunner of the outer layers of the mature epidermis and constitutes the layer of stem cells that will continue to replenish the epidermis throughout life. 196, 197f

Gestational diabetes. Diabetes mellitus that first appears during the second or third trimester and often disappears following birth. Woman with gestational diabetes usually do not have an increased frequency of children with birth defects. However, if the diabetes is poorly managed during pregnancy, there is an increased risk of delivering a very large baby (greater than 10 pounds). Such babies may have an increased risk for obesity and diabetes in later life. 178

Growth factor receptor α (Gfrα). The coreceptor to the Ret receptor that, along with its ligand, Gdnf, induces formation of the ureteric bud from the mesonephric duct. Gfrα and Ret are expressed within the mesonephric duct, whereas the ligand, Gdnf, is found within the metanephric mesenchyme. 490b

Gallus homeobox 6 (Ghg). A transcriptional control gene that plays a part in patterning the cranial-caudal axis of the avian neural plate. 276b

Gillespie syndrome. An rare autosomal recessive cerebellar ataxia syndrome consisting of aniridia, cerebellar ataxia, and mental retardation.* 269b

Gli3. A component (repressor) of Shh signaling pathway; a gene that when mutated manifests as Greig cephalopolysyndactyly (postaxial or preaxial polydactyly, syndactyly, broad digit 1) or Pallister-Hall syndrome (post-axial polydactyly, syndactyly). 550b, 635t

Glenoid blastema. A protuberance on the temporal bone that is involved with the mandibular condyle in formation of the temporomandibular joint. 554

Gli2. A component of the Sonic hedgehog signaling pathway that when mutated results in polydactyly (duplicated digits). 157, 549b

Glia. The supporting structure of nervous tissue consisting of (in the central nervous system), astrocytes, oligodendrocytes, and microglia.* Glia first begin to differentiate from the neuroepithelium of the neural tube during the 4th week and provide metabolic and structural support to the neurons of the central nervous system . 257

Glial cell line-derived neurotrophic factor. A chemotactic factor that attracts neural crest cells. 121b

Glial cells. The branching non-neural cells of the neuroglia (the supporting tissue of the central nervous system). They consist of three types: astroglia (macroglia), oligodendroglia, and microglia. 127f, 255, 284, 299b

Glioblasts. A new cell type that develops once production of neurons wanes in the ventricular layer of the differentiating neural tube. These cells differentiate into the glia of the central nervous system (astrocytes and oligodendrocytes). 256f, 257, 258

Globose nucleus. A deep cerebellar nucleus lying between the emboliform nucleus and the nucleus fastigii and projecting its fibers via the superior cerebellar peduncle.* It serves as a pathway for relaying input to the cerebellar cortex. 263

Globus pallidus. One of the large neuronal nuclei of the basal ganglia that are crucial to executing commands from the cerebral hemispheres. 250b, 282

Glomerulus. A knot of capillaries. 484f, 485, 487f

Glossopharyngeal nerve. Cranial nerve IX, which innervates the stylopharyngeus, vallate papillae, and the general sensory endings over most of the posterior one third of the tongue. 260f, 558f, 559, 575

Glottis. A passageway formed at the original point of evagination of the diverticulum of the pharynx. 321

Glucocorticoid. Any corticosteroid, including cortisol, cortisone, and corticosterone, that increases gluconeogenesis, raising the concentration of liver glycogen and blood glucose. The principal glucocorticoid hormone is cortisol, which regulates metabolism of proteins, carbohydrates, and lipids. Many physiologic processes within the body can occur only in the presence of, or with the "permission of," the glucocorticoids; for example, the secretion of digestive enzymes by gastric cells and the normal excitability of heart muscle and central nervous system neurons require a certain level of glucocorticoids.* 449b, 500b

Glycocalyx. A polysaccharide matrix surface coating of epithelial cells including (in the case of the uterine epithelium) abundant high–molecular weight mucin glycoproteins. 55b

Glycosaminoglycan. Any of the carbohydrates containing amino sugars occurring in proteoglycans, such as hyaluronic acid or chondroitin sulfate.* 238b, 611, 640

Glycosylation. The formation of linkages with glycosyl groups.* Congenital disorders present with gross cerebellar malformations that can be diagnosed after birth with computed tomography (CT) or magnetic resonance imaging (MRI). 269b

Glycosyltransferases. Enzymes that add sugars to or remove sugars from proteins. 159

Goldenhar syndrome. A particularly severe member of a group of more extensive deformities collectively known as hemifacial microsomia, which include defects of the eye (scleral dermoids and coloboma of the eyelids) and vertebral column. 580b, 613b

Golgi cells. (Type I) Pyramidal cells with long axons, which leave the gray matter of the central nervous system, cross through the white matter, and go out to the periphery. (Type II) Star-shaped neurons with short axons, found in the cerebral cortex and the cerebellar cortex.* 264, 268f

Goltz syndrome. A disease typified by skin atrophy and skeletal malformations that occurs in children who inherit a dominant X-linked mutation from one parent. 67b

Gonads. The gamete-producing glands, or "sex glands," of females (the ovaries) and males (the testes). In addition, gonads secrete hormones that influence the development of the reproductive organs at puberty, and they control other physical traits that differentiate men from women, such as pitch of the voice and body form and size.* 7, 18f

Gonadal arteries. Arteries that develop to vascularize the gonads. They initially arise at the 10th thoracic level but during descent of the gonads they become fixed at the third or fourth lumbar level. As the gonads continue to descend, the gonadal arteries elongate. 410f, 411

Gonadotropin. Also called gonadotropic hormone. Any hormone having a stimulating effect on the gonads. Two such hormones are secreted by the adenohypophysis (anterior pituitary): follicle-stimulating hormone and luteinizing hormone; both are active, but with differing effects, in the two sexes. 35, 38f

Gonadotropin-releasing hormone (GnRH). A decapeptide hormone of the hypothalamus that stimulates the release of follicle-stimulating hormone and luteinizing hormone from the adenohypophysis (anterior pituitary). It can be used in the differential diagnosis of hypothalamic, pituitary, and gonadal dysfunction.* 28, 287b

Gonocytes. Also called primordial germ cells. In males, gonocytes remain dormant from the 6th week of embryonic development until puberty, when seminiferous tubules mature and gonocytes differentiate into spermatogonia. In females, the gonocytes undergo a few more mitotic divisions after they are invested by the somatic support cells. They then differentiate into oogonia, and by the 5th month of fetal development all oogonia begin meiosis, after which they are called primary oocytes. 20, 20b

Goosecoid. Transcription factor involved with development of the cardiac neural crest. 95b, 376b

Gorlin syndrome. Also called nevoid basal cell carcinoma syndrome (NBCCS). An autosomal dominant disorder occurring in about 1:50,000 to 1:100,000 individuals. Those affected have basal cell carcinomas that begin forming early in life. NBCCS patients also have increased susceptibility to other carcinomas such as meningiomas, fibromas, and rhabdomyosarcomas. 207b

Granular layer. Also called stratum granulosum. The middle layer of the outer epidermis. 193b, 196, 197f, 201f

Granule cells. Cells found in the granular layers of the cerebellar and cerebral cortices. 261, 263, 285

Granulocyte-macrophage colony-stimulating factor (Gm-Csf). A colony-stimulating factor that binds to stem cells and most myelocytes and stimulates their differentiation into granulocytes and macrophages.* 197b

Gray matter. The term for layers of the cortex of the brain that contain mainly cell bodies. 256f, 257, 263

Gray ramus. A small branch formed from postganglionic fibers that originate in each chain ganglion. It grows dorsally to rejoin the spinal nerve and then grows toward the periphery. 297b, 304, 306, 307f

Grebe type chondrodysplasia. A type of chondrodysplasia that specifically affects the appendicular skeleton. 239b, 239f, 240b

Greig cephalopolysyndactyly. A human syndrome resulting from a mutation in Gli3, indicated by postaxial (hands) or preaxial (feet) polydactyly, syndactyly, and broad first digit. 550b, 634b, 635t

Gremlin. A secreted Bmp antagonist that blocks the repressive actions of Bmps on the function of the limb apical ectodermal ridge. 630b, 631f

Gridlock. A mutant of the Hey2 homolog that, in zebrafish, has defects in the aorta resembling human coarctation. 416b

Growth. The progressive development of a living thing, especially the process by which the body reaches its point of complete physical development.* 80b

Growth cone. The swollen central core found at the tip of the nerve sprouts, from which extend flattened, webbed processes called lamellipodia and numerous stiff, fine processes called filopodia (composed of actin). The growth cones interact with laminin and fibronectin

present in the basal lamina of the Schwann cells. These glycoproteins play a key role in promoting the growth and advancement of the regenerating axons.‡‡ 277b, 277f, 640

Growth differentiation factors (Gdf). Factors involved in bone development. Gdf5 is necessary for development of some of the appendicular joints, but its precise role in this process is unknown because overexpression of Gdf5, unlike that of Wnt9a, does not induce/maintain joint formation. Gdf6, along with Gdf5, is expressed in developing joints, and both promote chondrogenesis by increasing the size of the initial chondrocyte condensations and increasing chondrocyte proliferation. Gdf7 is necessary for epididymis and seminal vesicle development. 238b, 238f, 512b, 513f

Growth factors. Any substances that promote skeletal or somatic growth, usually a mineral, hormone, or vitamin.* 154

Growth plate. Also called epiphyseal cartilage plate, or physis. A layer of cartilage that persists between the epiphysis and the growing end of the diaphysis (metaphysis). 235

Gubernaculum. Also known as caudal genitoinguinal ligament. One of the ligaments that keeps the mesonephric-gonadal complex anchored as it becomes more segregated from the adjacent intermediate mesoderm. The gubernaculum is attached to the caudal portion of the male and female mesonephric-gonadal complex and extends to the peritoneal floor where it is attached to the fascia between the developing external and internal oblique abdominal muscles in the region of the labioscrotal swellings. 481f, 502t, 519f, 525, 526f

Gut tube. The central early structure of the formation of the tube-within-a-tube body plan, fifth in the phases of human embryogenesis. It consists of cranial and caudal blind-ending tubes, the presumptive foregut and hindgut, and a central midgut, which opens ventrally to the yolk sac. 1b, 8f, 10–11t, 101b, 104f, 409f, 436f, 437, 438f, 439, 439t

Gynecomastia. Development of breasts in males. 536b

Gyri. The ridges on the surface of the brain separated by sulci.

‡‡ Godding GC. 2005. Laryngeal Reinnervation. In: Cummings CW, et al, eds. Otolaryngology: Head & Neck Surgery, 4th ed, pp 2210-2211. Philadelphia, Mosby.

H

Habenular commissure. One of the small nerve bundles that is part of a structure called the trigonium habenulae. 273f, 274, 289f

Hair cell. A type of sensory cell in the inner ear that has hairlike processes and plays an important role in the process of hearing, having nerve fiber connections to either the cochlear nerve or the vestibular nerve. These cells are found in the organ of Corti, ampullar crest, utricle, and saccule.* 588, 592, 593

Hair follicle. A specialized structure that develops within the skin, originating as a rod-like downgrowth of the stratum germinativum into the dermis. 193b

Hair germ. A small concentration of ectodermal cells in the basal layer of the primitive, two-layered epidermis, where the hair follicle first appears. 194f, 203, 204f

Hair peg. A rod-like structure formed when the hair germ recruits dermal cells to form a dermal condensate that promotes further differentiation of the hair germ. The hair germ proliferates to form the rodlike hair peg that pushes down into the dermis. 194f, 203, 204f

Hairy. A Drosophila segmentation gene. 91b, 159, 452b

Hairy1. An ortholog of the Drosophila segmentation gene Hairy and a member of the Notch family. 91b

Hairy and enhancer-of-split-like-1 (Hes1). A transcription factor that downregulates the proendocrine bHLH transcription factor Neurogenin-3 (Ngn3), a member of the Neurogenin/NeuroD family. 452b

Hand plate. The earliest formation structure of the hand, visible by day 33, before the fingers form. 10t, 617b, 626

Handed asymmetry. The term used to denote anatomic differences on the left and right sides of the body. 73b

Hand-foot-genital syndrome. An dominant autosomal disorder characterized by malformed distal limbs and hypospadias. 524b, 635t, 637b

Haploid cell. A cell that contains half the number of chromosomes contained in typical body cells. 7, 15b, 21, 22f

Hassall's corpuscles. Whorl-like bodies in the medulla thought to arise from the ectodermal cells of the third pharyngeal cleft. Hassall's corpuscles produce signals necessary for the development of regulatory T cells. 577

Hay-Wells syndrome. Ankyloblepharon-ectodermal dysplasia clefting (AEC) syndrome, caused by mutations in transcription factor Tumor protein P73-like (Tp73l, also known as P63). Ankyloblepharon refers to fusion of the eyelids. 203b

Head fold. The fold of blastoderm at the cephalic end of the developing embryo.* 329, 344f

Hearing loss. The complete or partial loss of hearing, which occurs in 1 in 1000 live births. Conductive hearing loss is the result of malformations in the external and/or middle ear; sensorineural hearing loss can arise from defects in the inner ear, vestibulocochlear nerve (cranial nerve VIII), or the auditory regions of the brain. About half of all hearing loss has genetic causes, with the other half attributed to environmental factors. 596b–597b

Heart field. Also called cardiac crescent. The primary heart field, a cardiac primordium formed from cardiogenic precursors within the splanchnic mesoderm at the cranial end of the embryonic disc in response to inductive and permissive signals that emanate from the endoderm, ectoderm, and midline mesoderm. The *secondary* heart field is the source of cardiac precursor cells from outside the original cardiac crescent at both the arterial (cranial) pole and venous (caudal) pole that drive lengthening of the primitive heart tube and proper cardiac looping. 337b, 341f

Heart murmur. Any sound in the heart region other than normal heart sounds. Common causes include movement of blood through narrowed or stenotic heart valves and blood leaking through a valve that does not close properly. In many cases a murmur may be of the innocent or functional type, with no heart disease at all, so that it causes no trouble; this type is only sporadically present and in time may go away completely.* 379b

Heart tube. The earliest rudiment of the heart. 10t, 337b, 338f, 339, 344f, 345f, 348f.

Heat shock transcription factor 4 (Hsf4). A transcription factor that, if mutated, can lead to congenital cataracts. 614b

Hedgehog. A family of genes. Indian hedgehog (Ihh) is one of the crucial genes that regulates the differentiation of the chondrocytes; it signals through the Patched (Ptc) receptor. Sonic hedgehog (Shh) signals the formation of prethalamus cranially and thalamus caudally. Desert hedgehog (Dhh), released by fetal Sertoli cells, plays a central role in fetal and adult Leydig cell differentiation. 156f, 156–157, 510b.

Helix. The spiral shape most often associated with the structure of DNA. 601

Hemangioblasts. Aggregates that develop adjacent the endoderm at about day 17, which are the earliest evidence for blood and blood vessel formation in the extraembryonic splanchnic mesoderm of the yolk sac. 385b, 388, 388f

Hemangioma. A common type of congenital vascular malformation or benign tumor made up of newly formed blood vessels clustered together. It may be present at birth or appear a little later. The most common type appears as a network of small blood-filled capillaries near

the surface of the skin, forming a red to purple birthmark. Other types are sometimes found in the liver and in bones.* 399b–401b, 401f

Hemangiosarcoma. Also called metastatic angioma or angiosarcoma. A malignant tumor of vascular tissue. 399b

Hematopoiesis. Also called hemopoiesis. The formation and development of blood cells. In the embryo and fetus it takes place in a variety of sites (the hematopoietic organs) including the liver, spleen, thymus, lymph nodes, and bone marrow. From birth throughout the rest of life it is mainly in the bone marrow, with a small amount occurring in lymph node.* 58, 385b, 388, 388f, 448

Hematopoietic stem cells (HSCs). Stem cells that have the capacity for replication and differentiation and give rise to precursors of various blood cell lines.* 122b, 385b, 388

Hematopoietic system. The network of tissues involved in the production of blood, including the bone marrow, liver, lymph nodes, spleen, and thymus.* 219

Hemiazygos vein. The vein derived from the left thoracic supracardinal vein. 423f, 424

Hemidesmosomes. Cell-to-cell membrane junctions containing Integrins that connect cells of the stratum germinativum to the basement membrane. 199

Hemifacial microsomia. Also called oculoauriculovertebral spectrum. A group of disorders in which the lateral cleft of the face is not large, but the posterior portion of the mandible, temporomandibular joint, muscles of mastication, and outer and middle ear may all be underdeveloped. Goldenhar syndrome is a particularly severe member of this group. 580b

Hemolytic disease of the newborn. Also called hemolytic disease of the newborn. A disorder that occurs when the mother's anti-Rh antibodies cross the placenta and destroy the fetal red blood cells of the Rh+ fetus, thus causing anemia in the fetus and newborn. 175–176

Hemopoiesis. Also called hematopoiesis. The formation and development of blood cells. In the embryo and fetus it takes place in a variety of sites (the hematopoietic organs) including the liver, spleen, thymus, lymph nodes, and bone marrow. From birth throughout the rest of life it is mainly in the bone marrow, with a small amount occurring in lymph node.* 58, 385b, 388, 388f, 448

Heparan sulfate. A proteoglycan known to have a high degree of specific binding to various extracellular matrix proteins and growth factor/cytokines, which thus could serve as attachment factors. 55b

Heparin-binding epidermal growth factor-like growth factor (Hb-Egf). A factor upregulated at the implantation site, presumably in response to blastocyst signaling. 55b

Hepatic duct. An outgrowth of the gut tube endoderm at the duodenal level that gives rise to the liver. 439t, 446, 448f

Hepatic nuclear factor (Hnf). A group of transcription factors important in mediating metabolic and detoxifying functions of the liver as it begins to shift away from hematopoiesis. Hnfs activate specific liver genes. 449b

Hepatic plate. A small endodermal thickening that forms on the ventral side of the duodenum on about day 22. 10t, 446

Hepatoblasts. The liver primordial cells that express several genes that are specific to the development of hepatocytes (parenchyma). 446

Hepatocytes. Cells that begin upregulating the expression of numerous genes related to mature liver function (e.g., those associated with amino acid metabolism and detoxification) as the hematopoietic function is shifted to the peripheral organs. 446

Hepatocyte growth factor (Hgf). An extraneous growth factor required for the migration and proliferation of hepatocytes. 448

Hepatoduodenal ligament. The caudal border of the lesser omentum, connecting the liver to the developing duodenum. 455, 455f

Hepatogastric ligament. The region of the lesser omentum between the liver and the stomach. 455, 455f

Hereditary hemorrhagic telangiectasia (HHT). Also known as Osler-Weber-Rendu disease. A syndrome (with a prevalence of 1:5000 to 1:8000) manifesting most often as nosebleeds and small vascular anomalies called telangiectases. However, gastrointestinal bleeding and arterial-venous malformations in the lung, brain, and liver progressively develop. 387b, 401b

Hereditary motor-sensory neuropathy (HMSN). Also called Charcot-Marie-Tooth (CMT) hereditary neuropathy. A group of chronic demyelinating polyneuropathies (i.e., motor and sensory) that present in the first and second decades with slowly progressive distal weakness, wasting, and sensory loss, which is worse in the legs. High arches (pes cavus), hammer toes, ankle instability, and eventually, deformity, are common. 307b–308b

Hereditary surfactant protein B deficiency. A fatal disease described as an uncommon cause of respiratory failure in full-term newborn infants. Alveolar air spaces become filled with granular eosinophilic proteinaceous material, and tubular myelin is absent. 326b

Herg. A gene that encodes cardiac ion channels. 383b

Hermaphrodites. Also called intersex individuals. Individuals having sex chromosomes, genitalia, and/or secondary sex characteristics that are a mixture of both male and female. 508b

Hernia. Protrusion of part of an organ or tissue through the structures normally containing it because of a weak spot or other abnormal opening. It may be either congenital or acquired.* 106f, 114f, 187, 187f, 324b, 334b, 335f, 461b, 509, 526, 529f, 530

Herp. Also called Hey2, a basic helix-loop-helix (HLH) transcription factor important for mediating Notch signaling. 416b

Herpes simplex virus. A virus capable of crossing the placenta and infecting the fetus, which causes canker sores and genital warts.176

Hes. An ortholog of Drosophila Hairy and Enhancer-of-split proteins that inhibits Atoh gene activity, thereby preventing hair cell differentiation and allowing cells to develop as supporting cells. When combined with Hes-related proteins (Hesr), together they regulate the expression of basic helix-loop-helix (bHLH) transcriptional repressors. 159

Heterotaxy. The condition in which different organ systems exhibit a discordance of sidedness, i.e., defects ascribed to abnormal left-right axis formation, be it a reversal of some organs (situs ambiguous) or a reversal of all viscera (situs inversus totalis). 74b, 353b, 353f

Heuser's membrane. Also called exocoelomic membrane. The primary yolk sac that forms on day 8. 51b, 55f, 57, 58f

High-resolution chromosome banding. Also known as karyotyping. A method used to detect complex chromosomal abnormalities. 37f

Hindbrain. Also called rhombencephalon. (1) The portion of the brain developed from the most caudal of the three primary brain vesicles of the early embryo, comprising the metencephalon and myelencephalon. (2) The most caudal of the three primary vesicles formed in the embryonic development of the brain, which later divides into the metencephalon and the myelencephalon. * 5f, 94, 101b, 251

Hindgut. A pocket formed beneath the caudal portion of the developing embryo, which develops into the distal portion of the small intestine, colon, and rectum.* 69b, 101b, 104f, 106, 408, 409f, 435b, 439, 472–475, 473f, 474f

Hindgut endoderm. One of the three subdivisions of the primitive gut. 495, 496f, 497, 497f

Hinge points. Localized regions where neuroepithelial cells change their shape from column-like to wedge-like and where the wedge-shaped cells become firmly attached to an adjacent structure through deposition of extracellular matrix. 107, 109f, 110b

Hippocampal commissures. Also called fornix commissures. Junctions that form during the 9th week between the right and left hippocampi (a phylogenetically old portion of the cerebral hemisphere located adjacent to the choroid fissure). 288, 289f, 290

Hirschsprung disease. A term for congenital megacolon, a defect that results when lumbosacral neural crest cells fail to innervate the terminal portion of the colon, resulting in impaired gut motility. 128b, 470b, 471f, 472b

Hirsutism. Abnormal hairiness, especially in women.* At puberty vellus hairs can be transformed into terminal hairs, for example, on the upper lip and lower leg. 207b

Hmx2/3. Homeobox genes expressed in the dorsal otocyst, which are required for development of the vestibular apparatus. 592b

Holoprosencephaly. The most common developmental defect of the forebrain, affecting 1 in 16,000 births. In its most severe form, only a single cerebral lobe forms (hence the name of the condition), rather than paired right and left hemispheres. Defects of the olfactory nerves, olfactory bulbs, olfactory tracts, basal olfactory cortex, and associated structures including the limbic lobe, hippocampus, and mammillary bodies are also found. The corpus callosum is sometimes affected; the hindbrain is usually normal. 134b, 134f, 157, 547b, 549f, 549b–550b, 602b

Holt-Oram syndrome. An autosomal dominant heart disease of varying severity, usually an atrial or ventricular septal defect that is associated with skeletal malformation (hypoplastic thumb and short forearm).* 355b, 636t, 638b

Homeobox. A highly conserved 183-base pair region of DNA that encodes the 61-amino acid homeodomain. 152

Homeobox expressed in ES cells-1 (Hesx1). A transcription factor that when mutated in humans can cause septo-optic dysplasia (also called De Morsier syndrome), an optic nerve hypoplasia that occurs in conjunction with pituitary hypoplasia and midline brain abnormalities. 605t, 615b

Homeodomain. Proteins that recognize and bind to the specific DNA sequences of other genes. 152

Homeotic complex (HOM-C). A special subset of Drosophila homeotic selector genes organized in two clusters on chromosome 3. 152, 153f, 153–154

Homeotic selector genes. A class of zygotic genes that act in establishment of the basic anterior-posterior body plan. 151–153

Homologous recombination. A technique that makes it possible to inactivate (knock out) any gene of interest or to replace one gene with another (knock in). 142, 148, 327b

Horizontal cells. A type of nerve cell found in the retina. There are two types, each with one long neural process and several short ones.* 607

Hormones. Chemical transmitter substances produced by cells of the body and transported by the bloodstream to the cells and organs on which they have a specific regulatory effect. Hormones act as chemical messengers to body organs, stimulating certain life processes and retarding others. Growth, reproduction, control of metabolism, sexual attributes, and even mental conditions and personality traits are dependent on hormones.* 4b, 5b, 15b, 25, 28, 30f, 167b, 179

Horny layer. Also called stratum corneum. The definitive outer layer of the epidermis. 193b, 196, 197f, 198b

Hox. The four complexes of homeobox genes in mammals. 152, 153f, 153–154, 518b, 520b

Human chorionic gonadotropin (hCG). Hormone that supports the secretory activity of the corpus luteum and thus maintains the supply of progesterone (i.e., maternal recognition of pregnancy). 44, 179, 182, 530b

Human immunodeficiency virus (HIV). The agent of acquired immune deficiency syndrome (AIDS) and related syndromes. This virus can sometimes cross the placenta from an infected mother to infect the unborn fetus. 176

Hunter-Thompson type chondrodysplasia. An autosomal recessive syndrome that can affect all limb skeletal elements with increasing severity in a proximal-to-distal direction, resulting in loss of function. Characterized by shortening of the appendicular skeleton (brachydactyly), it may result from mutations in Gdf5. 240b

Hyaline membrane disease. A condition resulting from continued injury that may lead to detachment of the layer of cells lining the alveoli. 326b

Hyaloid artery. The terminal branch of the ophthalmic artery that enters the optic vesicle via a groove called the choroidal fissure. The hyaloid artery vascularizes the developing retina and initially also vascularizes the lens vesicle. 585f, 586b, 604f, 611

Hyaloid canal. A passage running from in front of the optic disk to the lens of the eye. In the fetus, it transmits the hyaloid artery.* 604f, 611

Hyaluronan. Also called hyaluronic acid or hyaluronate. A glycosaminoglycan that readily absorbs water, which creates tissue spaces causing the stroma's cumulus cell mass to expand severalfold. 35, 238b

Hyaluronidase. An enzyme that catalyzes the hydrolysis of hyaluronan. 611

Hydantoin. An anticonvulsant linked to craniofacial anomalies in humans. 579b

Hydatidiform moles. Conceptus consisting of placental membranes, but absent the fetus (complete hydatidiform mole) or containing some remnant evidence of embryo development (partial hydatidiform mole). 60b, 63b–64b

Hydramnios. Also called polyhydramnios. An excess of amniotic fluid. 179

Hydrocele. A circumscribed collection of fluid; especially, a painless swelling of the scrotum caused by fluid in the serous membrane covering the front and sides of the testis and epididymis, the outermost covering of the testes. The hydrocele can be removed by withdrawing the fluid by tapping through the outer layer of tissue, or by cutting away the outer layer of tissue. 526, 529f

Hydrocephalus. Also called water on the brain. A congenital condition in which the third and lateral brain ventricles become enlarged due to blockage of the flow of cerebrospinal fluid. The cerebral cortex is abnormally thin and the sutures of the skull are forced apart, allowing the calvarial bones to increase in size. The condition can be corrected with shunts inserted either in utero or usually postnatally. 115b, 186, 270, 272f

Hydronephrosis. A condition identified by dilation of the ureter and renal pelvis. 169b

Hydrops fetalis. A condition in the fetus involving the accumulation of water. It is a sometimes fatal consequence of hemolytic disease of the newborn, also called erythroblastosis fetalis. 175

21-Hydroxylase deficiency. A condition involving enzyme deficiency in the pregnant mother that causes congenital adrenal hyperplasia (CAH), which results in a reduction of cortisol production by the suprarenal cortex and accumulation of 17-hydroxyprogesterone, that in turn results in suprarenal hyperplasia and excess production of suprarenal androgens. 188, 500b

Hyoid. A horseshoe-shaped bone at the base of the tongue, just above the thyroid cartilage.* 543b, 549f, 554f, 577f

Hypaxial muscles. The ventral and lateral muscles of the body wall (thorax and abdomen). 217b, 231

Hyperdontia. Excess or supernumerary teeth. A malformation resulting from Runx2 mutations (associated with cleidocranial dysplasia) can include the generation of a third set of teeth. 215b

Hyperglycemia. Excess glucose in the blood,* a condition associated with type 1 diabetes. Hyperglycemia inhibits release of Vegf from the myocardium, a growth factor essential for cushion tissue formation. 362b

Hyperinsulinism. Excessive secretion of insulin by the pancreas.* Compensatory hyperplasia caused by development of insufficient numbers of embryonic and fetal islet cells, this fetal maladaptation is frequently seen in neonates born to diabetic mothers. It can occur locally or diffusely throughout the pancreas, leading to life-threatening decreases in blood glucose levels (i.e., hypoglycemia). 454b

Hyperoxia. Excessive oxygen in the body. 397b

Hyperpyrexia. Lethal, extremely high body temperature; typically associated with hypohidrotic ectodermal dysplasia. 208

Hypertelorism. Wide-set eyes. A component of syndromes associated with holoprosencephaly: craniofrontonasal dysplasia, resulting from mutations in Efnb1 (Ephrin-B1), and Greig cephalopolysyndactyly, which results from mutations in Gli3 (a component of the Shh pathway). 550b, 581b

Hyperthermia. Overheating of the body; specifically, a potentially lethal condition whereby the body is no longer capable of maintaining normal temperature. 208

Hypertrichosis. Excess hair. 206b

Hypervascularization. Excessive vascularization. 393b, 395b

Hypoblast. The primitive endoderm, an internal (or lower) layer of cuboidal cells that forms when the embryoblast splits during the 2nd week. 51b, 52f, 54f, 56, 56b, 61f, 72f, 79f

Hypochondroplasia. A common disorder of cartilage development transmitted as an autosomal dominant trait. The clinical features resemble those of achondroplasia but are milder, such as short stature with a long trunk and short limbs, broad and short fingers; the face is normal in appearance.* 635t

Hypodermis. Also called the subcorium. The subcutaneous fatty connective tissue underlying the dermis. 201f, 202

Hypodontia. Too few teeth; a malformation that affects the secondary dentition, which can be the result of mutations in Wnt signaling component Axin2 or in transcription factors Pax9, Pitx2, or Msx1. 215b

Hypoglossal cord. Musculature formed when myoblasts from the myotomes of the occipital somites coalesce beside somite 4 and extend ventrally as an elongated column, eventually becoming located ventral to the caudal region of the pharynx. 559

Hypoglossal nerve. Cranial nerve XII, the cranial nerve associated with occipital somites. 260f, 559, 575

Hypoglycemia. Life-threatening decreases in blood glucose levels. 454b

Hypogonadism. Small gonads. A defect that results because the hypothalamus fails to produce sufficient GnRH (Gonadotropin-releasing hormone), a hormone required for normal development of the gonads. 287b

Hypohidrotic ectodermal dysplasia. An X-linked genetic disorder in which the sweat glands fail to develop. 208

Hypomere. (1) One of the anterolateral portions of the fusing myotomes in embryonic development, forming muscles innervated by the anterior rami of the spinal nerves. (2) The lateral plate of mesoderm that develops into the walls of the body cavities.* 217b, 218f, 224f, 231, 233f

Hyponatremia. A deficiency of sodium in the blood. It can occur as a result of inadequate sodium intake, as in a sodium-restricted diet, excessive water ingestion or retention, or excessive salt wasting. Symptoms include muscular weakness and twitching, progressing to convulsions if unrelieved; alterations in level of consciousness; mental confusion; and anxiety. When its cause is salt wasting, it is accompanied by loss of body fluids.* 500b

Hyponychium. The layer beneath the free edge of the nail. 210, 211f

Hypopharyngeal eminence. A midline swelling of the third and fourth pharyngeal arches that develops in the 5th and 6th weeks. 573f, 574, 575f

Hypophyseal cartilages. Cartilage of the chondrocranium that fuses to form the body of the sphenoid bone, and the prechordal cartilage that gives rise to the ethmoid bone. Together with the nasal and turbinate bones, they encapsulate the nasal cavity. 547, 548f

Hypoplastic left heart syndrome (HLHS). Congenital hypoplasia or atresia of the left ventricle, the aortic or mitral valve, and the ascending aorta, with respiratory distress, cardiac failure, and death in infancy. 339b

Hyposmia. Diminished sense of smell, a characteristic of Kallmann syndrome, which results because the olfactory bulbs and olfactory nerves fail to develop properly. 287b

Hypospadias. A developmental anomaly in which the penile urethra opens on the ventral surface of the penis. 521b, 525f, 524b–525b, 532b, 533f–634f, 535b

Hypothalamic sulcus. The deep groove that divides the alar plate of the diencephalon into dorsal and ventral portions. 249f, 250b, 272, 273f

Hypothalamic swelling. Swelling ventral to the hypothalamic sulcus that differentiates into the nuclei collectively known as the hypothalamus. 250b

Hypothalamus. The part of the brain that functions to control visceral activities such as heart rate and pituitary secretion. 250b, 272, 273f, 274

Hypotrichosis-lymphedema-telangiectasia. A rare syndrome that results from a mutation in transcription factor Sox18. Hair is the only abnormal ectodermal derivative. 203b

Hypoxia. Lower tissue oxygen content in the decidua. 171, 362b

Hypoxia-inducible factor-1α (HiF1α). The transcription factor that upregulates VegfA expression and nitric oxide synthase expression. 397b

I

Ichthyosis. Excessive keratinization of the skin. 198b, 308b

Id1. A basic helix-loop-helix (bHLH) transcription factor that promotes endothelial cell proliferation and migration. 396b

Ids1, 2, 3. Transcription factors that inhibit hair cell differentiation by binding to basic helix-loop-helix (bHLH) proteins. 593b

IkBKG. The gene that produces Ikkγ/Nemo; mutations cause X-linked incontinentia pigmenti. 198b

Indian hedgehog (Ihh). A member of the Shh family expressed by the prehypertrophic chondrocytes, signals to the periarticular perichondrium to induce Parathyroid hormone–related protein (Pthrp) expression. Ihh regulates chondrocyte proliferation and promotes hypertrophy, and induces development of the bone collar around the diaphysis of the cartilage element. 236f, 237b

Ileum. The distal portion of the small intestine that extends from the jejunum to the cecum (the beginning of the large intestine).* 435b

Iliac arteries. The arteries that drain the lower extremities and pelvic organs. 411, 413, 414f, 422f, 423f, 424

Immunohistochemistry. A term that denotes the application of antigen-antibody interactions to histochemical techniques, as in the use of immunofluorescence.* It is also a technique used to show patterns of protein expression. 145–146, 146f

Implantation. The point on day 6 when the blastocyst attaches to the wall of the uterus. 4, 16f, 43

Imprinting. The marking of genes so that they are expressed according to the parent of origin. 64b–67b, 66f

Imprinting centers. Specialized chromosomal regions that allow groups of genes to be coordinately imprinted. 65b

In situ hybridization. A technique used to visualize patterns of RNA expression. 94f,146–147, 146f

In vitro fertilization (IVF). A technique used to impregnate a female via insertion of an egg into the uterus, which has been fertilized in a Petri dish. 17b, 46b–48b, 47f, 48f

Incontinentia pigmenti. Spotty pigmentation of the skin caused by mutations in Ikbkg. In this syndrome, the mutant cells are eliminated by apoptosis induced by the cytokine Tumor necrosis factor-α. These defects occur as ‘‘M-’’ or ‘‘V’’-shaped patterns on the abdomen and back, as proximally and distally oriented lines along the limbs, and as anteriorly and posteriorly curved lines along the face. 67b, 198b

Incus. The middle auditory ossicle that forms from the first pharyngeal arch mesenchyme between the stapes and malleus to comprise the chain of ossicles within the tympanic cavity. 543b, 546f, 549f, 553, 554f, 562f, 583b, 584f, 588

Indomethacin. A prostaglandin inhibitor sometimes used to treat premature infants in whom the ductus arteriosus does not constrict spontaneously. 432b

Inducible promoters. A technique used in conjunction with the *cre-lox* system so that the a gene can be knocked out at a desired time in development. 149–150

Induction. The ability of one area of an embryo to change the fate of another area through the secretion of signaling molecules. 71b, 145

Inductive interactions. Cascading signaling events that prevent a tissue from forming its ‘‘default” tissue type, such as Bmps preventing surface ectoderm from forming its default fate, neural ectoderm). 83, 12b, 130f, 145

Inferior ganglia. The lower ganglia of cranial nerves VII (geniculate), IX (petrosal), and X (nodose), which begin to develop in the 5th week. 315f

Infertility. The inability to conceive and produce viable offspring. The diagnosis of infertility is not usually considered valid until after 1 year of engaging in sexual relations with the same partner without contraception.* 25b, 46b, 48b, 49b, 74b

Infrahyoid muscles. The strap muscles of the neck. 234

Infundibular recess. A proximal pit in the floor of the third ventricle. 282

Infundibulum. A diverticulum, a circumscribed pouch or sac occurring normally,* that develops during the 3rd week in the floor of the third ventricle and grows ventrally toward the stomodeum. It forms the posterior pituitary gland. 250b, 282, 283f

Ingression. The movement of cells through the primitive streak and into the interior of the embryo. 71, 79f, 81b, 119b

Inguinal canals. Caudal evaginations of the abdominal wall that form when the vaginal process grows inferiorly, pushing out a socklike evagination consisting of the various layers of the abdominal wall. 482b, 525–526, 526f, 527f, 529f, 531f

Indirect inguinal hernia. A malformation in which loops of intestine may herniate into the vaginal process. Repair of these hernias is one of the most common childhood operations. 526, 529f, 530

Inhibin-A. A serum protein produced by the fetus and placenta and checked during pregnancy as part of quadruple maternal screening to detect the presence of a fetus with Down syndrome or a birth defect such as a neural tube defect. 182

Inhibition. Restraint or termination of a process. Typically it takes the following forms: competitive inhibition of enzyme activity by an inhibitor (a substrate analog) that competes with the substrate for binding sites on the enzymes; contact inhibition of cell division and cell motility in normal animal cells when in close contact with each other; and noncompetitive inhibition of enzyme activity by substances that combine with the enzyme at a site other than that utilized by the substrate.* 72b, 97b, 156, 303b, 328b, 343f, 593b

Inhibitory molecules. Molecules of the neural crest cell migration pathways found in the caudal somite. 121b

Injection chimera. To construct these, embryonic stem cells, derived from the inner cell mass of one embryo of a particular genotype, are injected into the blastocoel of another embryo with a different genotype at the blastocyst stage. The blastocyst is then placed into the uterus of a pseudopregnant female. 148

Inlet septum. The smooth-walled dorsal part of the interventricular septum. 368

Inner cell mass. Also called *embryoblast*. One of the two groups of cells formed at the 8- to 16-cell stage from the cleaving embryo (morula) that gives rise to the embryo proper and associated extraembryonic membranes. 15b, 43

Insula. The portion of the cerebral cortex that originally forms the medial floor of the fossa and is covered by the temporal lobe. 284

Insulin. The major fuel-regulating hormone of the body, formed from proinsulin in the beta cells of the islets of Langerhans in the pancreas. Insulin promotes the storage of glucose and the uptake of amino acids, increases protein and lipid synthesis, and inhibits fat breakdown and gluconeogenesis. Secretion of insulin is a response of the beta cells to a stimulus; the primary stimulus is the presence of glucose, and others are amino acids and certain hormones. After insulin is released from the beta cells, it enters the bloodstream and is transported to cells throughout the body. The cell membranes have insulin receptors to which the hormone becomes bonded, or “fixed.” An interaction between the insulin and its receptors leads to biochemical processes that include transport of glucose, amino acids, and certain ions into the cell body; storage of glycogen in liver and muscle cells; synthesis of triglycerides and storage of fat; synthesis of protein, RNA, and DNA; and inhibition of gluconeogenesis and breakdown of glycogen, protein, and fats.* 450, 453b–454b

Insulin gene enhancer protein-1 (Isl1). A growth-promoting transcription factor expressed by mesoderm surrounding the dorsal pancreatic bud, which is important to the growth and differentiation of the pancreas. 450

Insulin-like factor-3 (Insl3). A substance generated by Leydig cells. Underexpression in males causes the testes to not descend, but remain adjacent to the kidneys. Overexpression in females causes the ovaries to descend. 529b–530b

Insulin-like growth factor (Igf). An insulin-like substance in serum that does not react with insulin antibodies. It is growth hormone–dependent and possesses all the growth-promoting properties of the somatomedins.* 65b, 157

Interferon regulatory factor 6 (Ifr6). Protein needed for the phase of skin development that involves formation of the granular and horny layers. 197b–198b

Integrins. Cell-adhesion molecules consisting of noncovalently linked heterodimers of alpha and beta transmembrane subunits, which provide a link between the extracellular matrix and the cells' cytoskeletal network. Integrins form critical transmembrane links between extracellular matrix molecules such as Fibronectin and the intracellular Actin cytoskeleton (microfilaments). 159–161, 160f, 160–161

Interarticular disc. A cartilaginous disc contained within a joint; for example, that which separates the mandibular condyle from the glenoid blastoma in the temporomandibular joint. 554

Intercellular communication. A form of cell-to-cell interaction mediated by secretion of soluble signaling molecules that diffuse within the extracellular environment to reach adjacent cells. 150

Intercostal arteries. The arterial supply of the wall of the thorax. 411

Intercostal muscles. The thoracic muscles that comprise the three layers of hypaxial muscles (external and inner intercostals, and innermost intercostals). 234

Intercostal veins. The veins that drain the wall of the thorax. 423–424

Interleukin. One of several proteins important for lymphocyte proliferation. Interleukin-1 (IL-1), produced by macrophages, induces the production of interleukin-2 by T cells that have been stimulated by antigen or mitogen. Interleukin-2 (IL-2), produced by T cells, stimulates the proliferation of T cells bearing specific receptors for IL-2; these receptors are expressed in response to antigenic stimulation. IL-2 also seems to induce the production of interferon and is used as an anticancer drug in the treatment of a wide variety of solid malignant tumors. Another interleukin, interleukin-3 (IL-3), is necessary for the differentiation of suppressor T cells. 55b, 197b

Interleukin/Lif cytokine family. A cytokine is a regulatory protein released by cells of the immune system; it acts as an intercellular mediator in the generation of an immune response. Cytokines are grouped into families of different types based on their structure and/or function; each family contains multiple members. 20b

Intermaxillary process. The structure formed during the 7th week when the inferior tips of the medial nasal processes expand laterally and inferiorly and fuse. 11t, 564, 565f, 569f

Intermediate layer. A layer of skin produced during the 11th week by the basal layer to form between itself and the periderm. 193b, 194f, 196, 196f

Intermediolateral cell columns. Neurons that form in the dorsal regions of the spinal cord at all 12 thoracic levels, at lumbar levels L1 and L2, and at sacral levels S2 to S4. 257, 257f

Internal capsule. A massive axon bundle that passes through the corpus striatum (giving it its striated appearance), It carries axons from the thalamus to the cerebral cortex (and vice versa), as well as from the cerebral cortex to the lower regions of the brain and spinal cord. 275f, 282

Internalization. Also called emboly. The movement of cells into the interior of an embryo. 80b–81b

Interosseous arteries. The main arteries located between the bones of the forearm, which serve as the main source of blood for the limb. 411, 413f

Intersegmental arteries. The dorsolateral branches of the dorsal aorta that penetrate between the somite derivatives and give rise to part of the vasculature of the head, neck, body wall, limbs, and vertebral column. 226, 385b, 406f, 412f, 413f

Intersex individuals. Also known as true hermaphrodites. (i.e., individuals having sex chromosomes, genitalia, and/or secondary sex characteristics that are a mixture of both male and female). 508b

Interthalamic adhesions. Multiple points in the thalamus where two thalami meet and fuse across the third ventricle. 274, 275f

Interventricular foramen. Also known as foramen of Monro. The persistent opening between each lateral ventricle and the third ventricle. 275f, 284

Interventricular septum. The muscular protrusion into the cardiac lumen along the interface between the presumptive right and left ventricular chambers as the ventricular chambers expand. 368, 368f

Intervertebral discs. Discs composed of cells of notochordal origin that form at the intrasegmental boundary, then die, leaving a gelatinous core called the nucleus pulposus. 218f, 227, 227f, 236

Intervillous space. The space in the mature placenta that is lined with fetal syncytiotrophoblast and filled with maternal blood into which the villi project. It is formed from trophoblastic lacunae that grow and coalesce. 167b, 171, 174f

Intestinal malrotation. An idiopathic malformation that occurs when the midgut fails to complete its rotation during the 10th through 12th week of development as it returns to the peritoneal cavity from the umbilical herniation. This leaves the small intestine in the right side of the abdomen, tethered to the mesenteric vasculature by a narrowed mesentery. 437b

Intracytoplasmic sperm injection (ICSI). The in vitro fertilization technique used in cases in which a partner's spermatozoa are unable to penetrate the zona pellucida. 46b, 47b–48b, 48f

Intraembryonic coelom. The space formed within the lateral plate mesoderm and enclosed in the embryo when the edges of the ectoderm fuse along the ventral midline. 70f, 89f, 101b

Intraperitoneal viscera. The term for the abdominal gut tube and its derivatives when suspended in what will later become the peritoneal cavity. 440, 458f

Intraretinal space. The temporary space between the neural retina and pigmented epithelium that disappears by the 7th week. It is homologous to the proliferative neuroepithelium lining the neural tube. 607, 608f

Intrasegmental boundary. A line of transversely arranged cells that characterizes the division between the cranial and caudal portions of each sclerotome. Also known as von Ebner's fissure. 222

Intrauterine device (IUD). A mechanical device that is inserted into the uterine cavity for the purpose of contraception. These devices are made of metal, plastic, or other substances, and come in various sizes and shapes. Their effectiveness is based on their alteration of the endometrium and consequent disruption of implantation; generally there is no effect on the menstrual cycle.* 45b

Intrauterine growth restriction (IUGR). Also known as small for gestational age (SGA). A condition in which fetal growth is markedly retarded. IUGR carries a higher risk of perinatal mortality and morbidity, so is considered a life-threatening birth defect. 178

Intussusception. The folding in of an outer layer, typically involving the developing vasculature of the fetus. 357, 359f, 392, 396b, 396f, 398f, 488f

Invasive mole. A malignant tumor that forms from a complete hydatidiform mole. 64b

Inversions. Chromosomal aberrations due to the inverted reunion of an internal segment after breakage of a chromosome at two points, resulting in a change in sequence of genes or nucleotides.* 34b

In vitro fertilization (IVF). An assisted reproductive technology (ART) procedure in which fertilized embryos are inserted into the uterus. 17b, 46b–48b, 47f, 48f

Involucrin. An envelope protein, produced by cells of the stratum granulosum, that lines the inner surface of the plasma membrane. 197f, 200

Ion channel. A cell membrane protein with an ion-specific transmembrane pore through which ions and small molecules pass into or out of a cell by diffusion downward along their electrochemical gradient.* 383b, 597b

Ionizing radiation. A teratogen that can cause birth defects. 579b

Iris. The circular colored membrane behind the cornea, perforated by the pupil. It is made up of a flat bar of circular muscular fibers that surround the pupil, a thin layer of plain muscle fibers that dilate the pupil, and, on the side toward the interior of the eye, two layers of pigmented cells.* The iris stroma develops from anterior segment mesenchymal tissue of neural crest cell origin. 612f, 613

Irritable bowel syndrome. The most common disorder seen in patients with gastrointestinal complaints, consisting of altered bowel habits, such as diarrhea or constipation or alternation of the two, along with abdominal pain and intolerance to flatus, without any detectable organic disease. It should not be confused with colitis or other inflammatory diseases of the intestinal tract; in irritable bowel syndrome there is no inflammation, and it is not necessarily limited to the colon.* The reciprocal relationship between the enteric nervous system and the brain may be significant in the pathogenesis of this syndrome. 470b

Irx4. An Iroquois homeoprotein expressed only in the cranial portion of the cardiac crescent, and thought to maintain the cranial-caudal phenotype of the heart by suppressing atrial commitment. 355b–356b, 356f

Ischiadic artery. Also called small sciatic artery. A remnant of the axis artery that serves the sciatic nerve in the posterior thigh. 413, 414f

Islets of Langerhans. Irregular microscopic structures scattered throughout the pancreas that comprise its endocrine portion. They contain the endocrine cells (or islet cells): alpha cells, which secrete the hyperglycemic factor glucagon; beta cells, which secrete insulin and whose degeneration is one of the causes of diabetes mellitus; and delta cells, which secrete somatostatin.* 450, 454b

Isomerism. Having two of the same organs where normally a right and left organ would exist, such as right lung isomerism (having two right lungs) or right atrial isomerism (both atria having right atrial morphology). 353b

Isotretinoin. An teratogenic analog of vitamin A and antiacne medication that can cause craniofacial anomalies in humans. 579b, 580f, 601b, 601f

Isthmus. A name for the constricted zone (boundary) consisting of the caudal midbrain and cranial hindbrain. 146f, 252f, 254f–255f.

Izumo. A sperm-specific protein named after the Japanese shrine to marriage. Izumo is a member of the immunoglobulin superfamily and as such is likely to be an adhesion molecule. 39

J

Jackson-Weiss syndrome. A disorder caused by constitutive activation of Fgfr2 and characterized by syndactyly. 630b, 635t

Jagged. A ligand for Notch receptors. 158–159

Jagged1. A Notch ligand expressed in cells adjacent to Notch2-positive epithelium at the site of biliary differentiation. Its interactions with Notch2 likely have critical roles in hepatocyte/cholangiocyte determination. Mutations in Jagged1 result in Alagille syndrome. 383b, 416b, 449b

Jansen-type metaphyseal chondrodysplasia. A disorder caused by Pthrp receptor 1 mutations and characterized by short limbs and dwarfism. 237b

Jarcho-Levin syndrome. Also called spondylocostal dysostosis syndrome. An autosomal recessive condition caused by mutation of Delta-like3 in which abnormal segmentation of the vertebral column and ribs occurs. 92b, 230b

Jejunal-ileal loops. A series of folds in the lengthening jejunum and ileum. 456, 457f

Jejunum. The part of the small intestine extending from the duodenum to the ileum.* 435b

Jervell and Lange-Nielsen syndrome. A syndrome caused by a mutation in Kcnq1 and characterized by prelingual sensorineural hearing loss and cardiac arrhythmia. 597b

Joint. The site of the junction or union of two or more bones of the body. Its primary function is to provide motion and flexibility to the frame of the body.* 234, 235f-237f, 236-241, 237b-238b, 238f, 640

Joint capsule. The saclike envelope that encloses the cavity of a synovial joint by attaching to the circumference of the articular end of each involved bone.* 237

Joint spaces. Spaces within the joint formed by cavitation. The inferior joint space forms between the condylar process and interarticular disc; the superior joint space forms between the interarticular disc and temporal bone. 556

Joubert syndrome. An autosomal recessive cerebellar ataxia syndrome. 269b

Jugular veins. Large veins that return blood to the heart from the head and neck.* The internal jugular veins are formed by cranial portions of the anterior cardinal veins in the developing cervical region, while the external jugular veins are formed from capillary plexuses in the face. 423f, 424

K

Kal1. The gene responsible for the X-linked form of Kallmann syndrome. Kal1 encodes an extracellular matrix glycoprotein protein called Anosmin-1. 287b

Kallmann syndrome. A syndrome characterized by anosmia or hyposmia and hypogonadism. 287b–288b, 536b

Kartagener syndrome. A syndrome caused by autosomal recessive mutations in the Dnah5 gene, characterized by inverted laterality, immotile respiratory cilia, and sperm flagella. Those affected often exhibit male infertility and chronic respiratory tract infections. 74b, 321b, 383b

Karyotype. The full set of chromosomes in a cell nucleus; by extension, the photomicrograph of chromosomes arranged according to a standard classification.* 34b–35b

Keratins. Proteins characteristic of the differentiated epidermis, contained in the keratinocytes of the intermediate layer. 193b, 196, 197b, 197f, 198b, 199, 200, 207b

Keratinocytes. Cells of the intermediate layer that contain Keratins. 193b, 196

Keratocysts, odontogenic. A non-neoplastic disorder of epidermal derivatives, arising from the dental lamina, that characterizes nevoid basal cell carcinoma syndrome. 207b

Keratoderma, palmoplantar, epidermolytic. Thickening of the skin in the hands and feet, caused by mutation in Krt9. 198b

Kidneys. The two bean-shaped organs in the lumbar region that filter the blood, excreting the end-products of body metabolism in the form of urine, and regulating the concentrations of hydrogen, sodium, potassium, phosphate, and other ions in the extracellular fluid.* 479b, 489, 489f, 493b-495b, 495, 496f,

Kif3A/Kif3B. Kinesin genes required for node cilia assembly, which is necessary for normal left-right development. 74b

Klinefelter syndrome. A syndrome caused by a variety of sex chromosome anomalies involving the presence of an extra X chromosome. The primary defect is a failure of the Leydig cells to produce sufficient amounts of male steroids, which results in small testes and azoospermia or oligospermia. Many individuals also exhibit gynecomastia, eunuchoidism, and primary hypogonadism. 34b, 536b

Klippel-Feil anomaly. An anomaly that affects the cervical and thoracic vertebrae, such that the neck is shorter with restricted movement. Sometimes the cervical vertebrae are fused. 231b, 233b

Knocked out genes. Inactivated target genes. The transcription of the target gene is blocked by mutation of introduced DNA sequences. 148

Krt1. A keratin induced by Notch signaling. 197b, 197f

Krthb1. A hair keratin, mutations in which result in monilethrix. 207b

Krthb6. A hair keratin, mutations in which result in monilethrix. 207b

Kvlqt1. A gene that encodes cardiac ion channels, mutations in which can cause long QT syndrome. 383b

L

Labia majora. Elongated folds on the external female genitalia, one on either side of the rima pudendi,* formed from the labioscrotal swellings. 521, 523f

Labia minora. Small folds of skin on either side of the vagina, between the labia majora and the opening,* formed from the urethral folds. 521, 523f

Labioscrotal folds. Paired folds on either side of the urethral plate that fuse at the midline to form the scrotum. 482b

Labor, preterm. Early delivery of the fetus. Preterm labor occurs frequently in cocaine-using mothers. 177–178

Labyrinth, bony. A system of canals within the petrous part of the temporal bone formed by the ossification of the otic capsule. 583b, 588, 593

Labyrinth, membranous. The otic vesicle derivatives of the inner ear, which are suspended in the fluid-filled perilymphatic space within the bony labyrinth. The membranous labyrinth itself is filled with endolymph. 583b, 588, 593

Labyrinthine aplasia. The complete absence of the membranous labyrinth. 597b

Lacrimal glands. The glands that produce tears, formed from invaginations of the ectoderm at the superolateral angles of the conjunctival sacs. 613

Lacrimal sac. The dilated upper end of the nasolacrimal duct.* 564

Lactiferous ducts. The channels of the mammary glands that open onto the mammary pit. 209, 209f

LacZ. A reporter gene that encodes the enzyme beta galactosidase. 150

Lag1. One of the transmembrane proteins of the DSL family; a ligand for Notch receptors. 159

Lamellar granules. Lipid-containing particles that help seal the skin. 200

Lamellipodia. Flattened processes extended from ingressing cells during gastrulation. 78

Lamina terminalis. The zone of closure of the cranial neuropore. 250b, 274, 288

Laminin. A basement membrane protein. 121b, 160, 277b

Langer mesomelic dysplasia. A syndrome caused by mutations in Shox, which results in mesomelia, limb bowing, and fibular hypoplasia. 636t

Langerhans cells. Macrophage immune cells of the skin that arise from the bone marrow, which function both in contact sensitivity and immune surveillance against invading microorganisms. 193b, 200, 200f

Lanugo. The fine, unpigmented first generation of hairs formed on the skin. They are mostly shed before birth and are replaced by coarser hairs during the perinatal period. 205

Large vestibular aqueduct (LVA). An inner ear dysplasia that enlarges the bony canal that transmits the endolymphatic duct, causing sensorineural hearing loss and vestibular anomalies. It can be diagnosed radiographically, and is associated with Pendred syndrome. 597b, 598f

Laryngeal musculature, intrinsic. The lateral cricoarytenoids, thyroarytenoids, and vocalis muscles, which are mainly devoted to vocalization. 559

Laryngeal nerves, recurrent. Nerves that branch from the vagus nerves to innervate the intrinsic muscles of the larynx. The right and left recurrent laryngeal nerves are asymmetric because of the asymmetric development of the left and right sixth arches. 405, 405f, 407

Larynx. The muscular and cartilaginous structure, lined with mucous membrane, that is situated at the top of the trachea and below the root of the tongue and the hyoid bone. It contains the vocal cords and is the source of the sound heard in speech. The larynx is part of the respiratory system; air passes through it traveling from the pharynx to the trachea on its way to the lungs and again returning to the exterior.* 321

Lateral cerebral fossa. A small indentation that forms in the lateral wall of each cerebral hemisphere during the 4th month. Formation of this fossa initiates the folding of the cerebral cortex into an increasingly complex pattern of gyri (ridges) and sulci (grooves) as the hemispheres grow. 282, 284f

Lateral geniculate nucleus (LGN). A body within the thalamus in which retinal axons synapse with target neurons to reproduce the spatial information from the retina. 274b, 279b-280b

Lateral inhibition. A process involving Notch signaling in which a neuronal precursor cell inhibits its neighbors from differentiating as neurons. Lateral inhibition regulates the number of neurons born in any one region of the developing nervous system and allows for the generation of supporting glial cells. 303b

Lateral lingual swellings. Also called distal tongue buds. A pair of lateral protrusions that develop on the first arch and rapidly expand to overgrow the median tongue bud. They eventually form the anterior two thirds of the tongue. 574, 575f

Lateral medial columns (LMCs). Two motor columns in the spinal cord composed of medial (LMCm) and lateral (LMCl) neurons; these innervate the limb bud in response to retinoic acid signaling from the paraxial mesoderm. 642b–643b, 643f

Lateral plate mesoderm. An area of intraembryonic mesoderm formed from the primitive streak during gastrulation, which contributes to the body wall and the wall of the gut. 69b, 217b

Lbx1. A homeobox transcription factor necessary for migration in the migratory limb and tongue muscle precursors. 242b, 244b, 642b, 643f

Leaflets, of atrioventricular valves. Cusps firmly rooted in the rim of the right and left atrioventricular canals, which are thought to arise from proliferation and differentiation of the adjacent endocardial cushion tissues. The valve leaflets are designed so that they fold back to allow blood to enter the ventricles from the atria during diastole, but close to prevent backflow when the ventricles contract during systole. 369–370

Leber congenital amaurosis syndrome. A genetic syndrome affecting the retina that causes the photoreceptors to die. It can result from mutations in Rpe65. 614b

Left-right axis. Part of the medial-lateral axis that defines asymmetries between the left and right sides of the body. 69b, 71, 73f, 73b-76b, 75f-77f, 76b

Lefty. A Bmp signaling inhibitor expressed in early development and involved in important events such as neural induction and establishment of left-right asymmetry. 157

Lefty 1, Lefty 2. Tgfβ family members that show left-sided expression and play an essential role in establishing left-right asymmetry. 73b, 383b

Lens. The transparent, biconvex body that separates the posterior chamber and vitreous body of the eye. It refracts (bends) light rays so that they are focused on the retina.* 604, 604b, 606f, 607b, 611

Lens body. A rounded body formed by the lens vesicle. 604

Lens fibers. Fibers that make up the lens. Posterior cells of the lens vesicle form long, slender anteroposteriorly oriented primary lens fibers. Anterior cells develop into a simple epithelium that covers the face of the lens and gives rise to the secondary lens fibers, which make up most of the mature lens. 586b, 604, 606f

Lens pit. A depression formed by the invagination of the lens placode. 604, 606f

Lens placode. An area of thickening surface ectoderm that invaginates and pinches off to become a hollow lens vesicle. 583b, 586b, 604, 606f

Lens vesicle. A hollow vesicle formed from the lens placode that gives rise to the primary lens fibers. 586b, 604, 606f

Lentiretinal space. The area between the lens vesicle and the inner wall of the optic cup in which mesenchymal cells secrete the primary vitreous body. 604

Leopard syndrome. A syndrome characterized by pulmonary stenosis and conduction anomalies as well as craniofacial and skeletal anomalies. It can be caused by mutations in the Ptpn11 gene. 383b

Léri-Weill dyschondrosteosis. A syndrome caused by mutations in the Shox gene that results in mesomelia and brachydactyly. 636t

Leucine-rich repeat-containing protein-coupled receptor 8 (Lgr8). A G-protein-coupled receptor. It is a target of Insl3, and mutations lead to cryptorchidism in mice. 529b–530b

Levator veli palatini muscles. Muscles originating in the fourth and sixth arches that function in vocalization and swallowing. 559

Leydig cells. Male endocrine cells that differentiate from mesonephric mesenchymal cells recruited by pre-Sertoli cells, which produce testosterone. 479b, 510, 510b–511b

Lhx4. A Lim homeodomain factor (previously known as Gsh4) involved in the control of lung growth, differentiation, and branching. 327b

Lhx9 (Lim homeobox protein-9). A homeobox protein required for the early formation of the indifferent gonad. 505b

Lif. A cytokine involved in blastocyst adhesion. 55b

Ligamentum arteriosum. A ligament that attaches the pulmonary trunk to the aorta, which is formed after the closure of the ductus arteriosus. 405

Lim1. A nephric marker required for metanephric kidney development. 486b

Limb buds. Four lateral swellings appearing in vertebrate embryos, which develop into the two pairs of limbs.* 617b, 621b, 622f, 626, 627f, 628, 628f, 640-643, 640f-642f

Limb musculature. Two areas of limb tissue: upper limb musculature, formed when cells from cervical and thoracic somites invade the upper limb buds, and lower limb musculature, formed when cells from lumbar somites invade the lower limb buds. 234

Limb-body wall complex (LBWC). A syndrome characterized by limb defects and anterior body wall defects such as omphalocele or gastroschisis, and sometimes craniofacial defects, exencephaly, or encephalocele. It has a complex etiology and in some cases may result from rupture of the amnion and constriction of the limbs by fibrous amniotic bands. 107b

Limiting membranes. Membranes that cover the two surfaces of the neural retina. The external limiting membrane is interposed between the pigmented epithelium and the proliferative zone of the neural retina; the internal limiting membrane seals off the inner surface of the retina. 607, 608f

Lines of Blaschko. A developmental pattern of skin growth seen in functional X-chromosome mosaicism,* originally described in 1901 by the German dermatologist Alfred Blaschko. 198b

Lingual nerve. A branch of the mandibular nerve (cranial nerve V3) that supplies the general sensory receptors on the anterior two thirds of the tongue. 575

Lip(s), cleft. A congenital fissure of the lip, which usually results from failure of the axillary prominence to fuse with the intermaxillary process. 114f, 134b, 134f, 569b–571b, 571f, 572f

Lis1. A gene that maps to chromosome 17p13 and encodes a protein that functions as a regulatory subunit of Platelet-activating factor acetylhydrolase. It has been linked to lissencephaly and subcortical band heterotopia. 287b, 291b

Lisch nodules. Nodules on the iris, which can be a clue to the diagnosis of neurofibromatosis-type 1. 614b

Lissencephaly. A condition that results from incomplete neuronal migration to the cerebral cortex during the 3rd and 4th months of gestation. Brains of individuals with this condition exhibit pachygyria, agyria, and neuronal heterotopia. Enlarged ventricles and malformations of the corpus callosum are also common. Affected newborns often appear normal but sometimes have apnea, poor feeding, or abnormal muscle tone. They later develop seizures, profound mental retardation, and mild spastic quadriplegia. 287b

Liver. The large gland located in the upper right portion of the abdomen, just beneath the diaphragm. Among the many functions of the liver are storage and filtration of blood; secretion of bile; conversion of sugars into glycogen; synthesis and breakdown of fats, with temporary storage of fatty acids; and synthesis of serum proteins such as certain alpha and beta globulins, albumin, fibrinogen, and prothrombin.* 389, 435b, 446, 448, 448f, 455

Liver sinusoids. A dense network of anastomosing venous spaces that arise from the vitelline venous system. 419

Liver transplants, fetal. A procedure used to treat fetuses diagnosed with diseases that severely cripple the white blood cells of the immune system or thalassemia. Cells from the fetal liver obtained from normal aborted fetuses are infused via an ultrasound-guided needle into the umbilical vein of the affected fetus. These cells successfully colonize the liver of the developing fetus and proceed to manufacture the missing protein, alleviating the disease. 189

Lmx1b. A homeobox gene expressed in the dorsal mesenchyme. Its expression is involved in the transcriptional regulation of Collagen type α3(IV), Collagen type α4(IV), and Nphs2. Mutations in Lmx1b are responsible for nail-patella syndrome. 495b, 636t

Long bones. Bones whose length far exceeds their breadth and thickness.* Most of the endochondral bones of the limb are long bones. 234, 235f–237f, 236–241

Long QT syndrome. An autosomal dominant syndrome characterized by prolongation of the depolarization (Q) and repolarization (T) intervals diagnosed by electrocardiogram. It predisposes affected individuals to syncope and sudden death. Underlying genetic disruptions include mutations in Kvlqt1, Herg, Scn5a, and other genes that encode cardiac ion channels. 383b, 597b

Loop-tail. A mouse mutant that exhibits convergent extension defects. Loop-tail mice have a mutation in the ortholog of the Strabismus/Van Gogh gene, which encodes a transmembrane protein that interacts with Dishevelled in the cytoplasm. 111b

Loricrin. An envelope protein produced by cells in the stratum granulosum that lines the inner surface of the plasma membrane. 200

Louise Brown. The world's first "test-tube" baby, resulting from the first successful case of in vitro fertilization in 1978.

LoxP sites. Sequences placed to flank a gene of interest in transgenic mice. Used to conditionally excise a gene (knock out) when the mice are bred to other mice expressing *Cre* recombinase (*Cre*). 149–150

Lrd. Left-right dynein. A dynein gene that seems to encode an axonemal dynein and occupies a high-level position in the genetic hierarchy of left-right development. 75b, 77f

Lrp5. A Wnt coreceptor that controls osteoblast proliferation, differentiation, and survival. Mutations result in either an increase or a decrease in bone mass. 241b

Lumbar region. The region of the back lying lateral to the lumbar vertebrae.* 411, 412f

Lumbosacral plexus. A lower limb network formed by motor axons at the base of the limb bud. 640

Lunatic fringe. One of three Glycosyltransferases that regulate Notch signaling. 159, 231b

Lung buds. The rudiments of the two lungs and the right and left primary bronchi, formed by the bifurcation of the respiratory diverticulum. 319b, 321

Lung lobes. The subdivisions of the lungs, three lobes in the right lung and two in the left lung, that arise from the secondary bronchial buds. 321

Luteal cells. Cells of the corpus luteum that differentiate from follicle cells and secrete progesterone. 37, 38f, 39

Lymph sacs. Enlargements of the thoracic duct that collect fluid from the lymphatics of the limbs and trunk. 425, 426f

Lymphatic system. The lymphatic vessels and lymphoid tissues considered collectively.* 425, 426f–427f, 428, 428b, 428t

Lymphedema, hereditary. A major hereditary congenital disorder of the lymphatic system caused by hypoplasia of the lymphatic system. 428b

Lymphoid progenitor cells. B and T lymphocytes, generated by hematopoietic stem cells in the liver. 390b

Lyve1. A lymphatic specific Hyaluronan receptor. 428b, 428f

M

Macrophages. Any of the large, mononuclear, highly phagocytic cells derived from monocytes, occurring in the walls of blood vessels and in loose connective tissue; components of the reticuloendothelial system. Macrophages are usually immobile but become actively mobile when stimulated by inflammation. Their functions include phagocytosis and pinocytosis; presentation of antigens to T and B lymphocytes; and secretion of a variety of products, including enzymes, several complement components and coagulation factors, some prostaglandins and leukotrienes, and several regulatory molecules.* 307b, 388, 611

Macrophage colony stimulating factor. A factor expressed by osteoblasts that promotes the proliferation and survival of osteoclast precursors and upregulates the expression of Rank. 238b

Macrotia. A large auricle. 601b, 601f, 602b

Maculae. Areas of the saccule and utricle responsible for detecting gravity and linear acceleration. 592

MafA (Musculoaponeurotic fibrosarcoma oncogene homolog A). A transcription factor that may be involved in beta cell specification in the pancreas. 454b

MafB. A gene that mediates glomerular Nephrin and Podocin expression levels and is required for normal podocyte development in mice. 495b

Magnetic resonance imaging (MRI). A noninvasive nuclear procedure for imaging tissues of high fat and water content that cannot be seen with other radiologic techniques. The MRI image gives information about the chemical makeup of tissues, thus making it possible to distinguish normal, cancerous, atherosclerotic, and traumatized tissue masses in the image.* 393b, 394f

Male meiosis inhibitor. A diffusible signaling factor produced by Sertoli cells that inhibits meiosis in males. 21b

Malformations. Structural birth defects involving perturbation of developmental events directly involved in forming a particular structure. 133b, 135.

Malleus. One of the auditory ossicles in the tympanic cavity of the middle ear, formed from the proximal part of Meckel's cartilage. 543b, 553, 554f, 583b, 588, 598

Mammary glands. The milk-producing glands that develop in females and function to provide nutrition and a source of immunity for breastfeeding infants. 193b, 202, 208–209, 209f, 209b–210b

Mammary pit. A small superficial depression onto which the lactiferous ducts of the mammary glands open. It is usually converted to an everted nipple within a few weeks after birth. 209, 209f

Mammary ridges. A pair of epidermal thickenings that develop along either side of the body from the area of the future axilla to the future inguinal region and medial thigh. In humans, they normally disappear except at the site of the breasts, where they produce the primary bud of the mammary gland. 208, 209f

Mandibular condyle. The posterior process on the ramus of the mandible that articulates with the mandibular fossa of the temporal bone.* 554

Mandibular prominences. Swellings associated with the first pharyngeal arch that give rise to the lower jaw. 543b, 553, 563

Mandibulofacial dysostosis. A group of syndromes involving generalized underdevelopment of the first pharyngeal arches, resulting in defects of the eye, ear, midface, palate, and jaw. 580b

Manic fringe. One of three Glycosyltransferases that regulate Notch signaling in mammals. 159

Mantle zone. The precursor of gray matter, established when neurons from the ventricular zone migrate peripherally. 247b

Manubrium. One of the definitive bones of the sternum. 227

Map kinase. Also called Erk. One of three kinases that are sequentially phosphorylated in an Erk/Mapk cascade. Once map kinase is phosphorylated, it translocates to the nucleus to phosphorylate and activate transcription factors. 158

Mapk kinase (Mapkk; Mek). One of three kinases that are sequentially phosphorylated in an Erk/Mapk cascade. 158

Mapk kinase kinase (Mapkkk; Raf). One of three kinases that are sequentially phosphorylated in an Erk/Mapk cascade. 158

Marginal zone. The future white matter, established by axons extending from mantle layer neurons. 247b

Marinesco-Sjogren syndrome. An autosomal recessive cerebellar ataxia syndrome. 269b

Mash. A proneural gene. Mash is the mammalian ortholog of Drosophila Archeate-Scute genes. 302b

Mash1. A basic helix-loop-helix transcription factor required for forming enteric neurons containing Serotonin and Nitric oxide synthase. Mash1 is a member of the Notch pathway. 328b, 472b

Masseter muscle. One of the muscles of mastication, formed by paraxial mesoderm in the first pharyngeal arch. 559

Master control genes. The encoded amino acid homeodomain proteins, which function as transcription factors that regulate the activity of many "downstream" genes. 152

Mastoid air cells. Air cells in the mastoid portion of the temporal bone that form at around 2 years of age. 600

Mastoid antrum. An air space in the mastoid portion of the temporal bone communicating with the middle ear and the mastoid cells.* 600

Maternal diabetes. A condition existing in two forms, preexisting and gestational. Approximately 1 in 200 women of childbearing age have diabetes before pregnancy (preexisting diabetes); these women are three to four times more likely to have a child with a major birth defect than are nondiabetic women. Another 2% to 5% of women develop diabetes during pregnancy (gestational diabetes); these women usually do not have an increased frequency of children with birth defects. In either case, poorly managed diabetes increases the chances of delivering a very large baby (greater than 10 pounds), which increases the risk of obesity and development of diabetes in the child. 178

Maternal effect genes. Genes expressed before fertilization that encode signals to establish the axes of the embryo in Drosophila. 19b, 151, 152f

Maternal recognition of pregnancy. The response to an implanted embryo in which cells of the trophoblast produce human chorionic gonadotropin, which supports the corpus luteum and thus maintains the supply of progesterone. 44

Maternal serum alpha-fetoprotein (MSAFP). A screening test to detect elevated levels of alpha-fetoprotein in maternal serum after 12 weeks of gestation, an indication of neural tube defects. 114b, 180, 182

Maternal serum screening. A diagnostic technique that measures maternal serum alpha-fetoprotein, human chorionic gonadotropin, estriol, and (optionally) Inhibin-A. The levels of these serum components can suggest the presence of Down syndrome or a birth defect such as a neural tube defect. 180, 182

Math. A vertebrate proneural gene, expression of which is both sufficient and necessary for the formation of neurons. Math is a mammalian ortholog of the Drosophila Atonal gene. 302b

Math1. A basic helix-loop-helix transcription factor repressed by Hes1, essential for hair cell development. 465b, 466f, 593b, 595f

Matrix metalloproteinases. Proteases that play a major role in promoting proliferation and migration of endothelial cells by activating growth factors and receptors and increasing extracellular matrix turnover. 397b

Matrix metalloproteinase-type 2 (MMp2). An extracellular protease that degrades several basement membrane components and releases bioactive peptides and growth factors from the extracellular matrix. 509b

Maturation wavefront. The threshold-level point in the presomitic mesoderm. 91b

Mature intermediate villi. Slender side branches formed by tertiary stem villi that produce secondary villi. 171

Maxillary arteries. Arteries that originate in the external carotid artery and distribute to the jaws, teeth, muscles of mastication, ear, meninges, nose, paranasal sinuses, and palate.* 403, 405f

Maxillary prominences. Swellings associated with the first pharyngeal arch that give rise to part of the upper jaw. 543b, 553, 554f, 563

Maxillary sinuses. Hollow spaces that form during the 3rd fetal month as invaginations of the nasal sac that slowly expand within the maxillary bones. 571

Meatal plug. A solid core of tissue that completely fills the medial end of the external auditory meatus by week 26. Canalization of this plug begins almost immediately and produces the medial two thirds of the definitive meatus. 583b, 600

Mechanosensory model, of left-right development. A variation on the nodal flow model in which it is proposed that motile cilia drive the nodal fluid flow, which in turn activates a calcium flux on the left side of the node, rather than transporting a morphogen. 75b, 76f

Meckel's cartilage. The central cartilage of the mandibular prominence. Most of this cartilage eventually disappears, either being resorbed or becoming encapsulated by the developing mandibular bone. However, the proximal part forms the malleus, sphenomandibular ligament, and anterior ligament of the malleus. 543b, 553, 554f

Meckel's diverticulum. A remnant of the vitelline duct, of variable length and location. Most often, it is observed as a 1- to 5-cm intestinal diverticulum projecting from the antimesenteric wall of the ileum within 100 cm of the cecum. In other instances, part of the vitelline duct within the abdominal wall persists, forming an open omphalomesenteric fistula, omphalomesenteric cyst, or omphalomesenteric ligament connecting the small bowel to the umbilicus. 458b, 461b, 462f

Medial-lateral axis. One of the three major axes, which runs from the midline of the body toward the right and left sides, with the midline being the most medial level and the right and left sides being the most lateral levels. 7, 11, 71

Median artery. One of the arteries of the upper limb, which develops partly as a sprout of the axis artery. 411, 413f

Median sulcus. A groove on the anterior two thirds of the tongue that marks the line of fusion between the right and left distal tongue buds. 574

Medulla oblongata. The portion of the brain most similar to the spinal cord, which houses cranial nerve nuclei and serves as a relay center between the spinal cord and the higher brain centers. It also contains centers and nerve networks that regulate respiration, heartbeat, reflex movements, and other functions. 247b, 263

Medullary cord. A solid mass formed by the condensation of central tail bud cells during secondary neurulation. Subsequently, it undergoes cavitation to form a lumen. 117, 117b, 119

Megacystis. A dilated bladder. 169b

Megakaryocytes. Giant cells of bone marrow, with a greatly lobulated nucleus. They are generally supposed to give rise to platelets.* 388

Meiosis. A sequence of two specialized cell divisions by which the number of chromosomes in the gametes is halved. Meiosis produces haploid cells and allows shuffling of genetic information to occur, increasing genetic diversity. 15b, 21, 22f, 23t, 24f, 24–25, 40f, 41f

Meissner's plexus. The inner layer of the enteric nervous system, between the submucosa and smooth muscle layer. 467

Mek (Mapk kinase). One of three kinases that are sequentially phosphorylated in an Erk/Mapk cascade. 158

Melanin. A factor normally expressed by chiasm cells that influences the choice of axonal pathway at the chiasm. 279b

Melanocytes. Pigment cells. 193b, 200–201, 200f, 639

Melanoma. A highly malignant type of skin cancer. 201

Melnick-Frasier syndrome. Also called branchio-oto-renal (BOR) syndrome. A single-gene disorder recognizable by cup-shaped ears, preauricular pits, and small cysts over the sternocleidomastoid muscle. 494b, 586b, 587f, 602b

Membrana granulosa. The layer of follicle cells that lines the antral cavity and underlies the basement membrane of the follicle. 29, 30f

Membrane bone. A type of bone that develops by intramembranous ossification directly from the mesenchyme. It typifies the majority of the bones of the face and skull. 219, 234, 543b, 545, 546f

Menarche. Puberty in females. 28

Meningocele. An open neural tube defect in which neural tube membranes protrude from the vertebral canal, forming a fluid-filled sac. 113b, 116f

Menisci. The crescent-shaped disks of fibrocartilage in the knee joint.* 237

Menopause. The time at which a female's monthly menstrual cycles cease, usually at approximately 50 years of age. 28

Menstrual cycle. A 28-day cycle that results in the monthly production of a female gamete and a uterus primed to receive a fertilized embryo. 28, 29f, 37, 39

Menstrual phase, of menstrual cycle. A 4- to 5-day phase of the menstrual cycle during which the endometrium is sloughed, along with about 35 mL of blood and the unfertilized oocyte. By convention, it is considered the start of the next cycle. 39

Meox2. A homeobox gene needed for the development of the appropriate number of myogenic cells in the limb. 244b

Merkel cells. Pressure-detecting mechanoreceptors lying at the base of the epidermis, which are associated with underlying nerve endings in the dermis. They arise from neural crest cells and contain keratin and form desmosomes with adjacent keratinocytes. 193b, 200

Meromelia. A disorder resulting in the absence of part of a limb. 632b, 633f, 634t

Mesangial cells. Essential pericytes of the glomerular capillaries. 494b

Mesencephalic flexure. The sharp flexure separating the prosencephalon and mesencephalon. 119, 247b, 255

Mesencephalic trigeminal nucleus. A portion of the sensory nucleus of the trigeminal nerve (V) located in the mesecephalon. 270, 271f

Mesencephalon. The midbrain, one of the three primary brain vesicles. 119, 247b, 251, 252f, 259t, 270, 271f, 272f

Mesenchymal cells. The pluripotent cells that constitute the mesenchyme.* 377

Mesenchymal core. The central part of each pharyngeal arch, lined on the outside with ectoderm and on the inside with endoderm. 617b

Mesenchyme. The meshwork of embryonic connective tissue in the mesoderm, from which are formed the connective tissues of the body as well as the blood vessels and lymph vessels.* 78, 79f

Mesenchymal villi. Terminal protrusions that originate as sprouts of syncytiotrophoblast, similar in cross section to primary stem villi. 171

Mesenteric arteries. Vitelline artery derivatives that vascularize the abdominal gut. 409f, 410, 435b, 442

Mesenteric ganglia, inferior. Ganglia whose fibers innervate the hindgut, including the distal one third of the transverse colon, the descending and sigmoid colons, and the upper two thirds of the anorectal canal. 311

Mesenteric ganglia, superior. Ganglia whose fibers innervate the midgut, the ascending colon, and about two thirds of the transverse colon. 311

Mesenteric trunk, superior. An artery that supplies the midgut. 442

Mesenteric veins. Veins that develop from the vitelline vein. The inferior mesenteric vein drains the hindgut. 419, 420f

Mesentery. A membranous fold attaching an organ to the body wall.* 439–441, 440f, 441f, 454–455, 455f

Mesocardium, dorsal. The dorsal mesentery of the heart, formed by splanchnic mesoderm located beneath the foregut. It initially suspends the primitive heart tube in the developing pericardial cavity, then ruptures, leaving the heart suspended by its attached vasculature. 346, 358

Mesoderm. The middle of the three primary germ layers. 51b, 57, 69b, 78, 80f, 81b, 82f, 83b, 85, 87–88, 88b, 88f, 89f, 92, 101b, 106, 219, 220, 222, 479b, 483, 483f, 621b

Mesogastrium. The portion of the dorsal mesentery that suspends the stomach. 435b, 445

Mesomelia. A disorder resulting in a shortened zeugopod (comprising the radius and ulna and the tibia and fibula). 634t

Mesonephric ducts. Small passages generated by the epithelialization of some of the intermediate mesoderm along the fifth to seventh cervical axial levels that induces mesonephros formation. In females, the ducts regress. However, in males they persist, forming important elements of the male genital duct system. 479b, 483, 484f, 485f, 485–486

Mesonephric tubules. Tubular structures comprising the mesonephros, or temporary kidney, of amniotes.* They are produced in craniocaudal succession from mesenchyme in the caudal intermediate mesoderm. 483, 485, 485f, 511

Mesonephros. The embryonic kidneys. 479b, 485–486, 486b

Mesp1/Mesp2. Members of the basic helix-loop-helix family of transcription factors that are expressed transiently during the primitive streak stage and are required for migration of the cardiac progenitor cells into the cranial region of the embryo. 339

Metalloproteinases. Proteases that play major roles in promoting proliferation and migration of endothelial cells by activating growth factors and receptors and increasing extracellular matrix turnover. 55b, 397b, 509b

Metanephric blastema. A portion of the sacral intermediate mesoderm penetrated by the ureteric buds. 485f, 486

Metanephric excretory unit. The definitive nephron with its renal corpuscle. 489

Metanephros. The definitive kidneys. 479b, 486t, 486–489, 487f–489f, 490b–493b

Metaphase. The phase of cell division in which the chromosomes align along the equator. In mitosis, the centromeres replicate; in meiosis, they do not. 22f, 23t, 24

Metaphysis. The growing end of the diaphysis. 235

Metencephalon. The cranial division of the rhombencephalon, consisting of rhombomeres 1 and 2. It gives rise to the pons and cerebellum. 247b, 251, 252f, 259t

Methylation. The postsynthetic addition of methyl groups to specific sites on DNA molecules. The reaction is catalyzed by enzymes called DNA methyltransferases that are specific for nucleotide and position of methylation. Methylation is involved in gene expression, and plays a role in a variety of epigenetic mechanisms, including development, X chromosome inactivation, genomic imprinting, mutability of DNA, and uncontrolled cell growth in cancer.* 65b

***N*-Methyl-*D*-aspartate (NMDA) receptor**. A receptor required for matching coactive retinal inputs to the tectum/superior colliculus. 282b

Methylmalonic acidemia. A deficiency in fetal enzymes, often vitamin B12, which results in increased methylmalonic acid excretion in maternal urine. Treatment involves maternal intravenous administration of cyanocobalamin. 188–189

Mhc1a. Atrial myosin heavy chain-1, a myosin heavy chain selectively expressed within atrial cells of the chick embryo heart. Following formation of the primitive heart chambers, its expression becomes restricted to the primitive atrium. 354b–355b, 356f

Mhc1v. Ventricular myosin heavy chain-1, a myosin heavy chain initially expressed by all cells of the differentiating cardiogenic mesoderm. Its expression is eventually restricted to the presumptive ventricles of the developing heart. 355b, 356f

Microangiography. The radiologic visualization of an injected contrast medium, used to study blood vessel formation and patterning. 392b–393b, 394f

Microcephaly. Small head. 290f, 290b–291b

Microfilaments. Any of the submicroscopic filaments, composed chiefly of actin, found in the cytoplasmic matrix of almost all cells, often in close association with the microtubules.* 160–161

Micrognathia. Small jaw. 571, 581b

Microphthalmia. Small eyes. 602b, 613b

Microsurgical epididymal sperm aspiration (MESA). A technique used to remove sperm from the epididymis of males with cystic fibrosis for use in vitro fertilization. 48b

Microtia. Small auricle. 601b, 601f, 602b

Microvilli. Minute processes or protrusions from the free surfaces cells, found especially in the proximal convolution of renal tubules and the intestinal epithelium.* 55b

Midbrain. Also called mesencephalon. One of the three primary brain vesicles. 94, 101b, 117, 251

Midgut. One of three subdivisions of the primitive gut. At first, it remains broadly open to the yolk sac. However, as the gut tube forms, the neck of the yolk sac is gradually constricted, reducing its communication with the midgut. 69b, 74b, 101b, 104f, 106, 311, 408, 409f, 435b, 439, 456–461, 456b, 457f, 458b, 458f, 459f, 460f, 461b, 462f

Midpiece, of spermatozoon. The middle part of the spermatozoon, which contains large, helical mitochondria and generates energy for swimming. 25, 27f

Migration. The active displacement of cells from one region of an embryo to another. 80b–81b

Migration staging area. An area between the somite, surface ectoderm, and neural tube where migration of neural crest cells begins. 122b

Milroy disease. A primary lymphedema syndrome linked to mutations in the Vegfr3 gene. 428b

Mind bomb zebrafish mutant. A mutant with defective Notch signaling, in which all prosensory cells differentiate as hair cells. There is a total absence of supporting cells. 593b

Mirror symmetry. Having right and left sides that are identical mirror images of each other, as opposed to handed asymmetry, in which there are anatomic differences on the left and right sides. 73b

Mitf. A transcription factor required for pigmented epithelium specification and differentiation in vertebrates. 608b, 609f, 610b

Mitochondria. Small, round or oval, membrane-bounded cytoplasmic organelles, the principal sites of synthesis of adenosine triphosphate (ATP). Mitochondria also contain enzymes of the citric acid cycle and ones for fatty acid oxidation, oxidative phosphorylation, and other biochemical pathways. They also contain DNA, RNA, and ribosomes, and replicate independently, synthesizing some of their own proteins. 597b

Mitosis. The process of normal cell division, in which a diploid, 2N cell replicates its DNA (becoming diploid, 4N) and undergoes a single division to yield two diploid, 2N daughter cells. 21, 22f, 23t

Mitral valve. Also called the bicuspid valve. The left atrioventricular valve, which has only anterior and posterior leaflets. 337b, 370

Mixer. A paired homeobox-containing transcription factor involved in endoderm formation. 56b, 57b

Moderator band. Also called a septomarginal trabecula. The prominent trabecula that forms the boundary between the trabeculated primary fold and the inlet septum. It connects the muscular septum with the forming anterior papillary muscle attached to the right atrioventricular valve. 368f, 368–369

Molecular layer, of cerebellar cortex. The outermost layer of the cortex, formed by basket and stellate cells from the ventricular layer. 267

Mondini dysplasia. A birth anomaly in which the coiled cochlea has fewer turns than the normal. 597b

Monilethrix. A condition caused by mutation in Krthb6 and Krthb1, in which the hair is “beaded” and fragile, and thus easily lost. 207b

Monocilium. A single cilium contained in each cell of the organizer. They have been identified in several species, but whether they are contained in the primitive node of humans is unknown. 74b, 75f

Monosomy. The absence of a specific chromosome in a gamete that combines with a normal gamete to form a zygote, so called because the zygote contains only one copy of the chromosome rather than the normal two. 32b, 34b

Monosomy 21. A condition resulting from the fusion of a gamete lacking chromosome 21 with a normal gamete. This is invariably fatal during early embryonic development. 32b, 34f

Morphogen(s). A diffusible protein that affects tissue development based on its concentration. 74b, 81b, 112b, 161, 253b, 628b

Morphogenesis. The generation of form. 133b, 133–162, 136f, 137f, 138f, 139f, 140f, 141f, 142f, 143f, 144f, 146f, 147f, 152f, 153f, 154f

Morphogenetic movements. Four types of coordinated group movements that cells undergo during gastrulation: epiboly, emboly, convergence, and extension. Morphogenetic movements are each generated by a combination of changes in cell behaviors, including changes in cell shape, size, position, and number. 80b

Morpholinos. Stabilized antisense RNA, which can be injected into cells to knock down gene expression. 150

Morula. The second of three stages of development during the period of the egg, formed after the zygote cleaves by mitosis, giving rise to a cluster of blastomeres. 15b, 41, 43, 47b, 48f

Mosaicism. The presence in an individual of two or more cell lines derived from a single zygote that are karyotypically or genotypically distinct.* 32b, 67b

Motoneurons. Efferent neurons that convey motor impulses from the center to cause body parts to move.* 247b, 257

Motor columns. Cell columns (somatic and visceral) that form in the ventral plates. 247b

Mrf4. A myogenic regulatory factor expressed during striated muscle development. 221b

Muenke syndrome. A syndrome in which mutations in Fgf are associated with craniosynostosis. 239b, 550b

Müller glia. Non-neuronal cells produced by the inner neuroblastic layer of the neural retina. 607

Müllerian ducts. Also known as paramesonephric ducts. The paired embryonic ducts arising as a peritoneal pocket, extending caudally to join the urogenital sinus. In females they develop into the fallopian tubes, uterus, and superior vagina; in males they degenerate, leaving vestigial structures, such as the appendix testis and utriculus prostaticus.* 479b, 500, 501f, 502

Müllerian-inhibiting substance (Mis). Also called anti-Müllerian hormone (Amh). A member of the Tgfβ family expressed specifically by Sertoli cells, beginning in humans at about week 8, that causes the Müllerian ducts to regress in males. 509, 509b, 510f

Multifactorial abnormalities. Anomalies that stem from interaction of environmental or outside influences with a poorly defined constellation of the individual's own genetic determinants. 378b

Multiple synostoses syndrome, type I. A syndrome caused by mutations in Noggin and characterized by fusion of the limb joints and craniofacial anomalies that are typified by conductive hearing loss and a broad nose. It can also involve synostoses of the vertebrae. 240b

Murine vasa homolog (Mvh). One of three newly identified germ cell-specific genes expressed shortly after primordial germ cells enter the genital ridge. 20b

Murmur. An auscultatory sound, benign or pathologic, loud or soft, particularly a periodic sound of short duration of cardiac or vascular origin.* 379b

Muscle cells. Any contractile cells peculiar to muscle. Smooth muscle cells are elongated spindle-shaped cells containing a single nucleus and longitudinally arranged myofibrils.* 244b

Muscle fibers. Any of the cells of skeletal or cardiac muscle tissue. Skeletal muscle fibers are cylindrical multinucleate cells containing contracting myofibrils, across which run transverse striations. Cardiac muscle fibers have one or sometimes two nuclei, contain myofibrils, and are separated from one another by an intercalated disk. Although striated, cardiac muscle fibers branch to form an interlacing network.* 244b

Muscle regulatory factors (MRFs). Also called myogenic regulatory factors. Basic helix-loop-helix transcription factors expressed during striated muscle development. 221b

Muscles of facial expression. The orbicularis oculi, orbicularis oris, risorius, platysma, auricularis, frontalis, and buccinator. Head mesoderm in the second arch gives rise to the muscles of facial expression. 543b, 555t, 557f, 559

Muscles of mastication. The temporalis, masseter, and medial and lateral pterygoid muscles, which arise from head mesoderm in the first pharyngeal arch. 559

Muscular dystrophy. A muscular abnormality in which functional muscle mass is either not maintained or the satellite cells are defective. 244b

Musculoaponeurotic fibrosarcoma oncogene homolog A (MafA). A transcription factor that may be involved in beta cell specification. 454b

Musculoskeletal system. The system of skeletal muscle and bone. 217–244, 221b, 221f, 222b, 223f, 224, 225f–228f, 226b, 227b, 229b, 230b–231b, 230f–232f, 233b, 233f, 234b, 235f–237f, 237b–238b, 238f, 239f, 239b–241b, 240f, 241f, 242t, 242b, 243f, 244b

Myelencephalon. The caudal division of the rhombencephalon, consisting of rhombomeres 3 to 8, that differentiates to form the medulla oblongata. 247b, 251, 252f, 259t

Myelin. The lipid substance forming a sheath (the myelin sheath) around the axons of certain nerve fibers. It is an electrical insulator that serves to speed the conduction of nerve impulses in these nerve fibers.* 308b

Myeloid progenitor cells. Cells generated by hematopoietic stem cells in the liver that acquire myeloid cell-generating capacity. 390b

Myelomeningocele. A type of spina bifida in which the neural tube and its surrounding membranes protrude from the vertebral canal, forming a fluid-filled sac. 113b, 115f, 115b, 186

Myeloschisis. Also called spina bifida aperta. A condition in which the spinal cord is open to the body surface. 113b

Myenteric ganglia. Some of the ganglia of the enteric nervous system, which connect to the myenteric plexus. 470b

Myenteric plexus. A nerve plexus situated in the muscular layers of the intestines.* 470b

Myf5. A basic helix-loop-helix transcription factor, one of the myogenic regulatory factors involved in striated muscle development. 221b, 234b, 244b

Mylohyoid muscle. Muscle that elevates the hyoid bone and supports the floor of the mouth,* which is formed by paraxial mesoderm in the first pharyngeal arch. 559

Myoblasts. The myogenic cells, which proliferate and then exit the cell cycle and terminally differentiate to form myocytes. 217b, 219

Myocardialization. A process in which myocardial cell projections extend into the conal cushions, where it is thought that many of the cushion cells undergo apoptosis. This process also leads to a thinning of the inner curvature. 367, 367f

Myocardium. The heart muscle, derived from a mass of splanchnic mesoderm that encloses the endocardial heart tube. 342, 369b, 369f

Myocytes. Terminally differentiated postmitotic cells formed from myoblasts that express Actin, Myosin, and other contractile proteins and fuse to form myofibrils. 217b, 219, 221b, 244b

MyoD. A basic helix-loop-helix transcription factor, one of the myogenic regulatory factors involved in striated muscle development. 221b, 234b, 235f

Myoepithelial cells. Modified smooth muscle cells, contractile in nature, believed to be of ectodermal origin. They are located around the secretory units of certain glands (salivary, mammary, sweat, and lacrimal glands) between the gland cells and basement membrane, having long dendritic interweaving cytoplasmic processes, and containing myofilaments. It is assumed that contraction of these cells functions to help express secretion from the gland.* 208, 479b

Myofibers. Multinucleated syncytia containing the contractile myofibrils, formed by fusion of the myocytes. 219

Myofibrils. Contractile fibrils contained within the myofibers. 219

Myogenesis. Striated muscle development. Primary myogenesis occurs during the stage of the embryo; secondary myogenesis occurs during the stage of the fetus. 219–220

Myogenic regulatory factors (MRFs). Also called muscle regulatory factors. Basic helix-loop-helix transcription factors expressed during striated muscle development. 221b

Myogenin. A basic helix-loop-helix transcription factor, one of the myogenic regulatory factors involved in the development of striated muscle. 221b

Myosin heavy chain(s) (Myhc). Contractile proteins involved in the formation of myocytes. 221b, 244b

Myostatin. Also known as Gdf8. A member of the Tgfβ family and a negative regulator of muscle differentiation. Mutations in humans are linked to increased muscle strength. 234b

Myotomes. One of three kinds of mesodermal primordia subdivided from somites. Myotomes develop into the segmental musculature of the back and ventrolateral body wall, and give rise to cells that migrate into the limb buds to form the limb musculature. 101b, 128, 217b, 231, 233f, 234

N

N number. The number of copies of each unique double-stranded DNA molecule in the nucleus. 21

Nail. A hardened or horny cutaneous plate overlying the dorsal surface of the distal end of a finger or toe. It is a part of the outer layer of the skin and is composed of hard tissue formed of keratin.* 210, 211f

Nail field. A shallow depression formed by the nail anlage. It is surrounded laterally and proximally by the nail folds. 210

Nail folds. Ectodermal folds that laterally and proximally surround the nail field. 193b, 210, 211f

Nail plate. A horny plate made of compressed keratinocytes, formed by the stratum germinativum of the proximal nail fold. 210, 211f

Nail-patella syndrome. A syndrome caused by mutations in the Lmx1b gene, characterized by skeletal anomalies and glomerular dysfunction. 495b, 630b, 636t

Nail-tooth dysplasia. A condition caused by mutations in Msx1in which the nails and teeth are dysplastic. 203b

Nanog. A homeobox-containing transcription factor expressed uniformly throughout all blastomeres. The first overt differentiation event that occurs in the morula requires Nanog expression to be maintained in the inner cell mass, but turned off in the trophoblast. 43b

Nanos. An mRNA involved in germ line determination. 19b

Nasal cavity. The proximal portion of the passages of the respiratory system, extending from the nares to the pharynx. It is divided into left and right halves by the nasal septum and is separated from the oral cavity by the hard palate.* 568, 569f

Nasal discs. Also called nasal or olfactory placodes, or nasal plates. A pair of ectodermal thickenings that form on the frontonasal prominence. 563

Nasal fin. A thickened, platelike fin of ectoderm separating the nasal sac from the oral cavity, formed by the proliferation of the floor and posterior wall of the nasal sac. 568, 569f

Nasal passages. Two channels, formed by the division of the nasal cavity by the nasal septum, which open into the pharynx behind the secondary palate through the definitive choana. 569

Nasal pits. Oval depressions formed by invagination of the ectoderm at the center of each nasal placode. 563

Nasal placodes. Also called olfactory placodes, nasal plates, or nasal discs. A pair of ectodermal thickenings that form on the frontonasal prominence. 563

Nasal plates. Also called nasal or olfactory placodes, or nasal discs. A pair of ectodermal thickenings that form on the frontonasal prominence. 563

Nasal processes. Divisions, medial and lateral, of the frontonasal prominence. During development, the medial nasal processes merge to generate the bridge of the nose, philtrum, and primary palate; the lateral nasal processes give rise to the side of the nose. 56f, 543b, 545b, 563

Nasal septum. A plate of bone and cartilage covered with mucous membrane that divides the nasal cavity into the nasal passages.* 569

Nasolacrimal duct. A tube formed when the ectoderm at the floor of the nasolacrimal groove invaginates into the underlying mesenchyme. After birth, it functions to drain excess tears from the conjunctiva of the eye into the nasal cavity. 564

Nasolacrimal groove. Also called naso-optic furrow. The groove between the lateral nasal process and the adjacent maxillary prominence. 563–564, 565f

Naso-optic furrow. Also called nasolacrimal groove. The groove between the lateral nasal process and the adjacent maxillary prominence. 563–564, 565f

N-cadherin. A calcium-dependent cell-cell adhesion molecule involved in epithelial-to-mesenchymal transformation. 81b

Nde1. A gene formerly known as mNude and homologous to the Nude gene of *A. nidulans* that directly interacts with Lis1. Genetic ablation of Nde1 function in mice results in microcephaly. 291b

Neocortex. The newer, six-layered portion of the cerebral cortex, showing stratification and organization characteristic of the most highly evolved type of cerebral tissue.* 284–285, 286f

Nephrogenesis. The development of the nephron, the filtration unit of the kidney, which is complete by birth in humans. 489

Nephrons. The definitive urine-forming units of the kidneys, which differentiate from the metanephric blastema. 479b, 486, 487f, 488, 493b, 494b-495b

Nephrotome. Also called intermediate mesoderm. One of the segmented divisions of the embryonic mesoderm connecting the somite with the lateral plates of unsegmented mesoderm; the source of much of the urogenital system.* 78, 479b, 483, 483f

Nerve growth factor (Ngf). A neurotrophin necessary for the survival and differentiation of dorsal root ganglion cells and sympathetic chain ganglion cells. 128b

Nesidioblastosis. Also called congenital hyperinsulinism. A fetal maladaptation frequently seen in neonates born to diabetic mothers in which the islet cells respond to elevated blood glucose levels with compensatory hyperplasia. It can occur locally or diffusely throughout the pancreas and lead to life-threatening decreases in blood glucose levels. 454b

Netrins. A family of guidance molecules that can guide axons during the process of axon pathfinding. 277b, 312b

Neural cell adhesion molecule (N-Cam). A calcium-independent adhesion molecule. 160, 312b, 361b

Neural crest or neural crest cells. Cells that arise from the lateral edges of the neural plate during formation of the neural tube. Near the end of the 4th week, the cells detach from the lateral lips of the neural folds and migrate to numerous locations in the body, where they differentiate to form a wide range of structures and cell types. 10f, 69b, 85, 94, 101b, 107, 110f, 119–128, 217b, 219, 297b

Neural folds. Folds of neuroepithelium and surface ectoderm that form at the lateral edges of the neural plate. As the neural plate bends, they fuse to form the neural tube. 107, 109f, 110b, 119

Neural groove. The depression delimited by the bending neural plate. 107

Neural induction. The process of neural plate formation. 69b, 94, 94b–95b, 96f, 97b

Neural plate. A thickened plate of ectoderm formed by neural induction. During subsequent development, the neural plate will fold up into a neural tube. 69b, 78, 85, 94, 95b, 95f, 96f, 253b, 254f, 255b

Neural tube. A hollow channel covered by surface ectoderm. It is the precursor of the central nervous system, formed by the folding of the neural plate. 69b, 98, 101b, 107, 108f, 109f, 112b, 112f, 113f, 117, 119, 119f, 130b, 253b, 255, 256f, 257

Neural tube defects (NTDs). Malformations that result when neurulation fails to occur normally, such as craniorachischisis, spina bifida, anencephaly, myelomeningocele, and meningocele. 111b–112b, 113f–116f, 113b–117b, 182

Neuregulin. A chemotactic molecule that attracts neural crest cells. It is also expressed in the endocardium during trabecular development. 121b, 369b

Neurenteric canal. An opening at the level of the primitive pit through which the yolk sac cavity transiently communicates with the amniotic cavity. 85, 86f

Neuroblastic layers. Two cellular embryonic retinal layers (inner and outer) formed by the progenitor cells. The inner neuroblastic layer gives rise to the horizontal cells, amacrine cells, bipolar cells, and Müller glia. The rods and cones of the mature neural retina are derived from the outer neuroblastic layer. 607, 608f

Neurocranium. The bones surrounding and protecting the brain and sensory organs. 543b, 547

Neurocristopathies. Defects of neural crest cell development. 128b

Neurocutaneous signature. A hairy tuft, pigmented nevus, angioma, lipoma, or dimple in the lumbosacral region, which may be a sign of an underlying neural tube defect. 116b

NeuroD. A vertebrate proneural gene, expression of which is both sufficient and necessary for the formation of neurons. 302b

NeuroD1. A transcription factor expressed in all endocrine cells of the pancreas after their specification and differentiation. It plays an important role in mediating the expression of differentiated endocrine products of the islet (e.g., insulin), and mutations are associated with maturity-onset diabetes of the young and type II diabetes. 453b–454b

Neuroepithelial cells (neuroectoderm). The cells of the neuroepithelium,* formed as a result of neural induction. 94

Neuroepithelium. Epithelium made up of cells specialized to serve as sensory cells for reception of external stimuli.* 107, 109f, 297b

Neurofibromas. Benign cutaneous tumors containing multiple cell types, including Schwann cells, neurons, fibroblasts, and mast cells. 302b

Neurofibromatosis. One of two autosomal dominant disorders characterized by growth of neurofibromas along various types of nerves, and sometimes on bone, muscle, or skin.* 128b

Neurofibromatosis-type 1. A prevalent familial tumor disposition caused by mutations in neurofibromin (Nf-1). It is a progressive disease with multiple defects, including benign and malignant tumors of the peripheral and central nervous systems. 302b

Neurofibromin (Nf-1). A tumor suppressor gene that inactivates the proto-oncogene Ras. Nf-1 is mutated in neurofibromatosis-type 1. 302b

Neurogenin(s). A vertebrate proneural gene, expression of which is both sufficient and necessary for the formation of neurons. 302b

Neurogenin-3 (Ngn3). A proendocrine transcription factor that, in the absence of Notch signaling, is sufficient to initiate the endocrine pathway in pancreatic epithelium. 452b–453b

Neurohypophysis. The posterior lobe of the pituitary gland. 272, 282

Neurons. Highly specialized cells of the nervous system, having two characteristic properties: irritability (ability to be stimulated) and conductivity (ability to conduct impulses). They are composed of a cell body called the perikaryon, which contains the nucleus and its surrounding cytoplasm, and one or more processes called nerve fibers that extend out from the body.* 112b, 125, 128b, 247b, 255, 257, 264

Neuropilin(s). A family of receptors that Semaphorins signal through, which in turn bind Plexins. Neuropilins are important in targeting cardiac neural crest cells into the pharyngeal arches and outflow tract. 312b, 376b

Neuropores. Openings in the anterior (rostral) or posterior (caudal) ends of the neural tube of the developing embryo; the rostral neuropore is normally closed by 25 to 26 days and the caudal neuropore is usually closed by the end of the 4th week.* 107

Neurotrophin(s). Small growth factors required for the survival and differentiation of peripheral neurons. 128b

Neurulation. The process of neural tube formation, which involves four main events: formation of the neural plate, shaping of the neural plate, bending of the neural plate, and closure of the neural groove. 101b, 107, 108f–110f, 110–117, 110b–112b, 112f, 113f–116f, 113b–117b, 117f, 118f

Neurulation forces. Forces generated by changes in cell behavior involved in neurulation. Forces arising within the neural plate are called intrinsic neurulation forces; those arising outside the neural plate are called extrinsic neurulation forces. 110b

Nevoid basal cell carcinoma syndrome (NBCCS). An autosomal dominant disorder occurring in about 1:50,000 to 1:100,000 individuals who are afflicted with basal cell carcinomas that begin forming early in life. NBCCS patients also have increased susceptibility to other carcinomas such as meningiomas, fibromas, and rhabdomyosarcomas.

Nevus flammeus. A vascular anomaly that presents at birth as a birthmark and grows proportionately with the growth of the child. 399b

Nieuwkoop center. An early-forming organizing center that induces the organizer. 81b, 94b

Nipbl. A gene that encodes a protein called Delangin. Mutations occur in 50% of patients with Cornelia de Lange syndrome. 636t, 638b

Nipple, inverted. The condition in which the nipple remains depressed. 209, 209f

Nitric oxide. NO, a naturally occurring gas that in the body is a short-lived dilator released from vascular epithelial cells in response to the binding of vasodilators to endothelial cell receptors. It causes inhibition of muscular contraction, and thus relaxation. Excesses of nitric

oxide are toxic to cells of the central nervous system and also cause the drop in blood pressure seen in septic shock.* 429

Nitric oxide synthase. An enzyme involved in the generation of nitric oxide. 397b, 429

Nkx2.2. A gene that acts with Ngn3 to promote beta cell specification. 453b

Nkx2.5. Nkx2 transcription factor related, locus 5. An early cardiogenic transcription factor expressed in cardiac progenitor cells. 342b, 349b, 382b

Nkx3.1. A gene expressed in the epithelium, necessary for normal prostatic development. 513b, 514f

Nkx5-1. A homeobox gene expressed in the dorsal otocyst and required for development of the vestibular apparatus. 592b

Nkx6.1. A transcription factor specifically expressed in adult beta-islet cells. 453b

NMDA (*N*-methyl-*D*-aspartate) receptor. A receptor required for matching coactive retinal inputs to the tectum/superior colliculus. 282b

N-myc. A proto-oncogene implicated in the control of lung growth, differentiation, and branching. 327b

Nodal. A member of the Tfgβ family of growth factors necessary for endoderm formation. 56b–57b, 72b, 73b, 81b, 95b, 157, 383b

Nodal flow model, of left-right development. A model in which the leftward movement of fluid across the node generates an asymmetric distribution of an unknown morphogen. The resulting left-right morphogen concentration gradient is believed to break symmetry and initiate left-right development. 74b–75b, 75f

Nodal vesicular parcels (NVPs). Membrane-sheathed vesicles that carry morphogens. 75b, 77f

Nodose ganglion, of nerve X. The inferior ganglion of cranial nerve X, the neurons of which are derived from the third and fourth epipharyngeal placodes. 314, 315f

Noggin. A Bmp inhibitor involved in important events such as neural induction and the establishment of left-right asymmetry. 81b, 95b, 119b, 128b–130b, 157, 206b, 234b, 340b, 340b, 341b, 341f

Noonan syndrome. A syndrome caused by mutations in the Ptpn11 gene in which those affected exhibit pulmonary stenosis and conduction anomalies, as well as overlapping craniofacial and skeletal anomalies. 383b, 416b

Norrie disease. A disease characterized by retinal dysplasia and abnormal vascularization (and sensorineural hearing loss) that arises from mutations in Norrin. 614b

Notch. A signaling pathway. In the presence of a ligand such as Delta, Notch signaling occurs when the ligand produced by the signaling cell binds to a Notch receptor on an adjacent cell. Binding activates a protease that cleaves off a portion of the Notch receptor, which in turn translocates to the nucleus, where it regulates target gene expression in partnership with Hes. 158–159, 159f

Notochord. A cylindrical cord of cells on the dorsal aspect of an embryo, marking its longitudinal axis and serving as the center of development of the axial skeleton.* 69b, 85, 86f, 98, 110b

Notochordal plate. A flattened plate formed by the notochordal process, which later detaches from the endoderm and becomes the notochord. 85, 86f

Notochordal process. A hollow tube extending from the primitive node that eventually forms the notochordal plate. 69b, 78, 85, 86f

Nphs1/Nphs2. Genes that code for Nephrin (Nphs1) or Podocin (Nphs2), mutations in which can lead to defects in glomerular function. 495b

Nrp1/Nrp2. A pair of transmembrane receptors belonging to the class III Semaphroin family that act as axon repellant factors. 395b, 398b, 400f

Nuchal region. The clear area at the back of the neck. 184

Nuchal translucency screening. A procedure in which ultrasonography is used to measure the thickness of the nuchal region. It indicates the likelihood that Down syndrome, chromosomal anomalies, or major heart anomalies are present in the fetus. 184

Nuclear layers. Two of the three layers of the mature retina. The inner nuclear layer contains the amacrine, horizontal, and bipolar cells; the outer nuclear layer contains the rods and cone photoreceptors. 586b

Nuclear migration, interkinetic. A to-and-fro movement of the nuclei of the neuroepithelial cells as they divide during neurulation. 111b

Nucleus ambiguus. An elongated nucleus that supplies branchial efferent fibers for nerves IX, X, and XI. 260f, 261

Nucleus habenulae. Part of the trigonium habenulae, a structure formed from the epithalamus. 274

Nucleus pulposus. A gelatinous core left when cells of notochordal origin in the intervertebral discs die. 227, 227f

Nutrient artery. An artery formed by a dominant blood vessel from the limb vasculature that nourishes a bone. 234, 236

O

Obesity, maternal. A maternal body mass index greater than 30 kg/meter squared. It is a risk factor for birth defects, such as neural tube defects, heart defects, and omphalocele. 179

Oblique muscles. The external and internal oblique muscles, which flex and rotate the vertebral column and compress the abdominal viscera.* 234, 559

Oblique vein, of left atrium. A small remnant of the proximal connection of the left anterior cardinal vein with the left sinus horn, which lies directly on the heart. It collects blood from the left atrial region of the heart and returns it directly to the coronary sinus. 355, 423f, 424

Occipital sulcus. The groove that demarcates the occipital lobe of the brain. 284

Oct4. Also called Pou5f1. A POU domain transcription factor that maintains pluripotency within the precursors that will form the germ line. 19b, 43b

Ocular muscles, extrinsic. Muscles formed by differentiation of mesoderm adjacent to the optic cup that cause the movements of the eye. 586b

Oculoauriculovertebral spectra (OAVS). Also known as hemifacial microsomia. A group of disorders, in which the lateral cleft of the face is not large, but the posterior portion of the mandible, temporomandibular joint, muscles of mastication, and outer and middle ear may all be underdeveloped. Goldenhar syndrome is a particularly severe member of this group. 580b, 602b, 613b

Oculomotor nerve. Cranial nerve III, which originates from the mesencephalon and innervates the inferior oblique, medial rectus, superior rectus, and inferior rectus muscles. 260f, 314t, 559

Oculomotor nucleus. One of the two nuclei of the oculomotor nerve. It controls the movements of all but the superior oblique and lateral rectus extrinsic ocular muscles. 270

Oculopharyngeal muscular dystrophy. A disease caused by mutations in Pabpn1 that affects the neck, face, and proximal limb muscles. 244b

Odontoblast(s). Cells formed by differentiation of the dental papilla that produce the dentin of the teeth. 195b, 210, 213f

Odontoblastic processes. Long cell processes left by the odontoblasts as they migrate downward, extending through the thickness of the dentin behind them. 210

Ofd1. The gene that causes the oral-facial-digital syndrome type 1. 636t

Olfactory bulbs. An outgrowth formed at the tip of each cerebral hemisphere that becomes part of the rhinencephalon. 250b, 272

Olfactory nerve. Cranial nerve I, which originates from the nasal placode and is associated with the telencephalon. It innervates the olfactory epithelium of the developing nasal cavities. 314t, 559

Olfactory placodes. A pair of ectodermal thickenings that form on the frontonasal prominence. In the 6th week, the ectoderm at the center of each invaginates to form an oval nasal pit. 123, 563

Olfactory tracts. Stalk-like central nervous system tracts formed by the lengthening of the axons of the secondary olfactory neurons. 250b, 272

Oligodactyly. A disorder resulting in the absence of any number of fingers or toes. 634t

Oligodendrocytes. Part of the glia of the central nervous system, which form the fatty myelin sheaths that wrap around many axons. 257

Oligodontia. A condition in which more than six teeth are absent. 215b

Oligohydramnios. A condition in which there is too little amniotic fluid. 169b, 173, 179, 334b, 489, 639b, 639f

Oligospermia. Low sperm count. 536b

Olivopontocerebellar atrophy. Any of a group of progressive hereditary disorders involving degeneration of the cerebellar cortex, middle peduncles, ventral pontine surface, and olivary nuclei. They occur in the young to middle-aged and are characterized by ataxia, dysarthria, and tremors similar to those of parkinsonism.* 269b

Omentum, greater. A large, suspended fold of mesogastrium that hangs from the dorsal body wall and the greater curvature of the stomach and drapes over more inferior organs of the abdominal cavity. 435b, 445, 447f

Omentum, lesser. A translucent membrane formed when a portion of the ventral mesentery between the liver and stomach thins out. 447f, 455

Omphalocele. An anterior body wall defect involving herniation of the bowel or other viscera through the umbilical ring, which is covered by a thin avascular membrane that may rupture. 106b, 106f, 461b

Omphalomesenteric cyst. A cyst formed when part of the vitelline duct within the abdominal wall persists; part of Meckel's diverticulum. 461b

Omphalomesenteric fistula. An open, abnormal passageway formed when part of the vitelline duct within the abdominal wall persists; part of Meckel's diverticulum. 461b

Omphalomesenteric ligament. A fibrous band connecting the small bowel to the umbilicus that is formed when part of the vitelline duct within the abdominal wall persists; part of Meckel's diverticulum. 461b

Oncostatin M. A molecule that stimulates the expression of hepatic differentiation markers, promotes liver-like morphology, and induces liver-specific gene expression in liver progenitor explant cultures. 449b

Oocytes. Also called egg; the female gamete before fertilization. 15b, 20, 21, 24f, 24–25, 28, 39

Oogenesis. The process of gametogenesis in females, occurring in the ovaries and producing the eggs or oocytes. 15b, 20, 28–30, 29f, 30f, 31f

Oogonia. Gamete precursor cells in females. Oogonia are diploid cells that eventually produce gametes. 15b, 20

Optic capsules. The embryonic structures from which the sclera is developed.* 547

Optic chiasm. A midline structure in which axons from the inner side of each eye cross over to the other side of the brain, whereas those of the outer side of each eye remain on the same side. 274, 275f, 277b–278b, 278f, 279f, 610

Optic cup. A goblet-shaped invagination of the optic vesicle attached to the forebrain by the optic stalk. 123, 602, 603f, 604f, 611

Optic disc. The part of the optic nerve that is inside the eyeball, formed by fibers converging from the retina and appearing as a pink to white disk in the retina. There are no sensory receptors in the region and hence no response to stimuli.* 277b, 277f, 586b, 602

Optic nerve. Cranial nerve II, which originates from the sensory layer of the optic cup and is associated with the diencephalon. It innervates the developing retina of the eye. 277b, 277f, 559, 610–611, 614b–615b

Optic primordia. Two primordia formed by the separation of the initially single eye field, which eventually develop into the optic vesicles. 602b

Optic stalk. A narrow, hollow structure that attaches the optic cup to the forebrain. Later, axons from the neural retina grow through the optic stalk to the brain, converting the optic stalk to the optic nerve. 583b, 602, 603f

Optic sulcus(i). A pair of lateral grooves that evaginate from the forebrain neural groove to form the optic vesicles. 583b, 602, 603f

Optic vesicles. Lateral evaginations of the neural tube, which invaginate to become the optic cup. 272, 583b, 602

Oral cavity. The cavity of the mouth, bounded by the jaw bones and associated structures (muscles and mucosa).* 568–569, 569f, 570f

Oral contraceptive. A compound, usually hormonal, taken orally to block ovulation and prevent the occurrence of pregnancy.* 45b

Oral membrane. The membrane that separates the stomodeum from the gastrointestinal tract. 563, 564f

Oral-facial-digital syndrome type 1. A syndrome caused by mutation of the gene Ofd1, and consisting of brachydactyly, syndactyly, and pre- or postaxial polydactyly. 636t

Orbicularis oculi muscles. The oval sphincter muscles surrounding the eyelids that close the eyelids, wrinkle the forehead, and compress the lacrimal sac.* They arise from paraxial mesoderm in the second pharyngeal arch. 559

Orbicularis oris muscles. The orbicular muscles of the mouth that close and protrude the lips.* They arise from paraxial mesoderm in the second pharyngeal arch. 559

Orbitosphenoid. One of two cartilages that develop around the eye and ultimately contribute to the greater and lesser wings of the sphenoid. 547

Organ culture. A technique in which lung primordia can be removed from embryonic birds or mice and cultured in media free of serum and other exogenous growth factors. Under these conditions, the lung primordia will grow and branch for a few days, but cannot completely develop. It is possible to use these cultured lungs to analyze the roles of growth factors and other agents in the branching process. 327b

Organ of Corti. The structure that contains the sensory hair cells responsible for transducing sound vibrations into electrical impulses. 588, 592f

Organizers. **A**lso called organizing centers. Special regions of the embryo that are capable of determining the differentiation of other regions through secretion of signaling molecules.* 81b, 94, 94b, 95b, 97b

Organogenesis. The formation of organ rudiments and organ systems. 69b, 78

Organum vasculosum, of lamina terminalis. An area of the lamina terminalis hypothalami where many neurons pass through a double-layered capillary bed and the blood-brain barrier is modified. It is one of the circumventricular organs.* 274

Oriented cell division. Cell divisions that are oriented in a particular plane. During neurulation, these occur to place daughter cells into the length of the neural plate rather than into its width, resulting in cranial-caudal extension of the neural plate. 87b

Oronasal membrane. A thin membrane formed from the nasal fin that separates that nasal sac from the oral cavity. 568, 569f

Oropharyngeal membrane. A two-layered membrane that caps the cranial end of the foregut and ruptures at the end of the 4th week to form the mouth opening. 69b, 78, 83, 439, 563, 564f

Osler-Weber-Rendu disease. Also known as hereditary hemorrhagic telangiectasia (HHT). A syndrome (with a prevalence of 1:5000 to 1:8000) manifesting most often as nosebleeds and small vascular anomalies called telangiectases. However, gastrointestinal bleeding and arterial-venous malformations in the lung, brain, and liver progressively develop. 387b

Ossicles. The malleus, incus, and stapes of the middle ear, which are arranged in a chain in the tympanic cavity. They derive from neural crest cells populating the first and second pharyngeal arches. 588, 602b

Ossification. Bone formation, which can occur in two ways. During endochondral ossification, a cartilage model first forms and is eventually replaced with bone. During intramembranous ossification, bone forms directly from mesenchymal cells without the prior formation of cartilage. 217b, 219, 234, 236, 543b, 545, 547, 617b

Ossification centers, primary. Regions where bone formation first begins. 227

Ossification centers, secondary. Regions where bone formation begins secondarily to those constituting the primary ossification centers. 227, 235

Osteoblasts. Bone-forming cells that arise from mesenchymal stem cells and function in secreting bone matrix. 217b, 219, 238b

Osteoclasts. Bone-resorbing cells that arise from the hematopoietic system. 217b, 219, 235, 238b

Osteogenesis imperfecta. A skeletal dysplasia associated with defects of the middle ear, caused by multiple collagen mutations. 602b

Osteopetrosis. Excess bone mass. 241b

Osteoporosis. Loss of bone mass, associated with increased skeletal fragility and bone fracture. 241b

Osteoporosis-pseudoglioma syndrome. A syndrome resulting from a mutation in the Wnt coreceptor Lrp5, causing abnormal vascularization. 241b, 614b

Osteoprotegerin. A decoy receptor secreted by the osteoblasts that negatively controls the interplay between osteoblasts and osteoclasts. 238b

Osterix. A zinc finger transcription factor that is essential for osteoblast development; in its absence, osteoblasts also do not differentiate. 221b, 238b

Ostia, of venae cavae. The openings of the superior and inferior venae cavae. 357

Ostium primum. Also called foramen primum. The diminishing foramen between the atria. 363

Ostium secundum. Also called foramen secundum. Foramen formed before the foramen primum closes by the coalescence of small perforations near the dorsal edge of the septum primum. 364f, 365

Otic capsules. Cartilage formed from the mesenchyme surrounding the membranous labyrinth that eventually ossifies to form the petrous portion of the temporal bone. 547, 583b, 593

Otic disc. Also called otic placode. A thickening of the surface ectoderm next to the hindbrain that gradually invaginates to form first an otic pit and then an otic vesicle. 588, 589f

Otic ganglion, of nerve IX. A ganglion derived from neural crest cells originating in the caudal portion of the rhombencephalon. 314

Otic pit. An indentation formed by invagination of the otic placode. 588, 589f

Otic placode. Also called otic disc. A thickening of the surface ectoderm next to the hindbrain that gradually invaginates to form first an otic pit and then an otic vesicle. 123, 315f, 583b, 588, 588b, 589f

Otic vesicle. Also called otocyst. A detached ovoid sac formed by closure of the otic pit in the early embryo, from which the percipient parts of the inner ear develop.* 583b, 588, 588b, 589f, 592b, 592f

Otoconial membrane. An acellular matrix that overlies the hair cells in the maculae. 593

Otocyst. Also called otic vesicle. A detached ovoid sac formed by closure of the otic pit in the early embryo, from which the percipient parts of the inner ear develop.* 583b, 588, 588b, 589f, 592b, 592f

Otx2. A transcription factor required for pigmented epithelium specification and differentiation in vertebrates. Loss of function also results in missing forebrain, microphthalmia, and cyclopia in the mouse. 253b, 608b, 609f, 610b

Outflow tract. Also called conotruncal segment. The cranialmost segment of the primitive heart tube forming the distal outflow region for both the left and right ventricles. 337b, 346, 370–371, 373f, 374f, 375b–376b, 376f, 380f, 381f

Oval window. A small fenestra in the bony labyrinth of the ear. 599

Ovarian follicles. Tissues that will nourish and regulate the development of maturing sex cells in females. 19

Ovaries. The female gonad, in which oogenesis occurs. 530, 531f–532f

Overgrowth syndromes. Disorders that result from abnormal imprinting of human autosomes, such as Beckwith-Wiedemann syndrome. 68b

Oviducts. Also called Fallopian tubes. Slender tubes extending laterally from the uterus toward the ovary, one on each side, that allow passage of oocytes to the cavity of the uterus and of spermatozoa in the opposite direction.* 45b, 482b, 518

Ovulation. The process by which the oocyte is released from the ovary. 15b, 28, 29f, 35, 37, 38f, 46b

Ovulatory surge. The sudden, sharp rise of follicle-stimulating hormone and luteinizing hormone levels, which stimulates the primary oocyte of the remaining mature graafian follicle to resume meiosis. 35, 38f

P

p63. Also known as Tumor protein p73-like (Tp73l). A transcription factor expressed in the stratum germinativum that regulates cell proliferation, expression of cell-adhesion molecules, and differentiation. 197b, 199f, 202, 203b, 636t

Pacemaker pathways. Conduction pathways that control the timing of contraction in the various regions of the heart, based on the rate of the sinoatrial (SA) node and, secondarily, the atrioventricular (AV) node. The pathways include the bundle of His and branches of Purkinje fibers. 377

Pacemaker region. The region that sets the pace for the contraction of the heart. The primary region is the sinoatrial (SA) node, which has a higher spontaneous depolarization rate than the rest of the heart. Later, a secondary region is formed in the atrioventricular (AV) node. 376–377

Pachygyria. Broad, thick gyri. 287b

Pain, congenital insensitivity to. A condition caused by a mutation in the Ntkr1 gene, which is required for the development of nociceptive (pain) sensory innervation of the skin. 299b

Pair-rule genes. One of four classes of zygotic genes. 151

Palate. The partition separating the nasal cavity from the oral cavity, consisting of a hard (bony) part anteriorly and a soft (fleshy) part posteriorly.* 114f, 134b, 134f, 543b, 545b, 564, 565f, 568, 569, 569f, 570b, 570f, 571b, 571f, 572f

Palatopterygoquadrate bar. The central cartilage of the maxillary prominence. 553

Palatopterygoquadrate cartilage. The cartilage formed by the first pharyngeal arch that ultimately gives rise to the incus of the middle ear. 543b

Pallister-Hall syndrome. A syndrome caused by a mutation in Gli3 that results in post-axial polydactyly and syndactyly. 634b, 635t

Pallium. The thin, dorsal part of the telencephalon that gives rise to the cerebral hemispheres, olfactory bulbs, and olfactory tracts. 250b, 272

Palmar arch, deep. The part of the arterial system of the upper limb that is formed from the axis artery. 411, 413f

Palmar crease, transverse, single. A minor anomaly, a single transverse palmar crease, which is often seen in infants with trisomy 21 (Down syndrome), but is also found in 4% of normal newborns. 634b, 635f

Pancreas. A large gland situated transversely behind the stomach, between the spleen and the duodenum, that arises from the dorsal and ventral pancreatic buds in the abdominal foregut.* 435b, 451, 453b

Pancreatic bud. Endodermal diverticulum; the ventral and dorsal pancreatic buds originate in the duodenal foregut and give rise to the pancreas. 450, 450f

Pancreatic duct. The passage formed from the ventral pancreatic bud that empties pancreatic secretions into the duodenum. 451

Pancreatic ductal cells. The cells differentiated from the endoderm of the pancreatic buds that transport digestive enzymes. 450

Pancreatic endocrine cells. Those cells in the islets of Langerhans, differentiated from the endoderm of pancreatic buds, that produce insulin, glucagon, and somatostatin. 450

Pancreatic exocrine cells. The cells differentiated from the endoderm of pancreatic buds that produce digestive enzymes. 450

Papillary layer. The superficial region of the dermis. 201f, 201–202

Papillary muscle. The conical muscular projections from the walls of the cardiac ventricles that are attached to the cusps of the atrioventricular valves by the chordae tendineae.* 368

Parachordal cartilages. The caudalmost pair of prochordal cartilages. Derived from occipital sclerotomes and the first cervical sclerotome, they form the base of the occipital bone. 547

Paradidymis. A remnant of the degenerated paragenital mesonephric tubules, made up of a few convoluted tubules in the anterior part of the spermatic cord.* 511

Parafollicular cells. Calcitonin-producing C cells of the thyroid that are derived from neural crest cells. 578

Paramesonephric ducts. Also known as Müllerian ducts. The paired embryonic channels that arise as a peritoneal pocket, extending caudally to join the urogenital sinus. In females they develop into the Fallopian tubes, uterus, and superior vagina; in males they degenerate, leaving vestigial structures such as the appendix testis and utriculus prostaticus.* 479b, 500, 501f, 502

Paranasal sinuses. One of four pairs of cavities (the maxillary, ethmoid, sphenoid, and frontal sinuses) that develop from invaginations of the nasal cavity and extend into the bones. 571–572

Parasympathetic division, of autonomic nervous system. A craniosacral system consisting of two-neuron pathways that stimulates the visceral organs to carry out their functions during periods of peace and relaxation. 125–126, 251, 257, 297b, 299

Parasympathetic ganglia. Aggregations of cell bodies that contain the peripheral (postganglionic) neurons of the two-neuron parasympathetic division of the autonomic nervous system. They may be associated either with the Vagus nerve or with cranial nerves III, VII, and IX, innervating the visceral organs or structures of the head, respectively.* 126, 297b, 314

Parathyroid glands. Small endocrine glands apposed to the posterior surface of the thyroid gland. Most commonly they occur in two pairs: the inferior parathyroid gland, formed from the third pharyngeal pouch, and the superior parathyroid gland, formed from the fourth pharyngeal pouch.* 545b, 577

Paroöphoron. In females, a remnant of the mesonephric ducts and mesonephric tubules that is found in the mesentery of the ovary. 518

Parotid duct. Also called Stensen's duct. The channel that drains the parotid gland and empties into the oral cavity opposite the second superior molar.* 579

Parotid gland. One of three pairs of salivary glands, which develops from a groove-like invagination of ectoderm that forms in the crease between the maxillary and mandibular swellings. 578

Pars inferior. One of three subdivisions of the otic vesicle, which forms the cochlear duct and saccule. 583b

Pars intermedia. Part of the pituitary gland, formed from Rathke's pouch. 282

Pars superior. One of three subdivisions of the otic vesicle, which differentiates to form the three semicircular canals and the utricle. 583b

Parthenogenic embryos. Also known as gynogenic embryos. Embryos that developed in the absence of fertilization or in the absence of a male pronucleus. 65b

Parturition. The act or process of giving birth to a child, including both labor and delivery.* 389

Parvovirus. One of several types of viruses that can cross the placenta and infect the fetus. In school-age children, the virus can cause rashes. 176

Pasting experimental embryology. A manner of experimentation in which tissues are transplanted or genes are ectopically (over)expressed to determine whether a particular gene is sufficient to cause a specific developmental event to occur. 147, 147f

Patched. A transmembrane receptor. In the absence of Shh protein, it inhibits the transmembrane signaling protein Smoothened. 156, 157

Patent ductus arteriosus (PDA). An open ductus arteriosus, the connection between the aorta and the pulmonary trunk. The ductus arteriosus normally closes soon after birth but can be kept patent if necessary, in part by circulating Prostaglandins. 339b, 380b, 432b

Pathfinding. The activity of the growth cone, which guides the axon along the correct trajectory to its target by detecting and integrating various molecular guidance cues in and around the axon pathways. 312b

Pax genes. A group of paired-box transcription factors. 221b, 242b, 244b, 276b, 375b, 472b, 486b, 602b, 604b, 608b, 609b, 610b

Pdgf. Platelet-derived growth factor. One of several families of growth factors binding to receptors that has a cytoplasmic Tyrosine kinase domain. 122b, 157

PdgfA. A platelet-derived growth factor released by fetal Sertoli cells, important in Leydig cell differentiation. It is also required for the postnatal formation of alveolar septae-containing myofibroblasts. 328b, 510b–511b

Pdx1. Pancreas and duodenal homeobox gene 1. A pancreatic-promoting transcription factor expressed in the early stomach and in dorsal and ventral prepancreatic and preduodenal endoderm. 444b, 452b, 453f, 492f, 492b–493b

Pectinate line. The border between the cranial end of the anal pit and the caudal end of the rectum, demarcated by mucosal folds. 475

Pelvis. The inferior portion of the trunk of the body, bounded anteriorly and laterally by the two hip bones and posteriorly by the sacrum and coccyx.* 311, 311f

Pendred syndrome. A hereditary syndrome of congenital bilateral nerve deafness, in which there is development in middle childhood of goiter without hypothyroidism. The main biochemical feature is defective thyroxine biosynthesis.* 597b

Pendrin. A chloride-iodide transporter protein. 597b

Penile meatus. The opening at the tip of the glans penis, formed when the solid urethral plate canalizes. 521, 523f

Penis. The male organ of copulation and urinary excretion, comprising a root (radix penis), body (corpus penis), and extremity (glans penis).* 482b

Pentalogy of Cantrell. A constellation of five defects (omphalocele, diaphragmatic hernia, sternal cleft, ectopia cordis, and intracardiac anomaly). 106b, 461b

Periauricular pits. Also called preauricular pits. Anomalous derivatives of the first pharyngeal cleft in the area anterior to the external acoustic meatus. The pits may arise due to defects in the fusion of the periauricular hillocks during the formation of the outer ear. 573

Pericardial cavity. The potential space located between the parietal layer and the visceral layer (epicardium) of the serous pericardium, which forms as a subdivision of the intraembryonic coelum.* 319b, 329, 330f, 331, 331f

Pericardial sac. Also called pericardium. The fibroserous sac that surrounds the heart and the roots of the great vessels, which consists of an inner serous pericardium and an outer mediastinal pleura, separated by the fibrous pericardium.* 329, 331–332, 332f

Pericardial sinus, transverse. A passage behind the aorta and pulmonary trunk and in front of the atria, formed from the region of the ruptured dorsal mesocardium. It is lined by serous pericardium.* 346, 348

Pericardioperitoneal canals. A pair of canals passing dorsal to the septum transversum through which the pleural cavities and the peritoneal cavity initially communicate. They are later closed off by a pair of transverse pleuroperitoneal membranes. 319b

Pericardium. Also called the pericardial sac. The fibroserous sac that surrounds the heart and the roots of the great vessels, which consists of an inner serous pericardium and an outer mediastinal pleura, separated by the fibrous pericardium.* 331, 342

Periderm. An outer layer of simple squamous epithelium formed by the proliferation of the ectoderm, which is gradually shed into the amniotic fluid as the definitive epidermis develops. 193b, 195, 196f

Perilymph. The fluid that fills the perilymphatic space, which communicates with the cerebrospinal fluid. 593

Perilymphatic space. A cavity within the bony labyrinth of the petrous portion of the temporal bone, formed when the layer of cartilage immediately surrounding the membranous labyrinth undergoes vacuolization in the 3rd to 5th months of development. 593, 595f

Perineum. The pelvic floor and associated structures that occupy the pelvic outlet, bounded anteriorly by the pubic symphysis, laterally by the ischial tuberosities, and posteriorly by the coccyx. It is formed from the tip of the urorectal septum.* 307b, 311, 311f

Periodontal ligament. The ligament formed from the outermost cells of the dental sac that attaches a tooth to its bony socket. 214

Peripheral nervous system (PNS). One of two major structural divisions of the nervous system, consisting of all components of the nervous system outside the central nervous system (CNS), including the cranial nerves and ganglia, spinal nerves and ganglia, autonomic nerves and ganglia, and enteric nervous system. 251, 297–316

Peripheral neurons. One of four types of neurons (peripheral sensory neurons, sympathetic autonomic peripheral motoneurons, parasympathetic autonomic peripheral motoneurons, and enteric neurons) that are derived from neural crest cells and housed outside the central nervous system. 125, 128b

Peripheral neuropathies, hereditary. Functional disturbances or pathologic changes in the peripheral nervous system, generally caused by demyelination. 306b–308b

Peritoneal cavity. The potential space of capillary thinness between the parietal and the visceral peritoneum, which is normally empty except for a thin serous fluid that keeps the surfaces moist. It formed as the abdominal subdivision of the intraembryonic coelum.* 319b, 329, 331f, 440, 445

Peritoneum. The serous membrane that lines the abdominopelvic walls (parietal peritoneum) and invests the viscera (visceral peritoneum). A strong, colorless membrane with a smooth surface, it forms a double-layered sac that is closed in males and continuous with the mucous membrane of the uterine tubes in females.* 435b, 455

Perivitelline space. The area between the oocyte and the zona pellucida. 39

Perlecan. A Heparan sulfate proteoglycan expressed by mature blastocysts, which has a role in blastocyst attachment. 55b, 160

Permissive molecules. The extracellular matrix molecules that participate in establishing the path of neural crest cell migration, including the basement membrane proteins Tenascin, Fibronectin, Laminin, and Collagen. 121b

Permissive pathways. The courses that permit axons to travel into the limb bud. 640

Peroneal artery. A remnant of the axis artery that originates in the posterior tibial artery and distributes to the outside and back of the ankle, as well as the deep calf muscles.* 413

Persistent atrioventricular canal. The persistence of a common atrioventricular canal (the initial pathway between the future atrium and left ventricle) that arises from the failure of the dorsal and ventral endocardial cushions to fuse. The defect commonly occurs in Down syndrome and can lead to a variety of secondary abnormalities. 379b

Persistent foramen ovale. The failure of the foramen ovale, an opening in the septum secundum near the floor of the right atrium, to close at birth. 380b

Persistent Müllerian duct syndrome. The failure of the Müllerian ducts to regress in the male, exhibited by 46,XY individuals with mutations in Amh or Amh receptor genes. These individuals develop structures derived from the Müllerian duct in addition to those derived from the mesonephric duct. 504f, 509, 509b, 510f

Persistent truncus arteriosus. The failure of the truncus arteriosus to split, which is caused by ablation of cardiac neural crest cells and failure of the conotruncal septa to form. This malformation necessarily includes a ventricular septal defect, and results in the mixing of blood from the two sides of the heart in the common outflow tract, leading to pulmonary hypertension. 380f, 381f

Peters anomaly. A developmental defect in structures around the anterior chamber of the eye, characterized by corneal clouding and sometimes adhesions of the iris, lens, and cornea. It is often accompanied by other defects such as dwarfism and mental retardation and is caused by mutations in the transcription factor Pax6.* 614b

Petromastoid bone. Also known as periotic bone. The petrous portion of the temporal bone, formed when the primitive otic capsule ossification centers fuse with the parachordal cartilages. 547

Petrosal ganglion, of nerve IX. The inferior ganglion of nerve IX, the neurons of which are derived from the second epipharyngeal placode. 314, 315f

Pfeiffer syndrome. An Fgfr1 or Fgfr2 mutation that results in craniosynostosis with limb defects. 158, 550b, 630b, 635t, 638b

Phallic segment. The lower expansion of the urogenital sinus, which becomes the penile urethra in males and contributes to the vestibule of the vagina in females. 495, 496f

Phallus. Tissue formed by the genital tubercle generated by the expansion of the mesoderm anterior and cranial to the phallic segment of the urogenital sinus. In males, it elongates to form the penis; in females, it bends inferiorly to form the clitoris. 521, 522f

Pharyngeal apparatus. A structure composed of five pairs of pharyngeal arches and separated by pharyngeal clefts externally and pharyngeal pouches internally. 543b

Pharyngeal arches. Also called branchial arches. Five pairs of mesenchymal condensations that develop on either side of the pharyngeal foregut and become central elements in the development of the neck and face. Because of their evolutionary history from ancestors with six arches, these arches correspond to numbers 1, 2, 3, 4, and 6. Each arch has an outer covering of ectoderm, an inner covering of endoderm, and a core of mesenchyme derived from paraxial and lateral plate mesoderm and neural crest cell–derived ectomesenchyme, and is separated from adjacent arches by pharyngeal clefts externally and by pharyngeal pouches internally. 122, 403, 543b, 551–560, 552f, 554f, 555t, 566b, 568f

Pharyngeal clefts. Four ectoderm-lined grooves that externally separate the pharyngeal arches. With the exception of the first pharyngeal cleft, which forms the external auditory meatus, they are obliterated by overgrowth of the second pharyngeal arch, although they occasionally persist as abnormal cervical cysts or fistulae. 543b, 553, 572–573, 573f, 574f

Pharyngeal membranes. Thin, two-layered membranes, consisting of ectoderm and endoderm, that separate the external pharyngeal clefts from the internal pharyngeal pouches. 553

Pharyngeal pouches. Four endoderm-lined sacs that separate the pharyngeal arches internally. Each of the pharyngeal pouches gives rise to an adult structure: the first pouch becomes the tympanic cavity and auditory (eustachian) tube; the second gives rise to the palatine tonsils; the third forms the thymus gland and inferior parathyroid glands; and the fourth forms the superior parathyroid glands. 543b, 553, 576–578, 578f, 579f

Phenotype. The observable characteristics of an individual, such as eye color or the presence or absence of a birth defect. 136

Phenytoin. An anticonvulsant known to be teratogenic, which may induce cleft lip, cleft palate, and limb malformations. 638b

Pheochromocytoma. Tumors of the chromaffin cells of the suprarenal medulla. 128b

Philtrum. The structure between the upper lip and the nose, formed by the intermaxillary process. 545b, 564, 565f

Phocomelia. A disorder that results in the absence of proximal limb structures. 634t

Phosphylation. The addition of a phosphate group to a protein, which generally causes its activation. 154

Phrenic nerves. The paired nerves that innervate the diaphragm. Formed when the spinal nerves of cervical levels 3, 4, and 5 join together, they originally run through the portion of the body wall mesenchyme incorporated into the pleuropericardial folds. In the adult, they course through the fibrous pericardium. 241, 329, 331–332

Physis. Also called the epiphyseal cartilage plate or growth plate. A layer of cartilage that persists between the epiphysis and the growing end of the diaphysis (metaphysis). 235

Phytanic acid. A substance commonly present in foods, which can cause Refsum's disease if mutations in the gene encoding the enzyme Phytanoyl-CoA hydroxylase cause it to accumulate. 308b

Piebaldism. A congenital autosomal dominant pigmentary disorder of the skin due to the absence of functioning melanocytes and melanin, which is caused by a mutation in the c-Kit gene The disorder results in patchy areas of depigmentation or hypopigmentation, often occurring in association with white forelock.* 136f

Pierre Robin sequence. A secondary cleft palate that results from a smaller lower jaw and occurs with backward displacement of the tongue. It is often seen as part of syndromes such as Stickler and Treacher Collins. 571

Pigmentation defects. Abnormalities in pigmentation patterns. 136f

Pigmented epithelium. Cuboidal melanin-containing epithelium formed by the thin outer wall of the optic cup. 586b, 607, 608f

Pilomatricoma. A benign tumor of hair follicle matrix cells resulting from constitutive activation of β-Catenin. 207b

Pineal gland. An endocrine gland, formed from the epithalamus, that is located above the superior colliculi and below the splenium of the corpus callosum.* 274

Pinna. Also called auricle. The external flap of the ear, developed from six auricular hillocks. 583b, 588, 600, 600f

Pinopodes. Large apical protrusions formed when the apical microvilli in the uterus retract during the receptive stage. 55b

Pituitary gland. An epithelial body located at the base of the brain. It consists of two lobes of differing embryonic origin: the posterior lobe forms from a diverticulum of the diencephalic floor called the infundibulum, whereas the anterior lobe and pars intermedia form from an evagination of the ectodermal roof of the stomodeum called Rathke's pouch.* 250b, 272, 282

Pitx2. A homeobox-containing transcription factor that regulates the transcription of downstream targets. It is expressed on the left side and seems to be an effector gene, with its expression persisting later in development. Haploinsufficiency results in Rieger's syndrome. 73b, 76b

Pitx. Homeobox-containing transcription factors. 353b

Pitx2c. An isoform of Pitx2. 408b

Pkhd1. A gene that encodes the protein Polyductin. Mutations can lead to autosomal recessive polycystic kidney disease (ARPKD). 495b

Placenta. An organ, consisting of both maternal and fetal components, that allows the developing fetus to receive nutrients and eliminate metabolic waste. It consists of a mass of feathery fetal villi that project into an intervillous space lined with fetal syncytiotrophoblast and filled with maternal blood. The placenta also secretes hormones and allows maternal antibodies to enter the fetus. The placenta grows along with the fetus, weighing about one-sixth as much as the fetus at birth. 51b, 59, 167b, 170–171, 172f–174f, 175–178, 180

Placenta previa. "Low-lying" placenta; a condition in which the blastocyst implants near the uterine cervix and the placenta covers part of the opening of the cervix. 178

Placental septa. The wedge-like walls of tissue that make up the cotyledons of the intervillous spaces and grow inward from the maternal face of the placenta. 167b, 171, 174f

Placental villous tree. A tree-like structure formed by the placental villi. 171

Plakophilin1. A dermosomal protein. Mutations can affect differentiation and morphogenesis of the hair or cause skin fragility defects. 198b, 200f

Planar cell polarity (PCP) pathway. A signaling pathway that functions in the polarization within the plane of the epithelium. It is required for proper orientation of the stereocilia on the hair cells in the cochlea (essential for hearing) and for convergent extension during gastrulation and neurulation. 111b–112b, 205b–206b, 596b

Plasmin. A protease important in mediating endothelial migration and remodeling. 397b

Plasminogen activator inhibitor-1. A protein that blocks Plasmin formation. 396b

Plastic casting. A technique for studying the development of the vasculature by perfusing it with a soluble plastic that is then polymerized to form a solid cast that can be isolated, coated with metal, and examined by scanning electron microscopy. 393b, 394f

Platelet-endothelial–Cell adhesion molecule (Pe-Cam). A calcium-independent adhesion molecule expressed in the vascular system. 160

Platysma muscle. A platelike muscle that originates from the fascia of the cervical region and inserts in the mandible and the skin around the mouth. It is innervated by the cervical branch of the facial nerve, and acts to wrinkle the skin of the neck and to depress the jaw.* 559

Pleura. The serous membrane investing the lungs and lining the thoracic cavity, completely enclosing a potential space known as the pleural cavity. There are two pleurae, right and left, entirely distinct from each other. The pleura is moistened with a serous secretion that facilitates movements of the lungs in the chest.* 331

Pleural cavity. One of two hollow spaces, subdivisions of the intraembyronic coelom, in which the lungs develop. 319b, 329

Pleuropericardial folds. Coronal septae, consisting of mesenchyme sandwiched between two epithelial layers. They form on the lateral body wall of the primitive pericardial cavity and grow medially to fuse with each other and with the ventral surface of the foregut mesoderm, thus subdividing the primitive pericardial cavity into a definitive pericardial cavity and two pleural cavities. 319b, 329, 332f

Pleuroperitoneal membranes. A pair of membranes, arising along an oblique line connecting the root of the 12th rib with the tips of ribs 12 through 7, that grow ventrally to fuse with the septum transversum, thus sealing off the pericardioperitoneal canals and separating the definitive pleural cavities from the peritoneal cavity. 319b, 332, 333f

Plexins. A family of receptors important in targeting cardiac neural crest cells into the pharyngeal arches and outflow tract. 312b, 376b

Ploidy. The number of copies of each chromosome present in a cell nucleus. 21

Pluripotency. The ability to form many cell types. 18b, 83, 162

PNA-binding molecules. Inhibitory molecules that specifically bind the lectin Peanut agglutinin. 121b

Pod1. A gene involved in the development of the kidney, specifically expressed by stromal cells. 492f, 492b–493b

Podocytes. Glomerular epithelial cells. 489

Poland anomaly. The defect in which the pectoralis major muscle is absent on one side of the body, which may be due to vascular compromise in the fetus. 244b, 639b

Polar bodies. The small nonfunctional cells with a haploid chromosome complement, consisting of a small amount of cytoplasm and a nucleus, that result from meiotic division of the oocyte. Polar bodies contain only maternal genes.* 21

Polycystein2. A cation channel protein that is the product of Polycystic kidney disease type 2 gene (Pkd2). 75b, 77f

Polycystin 1/2 (Pdk1/2). Proteins, the precise roles of which are not yet known. However, Pdk1 seems to be required for normal elongation and maturation of tubular structures during renal development. 495b

Polycystic kidney disease (PKD). A disease, either autosomal dominant (ADPKD) or autosomal recessive (ARPKD). ADPKD is associated with the formation of cysts in the kidneys as well as in the ductal epithelia in the liver, pancreas, testis, and ovary, and is caused by mutations in the genes encoding Pdk1 and Pdk2. ARPKD is characterized by the development of renal, hepatic, and biliary cysts, and is caused by mutations in the Pkhd1 gene. 495b

Polydactyly. A disorder resulting in presence of extra digits or parts of digits. 134b, 134f, 157, 632b, 633f, 634b, 634t

Polyglutamine disorders. Conditions that occur when the tract of the amino acid glutamine residues reaches a disease-causing threshold. 269b

Polyhydramnios. Also called hydramnios. An excess of amniotic fluid. 179

Polymastia. The formation of supernumerary breasts along the line of the mammary ridges. 209, 209f

Polymerase chain reaction (PCR). A technique that amplifies DNA from a single cell, producing copies for sequence analysis. It is used to screen for mutations. 47b

Polyspermy. The fertilization of the oocyte by more than one spermatozoon. 39

Polythelia. The formation of supernumerary nipples along the line of the mammary ridges. 209, 209f

Pons. A bulbous expansion in the brain stem, formed by the metencephalon, that functions mainly to relay signals linking both the spinal cord and the cerebral cortex with the cerebellum. 247b, 258, 263, 264f

Pontine flexure. The third fold of the brain tube. A reverse, dorsally directed flexion that begins at the location of the developing pons and deepens to fold the metencephalon back onto the myelencephalon. 247b, 255

Pontine nuclei. Noncranial nerve nuclei of the rhombencephalon that arise from the rhombic lip and migrate to a ventral position, which relay input from the cerebrum to the cerebellum. 262f, 263

Popliteal artery. A continuation of the femoral artery that distributes to the knee and calf.* 413

Portal system. The arrangement of vessels that drain blood from the gastrointestinal tract to the liver sinusoids, formed by the right and left vitelline veins. 419

Positional address or value. A cell's unique "grid reference" along the cranial-caudal and medial-lateral axes of the neural plate. It is determined by measuring the ambient concentration of morphogen on each of the intersecting axes. 253b, 621b

Positional information. A Cartesian system in which cells may sense their position on orthogonal gradients of morphogens acting along the cranial-caudal and medial-lateral axes of the neural plate. 161, 253b, 621b

Postepithelial layer. An acellular stroma, formed between the corneal epithelium and the corneal ectoderm by the differentiation of the mesenchyme, that consists of a matrix of Collagen fibers, Hyaluronic acid, and Glycosaminoglycans. 611

Posterior chamber, of eye. Space formed when the deep layers of the pupillary membrane undergo vacuolization between the lens and the thin remaining pupillary membrane. This space communicates with the anterior chamber through the pupil, and eventually expands to underlie the iris and part of the ciliary body. 586b, 612, 612f

Posterior commissures, of epithalamus. A large fiber bundle that crosses the midline of the epithalamus just dorsal to the point where the cerebral aqueduct opens into the third ventricle.* 274

Posterior urethral valve. An abnormality of the urethra that prevents normal urine excretion and causes the urine to back up into the bladder, ureters, and kidneys. 169b

Posterolateral fissure. A transverse groove that separates the developing cerebellum into cranial and caudal portions. 263, 266f

Postganglionic fibers. Also called postsynaptic fibers. The axons of the peripheral sympathetic neurons. 251, 300, 316

Postsynaptic fibers. Also called postganglionic fibers. The axons of the peripheral sympathetic neurons. 251, 300

Potter sequence. A spectrum of abnormalities caused by oligohydramnios, including deformed limbs; wrinkly, dry skin; and an abnormal facies consisting of wide-set eyes with infraorbital skin creases, beak nose, recessed chin, and low-set ears. 489, 493b

Prader-Willi syndrome. A condition caused by deletions in the region of chromosome 15 (15q11.2-q13) inherited from the father. Symptoms include feeding problems in infancy and rapid weight gain in childhood, hypogonadism, and mild mental retardation. 53b, 67b–68b

Preaortic ganglia. Also called prevertebral ganglia. The peripheral ganglia of some specialized sympathetic pathways that develop from neural crest cells that congregate next to major branches of the dorsal aorta and contain the peripheral neurons of the two-neuron sympathetic pathway. 125, 297b

Preauricular pits. Also called periauricular pits. Anomalous derivatives of the first pharyngeal cleft in the area anterior to the external acoustic meatus. The pits may arise due to defects in the fusion of the periauricular hillocks during the formation of the outer ear. 573, 601b, 601f

Preauricular tags. Defects of the external ear caused by the formation of accessory hillocks derived from the first and second pharyngeal arches. 601b, 601f

Pre-B-cell leukemia transcription factor (Pbx1). A transcriptional marker for pancreatic endoderm. 451

Prechordal cartilages. One of three pairs of cartilaginous precursors that contribute to the cranial base. The prechordal cartilages give rise to the ethmoid bone. 547

Prechordal plate. A thickened area, formed by the cranial midline endoderm, that contributes to the oropharyngeal membrane during later development and is an important signaling center for patterning the overlying neural plate. 69b, 83

Predentin. The nonmineralized matrix of the dentin, secreted by odontoblasts in the 7th month of development, which later progressively calcifies to form dentin. 210

Preeclampsia. A maternal condition affecting about 5% of pregnancies, which is characterized by high blood pressure and protein in the urine. 178

Pre-formed pathway. A pathway in the chiasm, on which ipsilateral axons can adhere, that is formed by axons from the opposite eye that have already crossed over. 279b

Preganglionic fibers. Also called presynaptic fibers. The axons of the central sympathetic neurons, which synapse on the cell bodies of postganglionic neurons in the autonomic ganglia. 251, 300, 316

Prehypertrophic zone. The layer of chondrocytes near the diaphysis of the long bone in which the chondrocytes have enlarged. 234

Preimplantation genetic diagnosis (PGD). A diagnosis of genetic conditions prior to implantation, performed using first or second polar bodies or blastomeres removed during in vitro fertilization, which can be screened for aneuploidy, translocations, and mutations. This makes it possible to select only unaffected embryos for implanting. 47b, 48f

Premature infants. An infant, usually born after the 20th completed week and before full term, who is arbitrarily defined as one weighing 500 to 2499 g (2.2 to 5.5 lb) at birth and having poor to good chance of survival, depending on the weight.* 325b–326b

Prenatal diagnosis. The identification of fetal malformations and genetic diseases before birth, most often by maternal serum screening, ultrasonography, amniocentesis, or chorionic villus sampling. 35b, 114b, 169b, 180, 182–185, 186f

Prenatal pediatrics. Also called fetology. The study and treatment of the fetus. 169b, 180

Prenatal treatment. The use of either surgical or drug intervention to treat the fetus in utero to potentially lessen the impact of birth defects diagnosed prenatally. 186–189

Presbycusis. A progressive, bilaterally symmetric perceptive hearing loss occurring with age.* 596b

Pre-Sertoli cells. In males, cells that produce SRY protein, which causes the somatic support cells to differentiate into Sertoli cells. In females, they take on a follicle cell lineage. 479b

Prestin. A unique membrane protein that enables outer hair cells to change their length rapidly in response to sound. 593

Presynaptic fibers. Also called preganglionic fibers. The axons of the central sympathetic neurons, which synapse on the cell bodies of postganglionic neurons in the autonomic ganglia. 251, 300

Pretectum. An area at the junction of the mesencephalon and diencephalon that extends from a position dorsolateral to the commissure of the epithalamus toward the cranial colliculus, within which is situated the pretectal nucleus.* 272, 273f

Prethalamus. An area that forms at the junction of the diencephalon and telencephalon. 272

Prevertebral ganglia. Also called preaortic ganglia. The peripheral ganglia of some specialized sympathetic pathways that develop from neural crest cells that congregate next to major branches of the dorsal aorta and contain the peripheral neurons of the two-neuron sympathetic pathway. 125, 297b

Primary body development. The process in which the primitive streak gives rise to the three primary germ layers, which subsequently assemble into organ rudiments. 98

Primary bone collar. A band around the circumference of the bone, formed when the region surrounding the diaphysis ossifies. 235

Primary bronchi. The two main branches into which the trachea divides, each passing to the respective lung.*

Primary ciliary dyskinesia (PCD). Any of a group of hereditary syndromes characterized by delayed or absent mucociliary clearance from the airways. Often there is also lack of motion of sperm.* 321b

Primary intestinal loop. An anteroposterior hairpin fold that herniates into the umbilicus during the 6th week. As the primary intestinal loop herniates, it rotates around its long axis by 90 degrees counterclockwise (as viewed from the ventral side) so that the future ileum lies

in the right abdomen and the future large intestine lies in the left abdomen. 435b, 456, 457f, 458f

Primary ossification center. The region where ossification first begins. 234

Primitive fovea. The central macular depression that forms at 7 months. 608

Primitive groove. A trough-like depression that represents an area where cells leave the primitive streak and move into the interior of the embryonic disc. 69b, 71, 72f

Primitive node. The expanded cranial end of the cranial streak, containing the primitive pit. 69b, 71, 72f

Primitive pit. A circular depression in the primitive node, which represents an area where cells leave the primitive streak and move into the interior of the embryonic disc. It is continuous caudally down the midline of the primitive streak with the primitive node. 69b, 71, 72f

Primitive streak. A longitudinal midline structure formed during gastrulation in the epiblast near the caudal end of the bilaminar embryonic disc. 69b, 71, 72f, 94b, 94f

Primordial germ cells (PGCs). Specialized cells that first arise in the yolk sac and give rise to male and female gametes. Their lineage constitutes the germ line. 15b, 17–20, 19b–20b, 58, 122b

Proctodeum. Also called the anal pit. An invagination of the surface ectoderm of the embryo at the point where later the anus is formed.* 474, 474f

Proepicardial organ. A special group of splanchnopleuric mesodermal cells forming at the junction of the posterior dorsal mesocardium and the septum transversum, which is the progenitor of the epicardium. 377, 378f

Progesterone. A steroid hormone secreted by luteal cells that stimulates the thickening of the endometrial layer. 39, 45b, 179

Programmed cell death. Also called apoptosis. Cell death; a change (decrease) in cell number.

Progress zone(s). A narrow area of mesenchyme underlying the apical epidermal ridge of the limb bud where cells are thought to acquire positional information that will inform them of their final positional address along the proximal-distal axis. 62b, 625f

Progress zone model. A model to explain how patterning is specified along the proximal-distal axis of the limb. It states that cells acquire their positional address while residing in a progress zone. Cells that exit the progress zone after a short residence are destined to form proximal structures, while those that exit after a long residence form distal structures. 621b, 623b, 625f

Prokineticin2. A cysteine-rich protein that is secreted by the suprachiasmatic nucleus and involved in the circadian clock. Mutations in this gene can cause Kallmann's syndrome. 287b–288b

Proliferation. The reproduction or multiplication of similar forms, especially of cells and morbid cysts.* 610b

Proliferative phase. The stage of the menstrual cycle (generally days 5 to 14) in which the endometrial lining of the uterus proliferates and undergoes remodeling. 39

Pronators. Muscles formed from the ventral muscle mass that serve to turn the palm posteriorly (or inferiorly when the forearm is flexed) by medial rotation of the forearm.* 242, 242t

Pronephros. One of three sets of nephric systems that develop in craniocaudal succession from the intermediate mesoderm. It is the beginning of a developmental cascade that leads to the formation of the definitive kidney. 479b, 483, 484f, 485, 485f

Proneural genes. A group of basic helix-loop-helix transcription factors that act as negative regulators for neurogenesis. 302b–303b

Pronuclei. The nuclei of the oocyte (female pronuclei) and sperm (male pronuclei) that fuse to form the zygote. 39, 40f, 41, 41f

Prophase. The stage of mitosis or meiosis in which chromosomes condense into compact, double stranded structures (two chromatids joined by one centromere). 22f, 23t, 24

Prosencephalon. Also called forebrain. One of three primary brain vesicles, which subdivides into the telencephalon and diencephalon. 119, 247b, 251, 252f

Prosomeres. Subdivisions of the alar plates of the diencephalon. 251, 272

Prospective fate. The term for what a group of epiblast cells are destined to form during normal development based on their place of origin. 83

Prospective fate maps. Diagrams that show the locations of prospective groups of cells prior to the onset of gastrulation. 83, 84f

Prospective gut endoderm. Germ layer that moves from the epiblast surrounding the cranial half of the primitive streak into the primitive streak, then migrates into the hypoblast to displace that layer and form a new layer of definitive endoderm. 83

Prospective potency. The term for what a region of the blastoderm is capable of forming at a particular stage of development. 83

Prostaglandin(s). A family of compounds, derived from fatty acids, that performs a range of functions in various tissues of the body, including dilation of vascular smooth muscle. 179, 431, 432b

Prostaglandin D_2 (Pgd2). Protein that upregulates Sox9 expression, possibly reinforcing male gonadal development once it is initiated. 507b

Prostate gland. In males, a gland that surrounds the bladder neck and urethra, made up partly of glandular matter whose ducts empty into the prostatic part of the urethra and partly of muscular fibers that encircle the urethra. It contributes to the seminal fluid a secretion containing acid phosphatase, citric acid, and proteolytic enzymes that account for the liquefaction of the coagulated semen.* 28, 511, 511f, 512b–513b, 514f, 515b

Prostatic utricle. An expansion of the prostatic urethra that remains in males after regression of the Müllerian ducts. 504f, 509

Protanopes. Individuals with color blindness due to the absence of L-cones. 608

Proteases. Peptidases that catalyze the cleavage of internal peptide bonds in a polypeptide or protein.* 207b

Proteinuria. Excessive protein loss into the urine. 494b

Proteoglycans. Any of a group of polysaccharide-protein conjugates occurring primarily in the matrix of connective tissue and cartilage. They are composed mainly of polysaccharide chains, particularly glycosaminoglycans, as well as minor protein components.* 121b

Proto-oncogenes. A normal gene that when mutated can become an oncogene, resulting in the development of cancer. 302b

Prox1. Prospero-related homeobox 1; the transcription factor required for lymphatic cell specification, horizontal cell formation, and lens fiber differentiation. 428b, 428f, 607b, 610b

Proximal-distal axis. The axis running from the shoulder to the fingers in the upper limb and from the hip to the toes in the lower limb. The proximal end is close to the center of the body, while the distal end is far from the center of the body. 617b, 621b, 622f–626f, 623b

Prune-belly syndrome. A defect in which the abdominal wall muscles fail to develop. 106b–107b, 244b

Pseudoglandular stage. The period between 6 and 16 weeks of development in which the respiratory tree undergoes 14 more generations of branching, resulting in the formation of terminal bronchioles. 322t, 328b

Pseudohermaphrodism. A condition in which an individual's gonads and sex chromosomes are discordant with secondary sex characteristics, including the genital tract and external genitalia. 531b–536b

Psoriasis. Hyperproliferative skin disease with polygenic inheritance and a fluctuating course. The principal histologic findings are Munro microabscesses and spongiform pustules; also seen are rounded, circumscribed, erythematous, dry, scaling patches of various sizes, covered by grayish white or silvery white, umbilicated, and lamellar scales, usually on extensor surfaces, nails, scalp, genitalia, and lumbosacral region.* 198b

Ptch. The receptor that represses Hedgehog signaling. Mutations can cause nevoid basal cell carcinoma syndrome. 207b

Pterygoid muscles. Medial and lateral pterygoid muscles, which are formed by the paraxial mesoderm originating beside the metencephalon. The lateral pterygoid muscle serves to

protrude the mandible, open the jaws, and move the mandible from side to side; the medial pterygoid muscle serves to close the jaws.* 559

Pthrp. Parathyroid hormone–related peptide, which is essential for mammary gland development and the prevention of hypertrophy during bone formation. 209b-210b, 237b

Ptosis. An anomaly characterized by drooping eyelids. 613b

Ptpn11. A gene encoding an Shp2 protein. 83b, 416b

Puberty. A major hormonally controlled postnatal developmental period, during which the secondary sex characteristics begin to develop and the capability of sexual reproduction is attained.* 15b, 536b

Pulmonary agenesis. A severe anomaly that results when the respiratory diverticulum fails to split into right and left bronchial buds and continue growing. 324b

Pulmonary arterial-venous malformation. An anomaly causing a pulmonary arterial-venous shunt. 387b

Pulmonary artery. The vessel arising from the conus arteriosus of the right ventricle, which extends upward obliquely to divide into the right and left pulmonary arteries beneath the arch of the aorta, and conveys unaerated blood toward the lungs. It is formed by the splitting of the truncus arteriosus.* 346

Pulmonary hypertension. Increased pressure (above 30 mm Hg systolic and 12 mm Hg diastolic) within the pulmonary arterial circulation.* 401b

Pulmonary hypoplasia. Congenital malformation characterized by a reduced number of pulmonary segments or terminal air sacs. 169b, 173, 324b, 327b

Pulmonary stenosis. A narrowing of the opening between the pulmonary artery and the right ventricle, usually at the level of the valve leaflets; one of the four malformations in the tetralogy of Fallot.* 382b, 382f

Pulmonary surfactant. A mixture of phospholipids and surfactant proteins secreted by alveolar type II cells that reduces the surface tension of the liquid film lining the alveoli and thus facilitates inflation. 326b

Pulmonary vein. One of four veins (right and left superior and right and left inferior), that returns aerated blood from the lungs to the left atrium of the heart.* 357f–359f, 358

Pupil. The opening through which the anterior and posterior chambers of the eye communicate, formed by the regression of the pupillary membrane. 586b, 612, 612f

Pupillary membrane. The inner wall of the anterior chamber of the eye. 611–612, 614b

Pupillary muscles. Circumferentially arranged smooth muscle bundles that originate from the neuroepithelium of the optic cup. They act as a diaphragm, controlling the diameter of the pupil and thus the amount of light that enters the eye. 613

Purkinje cell(s). One of four types of neurons produced by the ventricular layer that migrate to the cortex. As it migrates, each Purkinje cell reels out an axon that maintains synaptic contact with neurons in the developing cerebellar nuclei, which will constitute the only efferents of the mature cerebellar cortex. 264

Purkinje cell layer. A layer formed by Purkinje cells that underlies the external germinal layer. It is initially multilayered, but becomes a single layer when foliation is complete. 267

Purkinje fibers. Modified cardiac fibers composed of Purkinje cells, occurring as an interlaced network in the subendocardial tissue and constituting the terminal ramifications of the conducting system of the heart.* 377

Pycnodysostosis. A condition characterized by enhanced bone mass, which is caused by mutations in Cathepsin K. 241b

Pyloric atresia. Congenital obstruction of the gastric outlet by an antral or pyloric membrane, characterized by vomiting of gastric contents only.* 161

Pyloric stenosis, hypertrophic, infantile. A disorder characterized by the development of pyloric hypertrophy and a gastric outlet obstruction (which classically presents with projectile vomiting in the first two months postnatally) and abnormal thickening of the pyloric muscle. 470b

Pyramidal cells. The principal excitatory neurons of the neocortex, which project to subcortical targets and to the contralateral hemisphere. 285

Q

Quadratus lumborum muscles. The muscles that fill the space between rib XII and the iliac crest on both sides of the vertebral column, overlapped medially by the psoas major muscles. Formed by the hypomeres in the lumbar region, they depress and stabilize rib XII and contribute to lateral bending of the trunk.[§§] 234

[§§] Adapted from Drake RL, Vogl W, Mitchell AWM. 2005. Gray's Anatomy for Students. Philadelphia, Churchill Livingstone.

R

Rac1. A member of the Rho family of GTPases, required for regulation of actin organization and development of lamellipodia of gastrulating cells within the primitive streak. 81b

Radial artery. The artery that originates in the brachial artery and distributes to the forearm, wrist, and hand. 411, 413f

Radial glia. Also called Bergmann glia. Glial cells that are formed in the cerebellum from neurons and glioblasts. 267, 267f

Radical fringe. One of three glycosyltransferases that regulate Notch signaling. 159

Radioulnar synostosis with amegakaryocytic thrombocytopenia. A syndrome caused by mutations to Hoxd11 that results in proximal fusion of the radius and ulna. 635t

Raf (Mapk kinase kinase). Also called Mapkkk. One of three kinases that are sequentially phosphorylated in an Erk/Mapk cascade. 158

Raldh-2 (Retinaldehyde dehydrogenase-2). A limiting enzyme in retinoic acid biosynthesis. Restriction of Raldh-2 expression to the caudal area of the heart is associated with atrial gene expression. 355b

Randomized laterality. Randomization of body plan. For example, mutation in Nodal, Lefty1, Lefty2, Cryptic, and Acvr2b causes half of the those affected to exhibit a reversed body plan, while the remainder have a normal body plan.[***] 383b

Rank. **R**eceptor **a**ctivator of **n**uclear factor **k**appa B. A receptor involved in the differentiation of osteoclasts and the activation of mature osteoclasts. 238b

RAR(s). **R**etinoic **a**cid **r**eceptors. Ligand-dependent transcription factors that exist as alpha, beta, and gamma isoforms, to which retinoic acid binds. 161

[***] Adapted from Wood WB. 2005. The left-right polarity puzzle: Determining embryonic handedness. *PLoS Biol* 3(8):e292.

Rarα1/Rarβ1-3. Retinoic acid receptors, expressed exclusively within the stromal compartment of the developing kidney. 375b–376b

Rares. Retinoic acid response elements. Response elements, located within gene promoters, to which RARs bind, thereby regulating the expression of target genes. 562b

Ras. A proto-oncogene. 302b

Rathke folds. A lateral pair of integrated mesodermal septal systems that forms the urorectal septum. 473

Rathke's pouch. A diverticulum of the stomodeal roof, which grows to meet the infundibulum and becomes the anterior pituitary. 250b, 282, 283f

Rax. A homeobox gene expressed in the eye field. When deleted it leads to the arrest of eye development at the neural plate stage, resulting in anophthalmia or microphthalmia. 602b

Reciprocal inductive signals. Signals from the metanephric blastema that regulate the orderly branching and growth of the bifurcating tips of the ureteric buds. 487

Recombination. The result of the process of crossing over, in which two homologous chromosomes exchange large segments of DNA during the prophase of meiosis I. The new combinations of genetic material increase the genetic variability of the future gametes. 24, 148

Rectoprostatic urethral fistulas. A narrow type of rectourethral passage, occurring in males, that connects the rectum to the prostatic urethra. 536b, 537f, 538b

Rectourethral fistulas. Abnormal passages formed when caudal portions of the urorectal septal folds fail to grow and fuse and the caudal part of the cloaca is not separated into the urogenital sinus and anorectal canal. 536b, 537f, 538b, 538f

Rectovaginal fistulas. Abnormal passages occurring in females that connect the rectum to the vagina. 537f, 538b, 538f

Rectovesical fistulas. Abnormal communications between the rectum and the bladder. 538b, 538f

Rectum. The distal portion of the large intestine, beginning anterior to the third sacral vertebra as a continuation of the sigmoid and ending at the anal canal.* 435b

Rectus abdominis muscle. Muscle formed by the ventral segment of the hypomere that flexes the lumbar vertebrae and supports the abdomen.* 234

Rectus muscle. Extraocular muscle derived from mesoderm that migrates to surround the developing eyes. 559

5α-Reductase. An enzyme that converts testosterone to 5α-dihydrotestosterone, which is necessary for development of the prostate. 510

Reduction defects. Anomalies in which a limb or part of a limb is missing. 632b, 633f

Reelin. A large glycoprotein secreted by Cajal-Retzius cells that orchestrates the inside-to-outside migration of neurons in the cortical plate. 285

Refsum disease. A hereditary peripheral neuropathy similar to Charcot-Marie-Tooth disease, with additional symptoms such as anosmia, deafness, retinitis, ichthyosis, and ataxia. 308b

Reichert's cartilage. Cartilage formed by the second pharyngeal arch that ultimately forms the stapes of the middle ear, the styloid process of the temporal bone, the fibrous stylohyoid ligament, and the lesser horns and upper rim of the body of the hyoid bone. 543b, 553, 554f

Relaxin-like factor. Also called Insulin-like factor-3 (Insl3). A factor generated by the Leydig cells, which plays a role in the development of the testes. 529b–530b

Renal agenesis. The failure of one (unilateral) or both (bilateral) kidneys to form. 179, 334b, 493b–494b, 489

Renal arteries. Arteries that originate in the abdominal aorta and distribute to the kidney, suprarenal gland, and ureter.* 410f, 411, 495, 496f

Renal columns. Also called columns of Bertin. Zones of nephron-containing cortical tissue that separate the renal pyramids of the kidney. 489, 489f

Renal corpuscles. Bodies forming the beginnings of the nephrons, each consisting of a glomerulus (a tuft of capillaries), surrounded by the glomerular capsule (an expanded portion of the renal tubule).* 485

Renal mesangial sclerosis. An abnormal thickening of the glomerular basement membrane and mesangial extracellular matrix. 494b

Renal papillae. The blunted apex of a renal pyramid, found in the inner zone of the renal medulla and projecting into a renal sinus.* 489, 489f

Renal pelvis. Part of the collecting portion of the metanephric kidney, formed by the first bifurcation of the ureteric bud. 487

Renal pyramids. The conical masses that make up the substance of the renal medulla, which contain the loops of Henle, the collecting ducts, and the straight arterioles of the kidney.* 489, 489f

Renal-coloboma syndrome. A rare autosomal dominant syndrome characterized by optic nerve coloboma, renal anomalies, and vesicoureteral reflux.††† 494b

Renal-splenic ligament. The mesenteric connection between the spleen and the left kidney, established by the rotation of the dorsal mesogastrium. 454

Reproductive cloning. A process in which the blastocyst is used to make embryonic stem cells and is then transplanted into the uterus of the donor animal (thus, only female donors can be used). If normal embryogenesis ensues, a clone will be delivered, that is, an offspring genetically identical to its mother. 162

Reproductive efficiency. The likelihood of an intercourse producing a term pregnancy. 44b

Resegmentation. A process in which the sclerotome of each somite subdivides into cranial and caudal segments, each of which fuses with the adjacent caudal or cranial segment, respectively, contributing to a vertebra. Resegmentation allows motor axons and dorsal root ganglia to lie between vertebrae, rather than running through them. 217b

††† From Wein AJ, ed. 2007. Campbell-Walsh Urology, .9th ed. Philadelphia, Saunders.

Respiratory distress syndrome. Pulmonary insufficiency that is accompanied by gasping and cyanosis. 326b

Respiratory diverticulum. A ventral evagination of the foregut, the primordium of the lungs, that is formed on day 22 of gestation. 319b, 321, 322f

Respiratory failure. A condition resulting from respiratory insufficiency, in which there is persistent abnormally low arterial oxygen tension or abnormally high carbon dioxide tension.* 326b

Respiratory system. The tubular and cavernous organs and structures by means of which pulmonary ventilation and gas exchange between ambient air and the blood are brought about. The chief organs involved are the nose, larynx, trachea, bronchi, bronchioles, and lungs.* 320

Respiratory tree. The branches of the respiratory system, generated when the primary bronchial buds undergo rounds of branching. 324b–325b, 325f

Ret. The gene expressed in the developing renal system and in all cell lineages of the peripheral nervous system, which is required for normal enteric nervous system development. 471b–472b, 490b, 491f

Rete testis. A set of thin-walled ducts formed by Sertoli cells in the region adjacent to the mesonephros and devoid of germ cells. It connects the seminiferous tubules with a limited number of mesonephric tubules and canalizes at puberty to form a conduit connecting the seminiferous tubules to the mesonephric ducts. 482b, 505

Reticular layer. A thick underlying layer of the dermis consisting of dense, irregular connective tissue. 201f, 202

Retina. The innermost of the three tunics of the eyeball, surrounding the vitreous body and continuous posteriorly with the optic nerve.* 176–277b, 274b, 277f, 277b–279b, 278f, 279f, 586b, 607-608, 608f, 611, 614b

Retinal dysplasia. A congenital defect resulting from the abnormal growth and differentiation of a retina that fails to develop into functioning tissue and forms tubular, acinic rosettes.* 614b

Retinal ganglion cells (RGCs). The projection neurons of the retinae, which produce axons that grow across the retinae and then through the optic nerves and tracts to synapse in the lateral geniculate nucleus. 274b, 276b–279b, 277f, 278f, 279f, 279b-281b, 281f, 607, 608f, 610b

Retinal progenitor cells. The layer of cells adjacent to the intraretinal space that forms two cellular embryonic retinal layers: an outer neuroblastic layer and an inner neuroblastic layer. 610b

Retinaldehyde dehydrogenase-2 (Raldh-2). A limiting enzyme in retinoic acid biosynthesis. 355b

Retinitis pigmentosa. A group of diseases, frequently hereditary, marked by progressive loss of retinal response (as elicited by the electroretinogram), retinal atrophy, attenuation of the retinal vessels, and clumping of the pigment, with contraction of the field of vision. It may be transmitted as a dominant, recessive, or X-linked trait and is sometimes associated with other genetic defects.* 597b, 614b

Retinoic acid (Ra). Protein derived from Vitamin A (retinol). 161f, 161–162, 229b, 328b, 560b, 562b, 563f

Retinoid(s). Vitamin A and its analogs. 253b

Retinoid X receptors (RXRs). One of two groups of receptors to which retinoic acid binds. RXRs exist as three isoforms: alpha, beta, and gamma isoforms. 161

Retinopathy of prematurity. A bilateral retinopathy typically occurring in premature infants treated with high concentrations of oxygen. It is characterized by vascular dilation, proliferation, and tortuosity, edema, and retinal detachment, with ultimate conversion of the retina into a fibrous mass that can be seen as a dense retrolental membrane. Usually, growth of the eye is arrested and may result in microphthalmia, and blindness may occur.* 614b

Retroperitoneal organs. The organs located behind the peritoneum from a viewpoint inside the peritoneal cavity, such as the kidneys and bladder. 440f, 440–441

Reverse genetic approach. The method in which an investigator begins with a known gene and mutates it to determine its function during development. 142

RH factors. A group of genetically determined surface molecules that are present on the plasma membrane of red blood cells in most, but not all, individuals. Individuals whose blood cells carry an RH factor are RH+; individuals whose blood cells lack one are Rh-. 173, 175–176

Rhinencephalon. Literally, the "nose-brain," made up of the olfactory bulbs and tracts along with the olfactory centers and tracts of the cerebral hemispheres. 272

Rhizomelia. A disorder resulting in shortened stylopod (humerus and femur). 219b, 634t

RhoA. The member of the Rho family of GTPases required to regulate actin organization and development of lamellipodia of gastrulating cells within the primitive streak. 81b

RhoB. A small GTP-binding protein implicated in assembly of the actin cytoskeleton. 119b

Rhombencephalon. Also called hindbrain. The part of the brain developed from the posterior of the three primary brain vesicles of the embryonic neural tube, comprising the metencephalon and myelencephalon.* 119, 247b, 251, 252f, 261, 263–267, 264f, 265f-268f

Rhombic lip. The dorsal margin of the alar plate, adjoining the massively expanded roof plate. 261

Rhombomeres. Small repetitive segments of the hindbrain that partition the neural tube into approximately equal-sized segments. Rhombomeres are transient structures, becoming indistinguishable by early in the 6th week. 247b

Rhythm method. An approach to preventing conception by restricting coitus to the so-called safe period, avoiding the days just before and after the expected time of ovulation.* 103b

Rieger syndrome. A condition in which defects form in both eyes and teeth, but laterality defects are absent. It is the result of haploinsufficiency of the Pitx2 gene. 76b

Ring chromosomes. A chromosome in which both ends have been lost (deletion) and the two broken ends have reunited to form a ring, resulting from an error during meiosis.* 34b

Risorius muscle. The muscle of facial expression formed from the second pharyngeal arch. 559

RNAi. Interfering, double-stranded RNA, which can be injected into cells to knock down gene expression. 150

Robinow syndrome. Dwarfism associated with increased interorbital distance, malaligned teeth, bulging forehead, depressed nasal bridge, and short limbs.* 636t

Robo2. The receptor for Slit2, expressed in the urogenital ridge mesenchyme. 490b, 491b

Rod photoreceptors. One of two types of photoreceptors formed in the outermost layer of the mature neural retina, and are necessary for vision in low light. 607, 608, 608f

Roof plate, of neural tube. A non-neurogenic structure, made up of dorsal cells that secrete Bmps, which connects the ventral and dorsal plates. 247b, 257, 257f

Ror2. A gene whose mutations can cause brachydactyly type B1 or Robinow syndrome. 636t

ROSA26 transgenic mice. Mice that express the reporter gene LacZ in all of their tissues during development. 150

Round ligament of the ovaries. Ligament that develops from the superior gubernaculum and connects the uterus to the ovary. 530, 532f

Round ligament of the uterus. Ligament that develops from the inferior gubernaculum and connects the fascia of the labia majora to the uterus. 530, 532f

RU-486. An antiprogesterone compound. When taken within 8 weeks of the last menses, an adequate dose will initiate menstruation, sloughing off a conceptus if one is present. 45b

Rubella virus. The agent of rubella, or German measles, which can cross the placenta and infect the fetus, possibly causing patent ductus arteriosus, hearing loss, or cataracts in the fetus. 176, 432b, 596b, 614b

Runx2. Also known as core binding factor 1 (Cbfa1). Runt-related transcription factor 2, a transcription factor important for bone development. 221b, 221f, 237b, 238b

Rx. A transcription factor expressed in the eye field that regulates normal eye development. Mutations or deletions result in anophthalmia or microphthalmia. 602b, 608b, 609f

S

Saccular stage. The level of lung development during which the terminal sacs form and mature. 322t

Saccule. Part of the membranous labyrinth, formed by the pars inferior, which is connected to the cochlea by the ductus reuniens. 583b

Sacral agenesis. Also called caudal agenesis, caudal regression syndrome, or caudal dysplasia. A condition characterized by varying degrees of (1) flexion, inversion, and lateral rotation of the lower extremities; (2) anomalies of lumbar and sacral vertebrae; (3) imperforate anus; (4) agenesis of the kidneys and urinary tract; and (5) agenesis of the internal genital organs except for the gonads. 92b, 93f, 94b, 94f

Sacral arteries. Three arteries: the lumbar and lateral sacral arteries formed by the ventral branch of each intersegmental vessel in the lumbar and sacral regions, and the medial sacral artery, a short continuation of the dorsal aorta beyond its bifurcation into the common iliac arteries. 411

Sacrum, ala of. The triangular bone that is just below the lumbar vertebrae. Its ala is the upper surface of the lateral part of the sacrum.* 227

Saethre-Chotzen syndrome. An autosomal dominant disorder characterized by acrocephalosyndactyly in which the syndactyly is mild, and by hypertelorism, ptosis, and sometimes mental retardation.* 550b, 636t

Salivary glands. The glands of the oral cavity whose combined secretion constitutes the saliva. Three pairs of salivary glands develop in humans: the parotid, submandibular, and sublingual glands.* 202, 578–579

Salivatory nerves. Cranial nerve nuclei located on the visceral efferent column that provide preganglionic parasympathetic innervation to the salivary and lacrimal glands via nerves VII and IX. 260f

Sall1. A gene whose mutation can cause Townes-Brocks syndrome, preaxial polydactyly, and bifid or finger-like thumb. 636t

Satellite cells. Small quiescent cells underlying the basal lamina of the muscle fiber. In response to exercise or muscle damage, satellite cells form myocytes, which permit further muscle growth. 217b, 220, 221b, 297b

Scala tympani. The perilymph-filled part of the cochlea that is continuous with the scala vestibuli at the helicotrema, is separated from other cochlear structures by the spiral lamina and basilar membrane of the cochlear duct, and ends blindly near the fenestra cochleae.* 593

Scala vestibuli. The perilymph-filled part of the cochlea that begins in the vestibule, is separated from other cochlear structures by the spiral lamina and Reissner's membrane of the cochlear duct, and becomes continuous with the scala tympani at the helicotrema.* 593

Scalene muscles. The strap muscles of the back that are formed by the hypaxial myoblasts in the cervical region. 234

Scanning electron microscopy. A form of microscopy in which electrons bounce off the surface of the specimen at an angle, producing a three-dimensional picture.‡‡‡ 393b, 394f

Scatter factor (Sf). One of several families of growth factors that bind to receptors and have a cytoplasmic Tyrosine kinase domain. 157

Scf. Stem cell factor. A trophic factor important for the survival and proliferation of hematopoietic stem cells. 390b

Schizophrenia. A mental disorder characterized by disturbances in form and content of thought (loosening of associations, delusions, and hallucinations), mood (blunted, flattened, or inappropriate affect), sense of self and relationship to the external world (loss of ego boundaries, dereistic thinking, and autistic withdrawal), and behavior (bizarre, apparently purposeless, and stereotyped activity or inactivity).* 269b

Schwann cells. Cells that form the myelin sheaths of peripheral nerves. 306b–307b, 639

Sciatic artery. Also called ischiadic artery. A remnant of the axis artery that serves the sciatic nerve in the posterior thigh. 413

‡‡‡ Adapted from Murray P, Pfaller M, Rosenthal K. 2005. *Medical Microbiology*, ed 5. Philadelphia, Mosby.

Sclera. The outer, fibrous layer of the mesenchymal capsule surrounding the optic cup, which supports and protects the inner structures of the eye. 611, 612f

Sclerocornea. Corneal clouding. 614b

Sclerotomes. One of three kinds of mesodermal primordia derived from the somites, which develop into the vertebrae and ribs. 92b, 101b, 128, 129f, 217b, 222, 222b, 223f, 225f–228f, 226b, 226–227

Scn5a. A gene that encodes cardiac ion channels. 383b

Scoliosis. Lateral bending of the spinal column. 230b

Scribble. A planar-cell polarity gene that plays a role in neurulation. 112b

Scrotum. The pouch that contains the testes and their accessory organs.* 482b, 521, 523f

Sdf1. Stromal cell-derived factor-1. A chemokine factor involved in the regulation of primordial germ cell (PGC) honing that also acts as a PGC survival factor. 20b

Sebaceous glands. Glands that secrete sebum, produced by the downgrowth of the epidermis. 193b, 201f, 202, 207

Sebum. An oily substance secreted by the sebaceous glands that protects the skin against friction and dehydration. 207

Secondarily retroperitoneal organs. Organs initially suspended by mesentery that later become fused to the body wall, taking on the appearance of retroperitoneal organs. These include the ascending and descending colon, duodenum, and pancreas. 435b, 441

Secondary body development. A period of development that involves the direct formation of organ rudiments from the tail bud without the prior formation of distinct germ layers. 98

Secondary cartilages. Cartilages that arise within the periosteum of a membrane bone and grow in response to mechanical stimulation. Many of the facial bones form from secondary cartilages. 556

Secretory phase. The stage of the menstrual cycle that occurs after ovulation in which estrogens and progesterone are secreted and the uterine endometrial layer thickens. 39

Segment polarity genes. One of four classes of zygotic genes, which act in establishing the basic anterior-posterior body plan. 151

Segmentation. The process that involves the formation of serially repeated, functionally equivalent units or segments. 88b, 90b

Segmentation clock. An oscillator whose periodic signal is used to specify somite boundaries at progressively more caudal levels where the signal coincides in both time and space with a traveling threshold level of expression of another signaling molecule. 91b, 229b

Selectins. A type of lectin possibly involved in blastocyst adhesion. 55b

Sema3C. The gene important in targeting cardiac neural crest cells into the pharyngeal arches and outflow tract. 376b

Semaphorins. A large family of cell surface and secreted guidance molecules defined by the presence of a conserved "Sema" domain. They are important in axon guidance as well as in directing neural crest cell migration. 121b, 312b, 376b, 642b–643b

Semicircular canals. Three canals, the anterior, posterior, and lateral), which are oriented perpendicularly to each other. Along with the utricle and the saccule, they comprise the vestibular apparatus of the ear. 583b, 588

Semilunar ganglion. Also called trigeminal ganglion. The general afferent ganglion of cranial nerve V. 314

Semilunar sinuses. Two cavities located at the origin of the ascending aorta and pulmonary artery, which are formed from intercalated cushion tissue. 375

Semilunar valve. A structure having semilunar cusps, e.g., the aortic valve and pulmonary valves. The term is sometimes used to designate the semilunar cusps comprising these valves.*

Semilunar valvular stenosis. Abnormal narrowing of either the aortic valve or the pulmonary valve. 380b

Seminal vesicles. The paired sacculated pouches that are attached to the posterior part of the urinary bladder. The duct of each joins the ipsilateral ductus deferens to form the ejaculatory duct.* 28, 505, 511f, 511–512, 512b

Seminiferous epithelium. The stratified epithelium that lines the seminiferous tubules.* 19, 27

Seminiferous tubules. Channels in the testis in which the spermatozoa develop and through which they leave the gland.* 9, 482b, 505

Sensory capsules. The bones encapsulating the sensory organs. 545

Sensory ganglia. Ganglia that contain the cell bodies of sensory neurons for the corresponding cranial nerves. 313–314

Sensory organs. The olfactory organs, eyes, and inner ears. 559

Septal cusp. The structure that is attached to the membranous interventricular septum.* 370, 372f

Septation. The generation of the membranous (or fibrous) portion of the interventricular and interatrial septa and the separation of the aorta from the pulmonary artery. 323

Septomarginal trabecula. Also called moderator band. The prominent trabecula that forms the boundary between the trabeculated primary fold and the inlet septum. It connects the muscular septum with the forming anterior papillary muscle attached to the right atrioventricular valve. 368f, 368–369

Septo-optic dysplasia. Also called De Morsier syndrome. Hypoplasia of the optic nerve that occurs in conjunction with pituitary hypoplasia and midline brain abnormalities. Children with this syndrome are short in stature due to growth hormone deficiency. The condition is caused by mutations in the Hesx1 gene. 614b–615b

Septum intermedium. Also called atrioventricular septum. The structure that divides the common atrioventricular canal into right and left atrioventricular canals. It is formed at the end of the 6th week when the endocardial-derived dorsal and ventral cushions meet and fuse. 364f–366f, 365

Septum primum. A crescent-shaped myocardial wedge that extends into the atrium from the cranial-dorsal wall as the primitive atrial chamber expands, separating the right and left atria. Eventually it fuses with the septum secundum to close the foramen ovale. 337b, 362, 363f

Septum secundum. A crescent-shaped ridge of thick, muscular tissue that forms from the ceiling of the right atrium and contributes to the separation of the right and left atria. Eventually it fuses with the septum primum to close the foramen ovale. 337b, 365, 365f

Septum spurium. A transient septum formed by the left and right valves cranial to the sinuatrial orifices. 357

Septum transversum. A thickened bar of mesoderm just caudal to the cranial margin of the embryonic disc that forms the initial partition separating the coelom into thoracic and abdominal cavities. It gives rise to part of the diaphragm and ventral mesentery of the stomach and duodenum. 103, 104f, 319b, 329, 330f, 455, 455f

Serous membranes. Two membrane layers that line the intraembryonic coelom: the somatic mesoderm lining the inner surface of the body wall and the splanchnic mesoderm ensheathing the gut tube. 101b, 106

Serrate. A ligand that binds to Notch receptors to initiate Notch signalling. 158, 159

Sertoli cells. The elongated cells in the seminiferous tubules to which the spermatids become attached. They provide support, protection, and possibly nutrition until the spermatids become transformed into mature spermatozoa.* 19, 479b, 482b

Severe combined immunodeficiency. A group of rare congenital disorders characterized by gross impairment of both humoral and cell-mediated immunity and the absence of T lymphocytes. Some forms are also characterized by a lack of B lymphocytes. In most cases, all classes of immunoglobulins are nearly or completely absent, and there is marked lymphocytopenia. Persistent diarrhea, chronic mucocutaneous candidiasis, and failure to thrive occur in infancy.* 189

Sex chromosomes. The two chromosomes that determine the sex of an individual. There are two kinds of sex chromosomes, X and Y: individuals with one X chromosome and one Y chromosome (XY) are genetically male; individuals with two X chromosomes (XX) are genetically female. 21

Sex determination, primary. Expression of the transcription factor encoded by the Sry gene in somatic support cells of the indifferent presumptive gonad, which triggers male development. 503

Sex reversal. A condition in which an XX individual develops as a male or an XY individual develops as a female. 508b

Sf1. Steroidogenic factor-1, a gene required for the early formation of the indifferent gonad that encodes a nuclear hormone receptor protein. It is expressed in the forming suprarenal gland and early somatic cells. 505b, 507b–508b

Shh. Sonic hedgehog, one of three orthologs of the Hedgehog gene expressed in mammals whose signaling determines the fate of cells. 73b, 74b, 128b–129b, 134b, 146, 147, 156f, 156–157, 206b, 214b, 253b, 254f, 255b, 328b, 340b, 442b, 444b–445b, 452b, 467, 468f, 513b, 514f, 515b, 522b, 524f, 524b–525b, 549b–550b, 592b, 602b, 608b, 609f, 610b, 628b, 630b, 631f, 632f, 636t

Shox. A gene involved in limb development, whose mutations can cause Léri-Weill dyschondrosteosis or Langer mesomelic dysplasia. 636t

Shp2. A nonreceptor Tyrosine phosphatase involved in intracellular signal transduction. 383b

Shroom. An actin-binding protein. Overexpression of Shroom in cultured epithelial cells is sufficient to cause apical constriction. 111b

Signal transduction proteins. A series of intracellular proteins that initiate an intracellular signaling cascade. 154

Signaling centers. Groups of cells in the early embryo that secrete growth factors that form morphogen gradients and inform cells about their position and fate. 253b, 254b

Signaling pathways. Families of secreted factors that diffuse through the extracellular space to cause intercellular communication. 133b, 150–162

Silent carriers. Females who inherit a recessive X-linked mutation from one parent and a wild-type allele from the other. They do not exhibit symptoms of the disease because of compensation by cells in their bodies that express the wild-type allele, but may transmit the disease to their sons. 67b

Sim1. A marker of nephrogenic mesoderm. 486b

Simpson-Golabi-Behmel syndrome. A syndrome that, in some cases results from a mutation in the gene for Glypican-3. This mutation causes a protruding jaw, broad nasal bridge, short hands and fingers, heart defects, renal defects, and hypogonadism. 67, 635t

Sinoatrial (SA) node. The primary pacemaker region of the heart. 357, 376–377

Sinus horns. Paired cavities of the sinus venosus into which the common cardinal veins drain. The left sinus horn becomes the coronary sinus, which drains the myocardium. The right sinus horn is incorporated into the posterior wall of the future right atrium. 346

Sinus venarum. The portion of the atrium that consists of the incorporated sinus venosus, which will give rise to the definitive right atrium. 357

Sinus venosus. The common venous receptacle in the embryonic heart, attached to the posterior wall of the primordial atrium. It receives the umbilical and vitelline veins and the common cardinal veins.* 346

Sinusal tubercle. A slight thickening formed by the wall of the pelvic urethra at the point where it contacts the distal tips of the Müllerian ducts. 518, 519f

Sinusoids, maternal. Space formed by expansion of the maternal capillaries near the syncytiotrophoblast. These sinusoids rapidly anastomose with the trophoblastic lacunae. 58f, 59–60, 62f

Sinuvaginal bulbs. A pair of evaginating swellings, formed by the thickening of the endodermal tissue of the sinusal tubercle in the posterior urethra, which fuse to form the vaginal plate. 482b, 518, 519f

Sirenomelia. A rare condition characterized by the fusion of the lower limb buds during early development, resulting in a “mermaid-like” habitus. 71b, 92b, 93f

Situs inversus. Reversal of normal left-right asymmetry. 321b, 353b

Situs inversus viscerum totalis. A rare human disorder in which the handedness of all of the viscera is reversed. 74b

Situs solitus totalis. Normal left-right asymmetry. 74b

Six1. Sine oculis homeobox homolog 1, a transcription factor that interacts with Eya1. Mutations in Six1 cause branchio-oto-renal (BOR) syndrome. 494b

Six3. A transcription factor that is sufficient and required for lens formation in the mouse. Mutations are associated with holoprosencephaly in humans. 549b

Six6. A transcription factor that regulates proliferation of the eye field in the frog. Haploinsufficiency causes anophthalmia in humans. 608b, 609f

Skeletal elements, of limbs. Elements of the limb skeleton that develop from mesodermal condensations that appear along the long axis of the limb bud during the 5th week.. 617b

Skeleton, appendicular. Bones of the limbs and girdles formed by endochondral ossification. 234

Skin fragility syndromes. Syndromes caused by mutations in keratins and desmosomal proteins that manifest as blistering or separation of the epidermis at the level at which the mutated gene plays a critical role in adhesion. 198b

Skull. The skeleton of the head, including the cranium and mandible.* 545, 546f, 547, 548f, 549f

Slug. A zinc-finger transcription factor that promotes neural crest cell delamination. 119b

Smads. A family of nine proteins that are orthologs of the Drosophila Mothers against Decapentalegic protein. Ligand binding results in the phosphorylation of Smads, which then enter the nucleus where they act either as transcriptional coactivators or corepressors. 97b, 157

Small for gestational age (SGA) infants. Infants whose fetal growth is markedly retarded. A newborn is considered to be SGA if he/she weighs less than 2500 grams at term or falls below the 10th percentile for gestational age. 178

Small patella syndrome. Hindlimb malformation caused by mutation in Tbx4. 638b

Smith-Lemli-Opitz syndrome. An autosomal recessive hereditary syndrome characterized by multiple congenital anomalies, including microcephaly, mental retardation, hypotonia, incomplete development of male genitalia, short nose with anteverted nostrils, syndactyly of second and third toes, and sometimes holoprosencephaly. It is caused by a mutation in the Dhcr7 gene.* 550b

Smoothened. A transmembrane signaling protein in the Hedgehog signaling pathway. 156–157

Snail. A zinc-finger transcription factor that is responsible for repressing epithelial characteristics in the mesenchymal cells of the primitive streak. 81b

Soho. Sense organ homeobox, a transcriptional control gene that plays a part in subdividing the cranial domain and patterning the craniocaudal axis. 276b

Somatic afferent neurons. Cranial nerve nuclei. Special afferent neurons subserve the special senses of hearing and balance, while general afferent neurons subserve general sensation over the head and neck, as well as the mucosa of the oral and nasal cavities and pharynx. 259f, 260f, 261

Somatic cell nuclear transfer. A cloning process in which the female pronucleus is removed from the egg and then replaced with a diploid nucleus obtained from a donor cell from an adult animal. 162

Somatic efferent neurons. Cranial neurons that innervate the extrinsic ocular muscles and the muscles of the tongue. 258, 259f, 260f, 261

Somatic nervous system. One of the two major functional divisions of the nervous system. The somatic nervous system innervates the skin and most skeletal muscles. 251, 297b, 299

Somatic support cells. Cells formed by the proliferation of coelomic epithelium, which in turn proliferate to form the genital ridges. They eventually differentiate into Sertoli cells in males and follicle cells in females. 18f, 19, 479b, 500, 515

Somites. A series of segmental blocklike mesodermal condensations, formed by paraxial mesoderm in the future trunk region. 85, 87–88, 98, 128–130, 128b–130b, 129f, 130f, 217b, 219-220, 222, 223f, 224f, 234b, 235f

Somitocoele cells. Loose core cells in the central cavity of the somites. 222, 223f

Somitogenesis. The process of formation of spermatozoa.* 87–88, 88b, 88f, 89f, 90f, 90b–92b, 91f, 91b–92b

Sox. A family of HMG box-containing transcription factors. 43b, 56b, 57b, 237b, 428, 593b, 602b

Sp-B. Surfactant protein B, one of the genes encoding surfactant proteins. The absence or mutation of this gene can lead to hereditary surfactant protein B deficiency, which causes respiratory failure in full-term newborns. 326b

Spemann-Mangold organizer. An area of the early embryo that sends out signals to pattern the newly formed mesoderm into its medial-lateral subdivisions. 81b

Sperm. The final cells produced by spermatogenesis in males. Following coitus, they fertilize the ovulated egg in the female. 15b

Sperm chemotropic factor. A currently unknown factor that evidence suggests is contained in the ovulated follicle. Only capacitated sperm are able to respond to this factor by directed swimming toward the egg. 39

Spermatic duct. Also called vas deferens. The excretory passage of the testis, formed by differentiation of the mesonephric duct, which joins the excretory duct of the seminal vesicle to form the ejaculatory duct.* 505

Spermatids. Two definitive spermatocytes produced by the second meiotic cell division in males. They undergo dramatic changes that convert them into mature sperm while they complete their migration to the lumen. 24–25

Spermatocytes. The mother cell of a spermatid.* 21, 24–25, 24f

Spermatogenesis. The process of gametogenesis in males, which produces the sperm or spermatozoa. Spermatogenesis takes place in the seminiferous tubules of the testes in puberty. 15b, 20, 25, 26f, 27–28, 27f

Spermatogonia. Gamete precursor cells in males. Spermatogonia are produced by differentiation of the primary germ cells. They undergo spermatogenesis and eventually mature into spermatozoa. 15b, 20

Spermatozoa. Also called sperm. The final cells produced by spermatogenesis in males. 15b, 20, 25, 25b, 27–28, 27f

Spermiation. The final step of spermatogenesis in which the last connections with Sertoli cells break, releasing the spermatozoa into the tubule lumen. 25

Spermiogenesis. The process of sperm cell differentiation. 25

Sphenoid sinuses. Extensions of the ethmoid sinuses that enlarge within the sphenoid bones throughout infancy and childhood. 571–572

Sphenomandibular ligament. Formed from the proximal part of Meckel's cartilage, the ligament extends from the angular spine of the sphenoid bone downward medial to the temporomandibular articulation and attaches to the lingula of the mandible.* 553

Sphenopalatine ganglion, of nerve VII. A visceral efferent neuron that originates from rhombencephalic neural crest cells. 314

Spin cycle. A type of mouse mutant that exhibits convergent extension defects. 111b

Spina bifida. The open neural tube defect of the spinal cord that results in an open spine in which the vertebral arches fail to form properly, forming a spinelike bony protuberance on either side of the open spinal cord. 130b, 186

Spina bifida aperta. Spina bifida in which the spinal cord is open to the body surface. 113b, 230b

Spina bifida occulta. Spina bifida in which the defect is hidden. 113b, 113f, 230b

Spina vestibuli. Also called the atrial spine. A projection of cells sent into the atrium from the dorsal mesocardium that joins the septum primum and contributes to the atrial septum. 358, 362–363

Spinal accessory nerve. Cranial nerve IX, a branchial efferent nerve that innervates the trapezius and sternocleidomastoid muscles. 260f

Spinal anomalies. Spinal defects caused by abnormal formation of the sclerotomes and neural tube, including scoliosis and spina bifida. 130b

Spinal cord. The part of the central nervous system that is lodged in the vertebral canal, formed from the caudal portion of the neural plate. It conducts impulses to and from the brain and controls many automatic muscular activities.* 94, 115b–116b, 117, 247b, 250b, 253, 257f, 257–258, 297b

Spinal nerves. The 31 pairs of nerves that arise from the spinal cord and pass out between the vertebrae, including 8 cervical pairs, 12 thoracic, 5 lumbar, 5 sacral, and 1 pair of coccygeal nerves.* 231, 258, 303–308, 305f

Spinocerebellar ataxia (SCA) syndromes. Any hereditary failure of muscular coordination with cerebellar malfunction that results in clinical manifestation. More than 30 have been mapped.* 269b

Spinous layer, of skin. Also called stratum spinosum. The inner keratinocyte layer of the epidermis. 193b, 196, 197f

Spiral arteries. Arteries through which maternal blood enters the intervillous spaces of the placenta. 173

Spiral organ of Corti. The structure that contains the sensory hair cells responsible for transducing sound vibrations into electrical impulses. 588

Splanchnic nerves. The preganglionic fibers that pass directly out of the chain ganglia at levels T5 to L2 to innervate neurons within the celiac, superior, mesenteric, aorticorenal, and inferior mesenteric ganglia. 310–311

Spleen. A large glandlike but ductless organ in the upper part of the abdominal cavity on the left side lateral to the cardiac end of the stomach. It has a flattened oblong shape and is about 125 mm long, the largest structure in the lymphoid system. Having a purple color and a pliable consistency, it is distinguished by two types of tissue: red and white pulp. The spleen disintegrates red blood cells and sets free hemoglobin, which the liver converts into bilirubin. It serves as a reservoir of blood and produces lymphocytes and plasma cells. During fetal life and in the newborn it gives rise to new red blood cells.* 435b, 454

Splenic vein. The vein that drains the spleen, part of the stomach, and the greater omentum. 419, 420f

Split-hand/split-foot type 4 syndrome. A syndrome caused by mutations in transcription factor Tp73l, which is characterized by longitudinal divisions of the autopod into two parts, often with absence of central digits. 634b, 637f

Splotch mouse. Pax3 mutant in which the limb and diaphragm muscles are absent. 242b, 375b

Spondylocostal dysostosis. An autosomal recessive condition characterized by vertebral defects such as hemivertebrae, rib fusions, and kyphoscoliosis. Because the vertebral column is short, the arms appear to be relatively long. It is caused by a mutation of the Notch pathway ligand Delta-like3 gene. 92b, 159, 230b, 231b

Spondyloepimetaphyseal dysplasia. The syndrome caused by a mutation in the Atpsk2 gene, which is characterized by bowed long bones, brachydactyly, enlarged knee joints, and joint degeneration. 635t

Spontaneous abortion. The unexpected or unintentional termination of a fetus caused by any of a number of natural causes (typically a result of chromosomal abnormalities), and not as the result of an intentional medically induced abortion procedure.

Sprouty. An endogenous Fgf inhibitor that provides negative feedback regulation by antagonizing Fgf signaling, thereby limiting the amount of tracheal branching that occurs. 158, 328b

Squames. Flattened, scalelike, and terminally differentiated keratinocytes. 200

Sry. The sex-determining gene of the Y chromosome. In males, the Sry gene is expressed in the somatic support cells, where it produces the Sry protein, which initiates a developmental cascade that leads to the formation of the testes, male genital ducts and associated glands,

male external genitalia, and the entire constellation of male secondary sex characteristics. 479b, 503, 504, 506f, 507b, 508b, 535b–536b

Stapedial artery. The artery that supplies blood to the primordium of the stapes bone in the developing ear, formed from a remnant of the second pharyngeal arch. 403, 405f, 406f

Stapedius muscle. The muscle that arises from the wall of a conical cavity in the pyramidal eminence on the posterior wall of the tympanic cavity and from its continuation anterior to the descending part of the facial nerve canal. It helps to damp down excessive sound vibrations, and is formed by the paraxial mesoderm in the second pharyngeal arch.[§§§] 599

Stapes. One of three auditory ossicles that develop in the mesenchyme adjacent to the tympanic cavity. The stapes is a second arch derivative. 543b, 553, 554f, 583b, 588, 598

Statoacoustic ganglion. The ganglion of the vestibulocochlear nerve (cranial nerve VIII) that innervates the sensory regions of the inner ear. 588, 592

Statoacoustic nerve. Also called the vestibulocochlear nerve (VIII). The nerve that arises from the otic placode and innervates the developing inner ear. 260f, 559, 583b, 588, 592

Steel. A stem cell factor that signals through the Tyrosine kinase c-Kit receptor and functions in the migration of melanoblasts. 157

Stellate cells. Cells produced in the ventricular layer that migrate radially to form the molecular layer of the definitive cortex. 264

Stellate ganglion. The ganglion formed when the inferior cervical ganglion fuses with the chain ganglion at T1. 310, 310f

Stem cell(s). Cells that can self-renew under appropriate conditions and produce daughters that can differentiate into multiple cell types.133b, 148, 162, 189, 219, 301b, 302f

Stem villi. One of the definitive types of chorionic villi, having trophoblastic cover, connective tissue (mesoblastic) core, and blood vessels.* 167b

[§§§] Adapted from Standring S, ed. 2005. *Gray's Anatomy: The Anatomical Basis of Clinical Practice*, ed. 39, Edinburgh, Churchill Livingstone.

Stensen's duct. Also called the parotid duct. The passage that drains the parotid gland and empties into the oral cavity opposite the second superior molar.* 579

Stereocilia. Specialized microvilli consisting of parallel dense bundles of actin filaments that are the mechanosensors of the hair cell. They are arranged in a "staircase" pattern at one edge of the cell. In the cochlea, the stereocilia on the different hair cells are all oriented in the same direction. This ordered and repetitive pattern is essential for hearing. 593, 593b, 596b, 597b

Sterilization. Any procedure by which an individual is made incapable of reproduction, such as vasectomy in males and ligation of the fallopian tubes in females.* 45b

Sternal bars. A pair of longitudinal mesenchymal condensations that form in the ventrolateral body wall. They eventually fuse and ossify to produce the definitive bones of the sternum. 227, 228f

Sternalis muscle. A band that is occasionally found parallel to the sternum on the sternocostal origin of the pectoralis major.* 234

Sternocleidomastoid muscle. Muscle that inserts on the mastoid process and superior nuchal line of the occipital bone, which flexes the vertebral column and rotates the head.* 559

Sternum. A longitudinal unpaired plate of bone comprising the middle of the anterior wall of the thorax. Formed by the sternal bars, it is made up of the manubrium, the body, and the xiphoid process.* 227

Steroidogenic factor-1 (Sf1). The gene required for the early formation of the indifferent gonad. 505b, 507b–508b

Stickler syndrome. Hereditary progressive arthro-ophthalmopathy.* 571

Stigma. A small, nipple-shaped protrusion on the projecting wall of the follicle, formed as ovulation approaches. 35

Stomodeum. An ectodermal lined space located near the future mouth opening, between the maxillary and mandibular processes. 563

Strabismus. The misalignment of gaze, which can be caused by abnormalities of the extraocular muscles or their innervation. 614b

Stratum corneum. Also called cornified layer of skin. The layer that forms as the third definitive (outer) layer of keratinocytes. 193b, 196, 197f

Stratum germinativum. The layer of stem cells that will continue to replenish the epidermis throughout life. 193b, 196, 197b–198b, 199f, 199–200, 201f

Stratum granulosum. Also called granular layer. The middle layer of the outer epidermis. 193b, 196, 197f, 201f

Stratum spinosum. Also called spinous layer. The inner layer of the outer epidermis. 193b, 196, 197f, 199, 201f

Stria vascularis. A specialized, thick epithelial layer above the spiral prominence of the ear.[****] 597b

Stroma. The matrix or supporting tissue of an organ.* 170, 446, 611

Stromal cell-derived factor-1. A chemokine expressed by cells along the migratory pathway that direct primordial gene cells from the yolk sac to the gut and dorsal mesentery and then to the gonadal ridge (presumptive gonad) in the posterior body wall. 20b

Stromal layer. A cellular layer formed when mesenchymal cells rapidly invade the corneal stroma. 611

Stylohyoid bone. A skull bone formed from the second pharyngeal arch. 543b

Stylohyoid ligament. A vertical fibroelastic aponeurotic cord attached superiorly to the tip of the styloid process of the temporal bone and inferiorly to the lesser horn of the hyoid bone.* 553, 554f

[****] Adapted from Standring S, ed. *Gray's Anatomy: The Anatomical Basis of Clinical Practice*, ed.39, Edinburgh, Churchill Livingstone.

Stylohyoid muscle. A muscle that originates from the styloid process, inserts into the body of the hyoid bone, and draws hyoid and tongue superiorly and posteriorly. It is formed from the paraxial mesoderm in the second pharyngeal arch.* 559

Styloid process. A long, pointed spine projecting downward from the inferior surface of the temporal bone, which is formed from the second pharyngeal arch.* 553, 554f

Stylopharyngeus muscle. A long, slender muscle formed by paraxial mesoderm in the third pharyngeal arch, which originates on the styloid process and inserts into the wall of the pharynx. This muscle raises the pharynx during vocalization and swallowing, and is innervated by the glossopharyngeal (IX) nerve. 559

Stylopod. The humerus or femur of the limb bud. 621b

Subcardinal system. A subsidiary venous network that grows caudally from the base of the posterior cardinal veins in the medial dorsal body wall. 385b

Subcardinal veins. A pair of veins that develops in the body wall medial to the posterior cardinal veins, replacing the posterior cardinal veins. 421, 421f–423f, 423

Subclavian artery. One of a pair of arteries that supplies the upper limb. The right subclavian artery is derived from the right fourth arch, a short segment of the right dorsal aorta, and the right seventh intersegmental artery. The left subclavian artery is formed by the left seventh intersegmental artery. 403, 405b

Subclavian vein. A vein that coalesces from the venous plexus of the left upper limb bud and empties into the proximal left anterior cardinal vein. 423f, 424

Subcommissural organ. A group of tall columnar ciliated ependymal cells lining the dorsal aspect of the cerebral aqueduct, which is situated dorsoventral to the commissure of the epithalamus. It is one of the circumventricular organs.* 274

Subcorium. Also called hypodermis. The subcutaneous fatty connective tissue that underlies the dermis. 202

Subcortical band heterotopia (SBH). A syndrome believed to result from the aberrant migration of differentiating neuroepithelial cells. Those affected have bilateral circumferential and symmetric ribbons of gray matter located just beneath the cortex,

separated from it by a thin band of white matter. Seizures, mild mental retardation, and some behavioral abnormalities are often present in infancy. 287b

Subfornical organ. A group of specialized ependymal cells, similar to those of the subcommissural organ, which projects toward the cavity of the third ventricle from its anterior wall between the columns of the fornix. It is one of the circumventricular organs.* 274

Sublingual gland. One of the three pairs of salivary glands that develop in humans. The sublingual gland is formed from invaginations of the endoderm in the paralingual sulci on either side of the tongue. 578

Submandibular ganglion. The visceral efferent ganglion of nerve VII formed by neural crest cells that migrate from the cranial rhombencephalon. 314

Submandibular gland. One of the three pairs of salivary glands that develop in humans, formed from invaginations of the endoderm in the floor of the oral cavity. 578

Submucosa ganglia. Enteric ganglia underlying the submucosa of the gastrointestinal tract. Its absence leads to Hirschsprung's disease. 470b

Submucosal plexus. Part of the enteric nervous system of the gastrointestinal tract. 470b

Subpallium. The thicker, ventral subdivision of the telencephalon, which budges into the neural canal to form the ganglion eminences that later make up the basal ganglia. 250b, 272

Substantia propria. A cellular stromal layer of the cornea formed when mesenchymal cells rapidly invade the stroma. 611

Subventricular zone. An accessory germinative zone lying deep to the ventricular zone. 285

Sulcus(i), in primitive heart tube. A series of constrictions. 342, 347f

Sulcus dorsalis. A shallow groove separating the thalamus from the epithalamic swelling. It is eventually obliterated by the growth of the thalamus. 274

Sulcus limitans. The groove at which the ventral and dorsal plates of the mantle zone of the spinal cord abut. 247b, 257

Superior combined ganglion. The ganglion of nerves VII and VIII, derived from both the first epipharyngeal placode and the rhombencephalic neural crest cells. 314, 315f

Superior ganglion. The ganglion of nerves IX and X, formed by rhombencephalic neural crest cells. 314, 315f

Superior segmental optic nerve hypoplasia. A syndrome caused by defects in the dorsal quadrant of the eye. It occurs in as many as 9% of children born to diabetic mothers. 615b

Superovulation. The development of multiple mature follicles by the ovaries. 46b

Supinators, of upper limb. Muscles that serve to turn the palm of the hand forward and upward.* 241, 242t

Suppressive interactions. Interactions that prevent a tissue from forming its "default" tissue type. 145

Supracardinal system. A venous system that grows caudally from the base of the posterior cardinal veins in the medial dorsal body wall. 385b, 387b

Supracardinal veins. A pair of veins sprouting from the base of the posterior cardinal veins and growing caudally just medial to the posterior cardinal veins. The veins drain the body wall via the segmental intercostal veins, thus taking over the function of the posterior cardinal veins. 421, 421f–423f, 423–424

Suprarenal arteries. The arteries that develop from the renal artery and the inferior phrenic artery. They comprise the major arterial supply to the suprarenal glands. 410f, 410–411

Suprarenal cortical cells, fetal. Cells formed when the delaminating gonadal ridge cells differentiate into large acidophilic cells. 499

Suprarenal gland. A crucial component of the hypothalamic-pituitary-suprarenal axis, which is responsible for coordinating mammalian stress response and metabolism. 499f, 499–500

Surfactant proteins. Proteins that enhance surfactant activity. Two of these proteins (A and B) seemingly act by organizing the surfactant phospholipids into tubular myelin; surfactant C enhances the function of surfactant phospholipids; and surfactants A and D apparently play important roles in innate host defense of the lung against viral, bacterial, and fungal pathogens. 326b

Surfactant replacement therapy. The administration of exogenous surfactant to critically ill newborns. 326b

Suspensory ligament, of lens. A radial network of elastic fibers that suspend the lens from the ciliary body. 613

Sutures. The soft fibrous areas that occur where two cranial membrane bones meet, which contain the progenitor cells that will give rise to the osteoblasts. They allow the skull vault to deform as it passes through the birth canal and to continue growing throughout infancy and childhood. 550b, 551f

Sweat glands. Glands that appear as buds of stratum germinativum, which grow down into the underlying dermis to form unbranched, highly coiled glands. They are widespread over the body and secrete sweat to regulate heat. 193b, 201f, 202, 208, 208f

Swyer syndrome. The syndrome caused by mutations in the Sry DNA-binding domain of human Sry in which there is total gonadal dysgenesis in XY individuals. These individuals are phenotypically female and have a female reproductive tract, but do not enter puberty. 535b–536b

Sympathetic chain ganglia. Trunk ganglia that flank the spinal cord ventrally. 297b, 304, 307f

Sympathetic division. The division of the autonomic nervous system that provides autonomic motor innervation to the viscera and exerts control over involuntary functions such as heartbeat, glandular secretions, and intestinal movements. It is activated during conditions of the “fight or flight” response and consists of two-neuron pathways. 124–125, 251, 257, 297b, 299, 316

Sympathetic fibers. Fibers of the sympathetic nervous system, which can be either preganglionic or postgangliotic. 308, 309f, 310–311, 468

Sympathetic trunk. Nerves comprising the chain ganglia and the preganglionic sympathetic fibers that synapse in a cranial or caudal chain ganglion or one of the prevertebral ganglia. 304

Symphalangism, proximal. The fusion of the interphalangeal, wrist, and ankle joints. 240b

Synapses. The sites of functional apposition between neurons, at which an impulse is transmitted from one neuron to another. 251

Syncope. Loss of consciousness. 383b

Syncytiotrophoblast. The expanding peripheral syncytial layer of the trophoblast, which aids in initiating formation of the placenta. 51b, 53, 54f, 55f

Syncytium. A mass of cytoplasm containing numerous dispersed nuclei. 219

Syndactyly. A disorder resulting in the fusion of digits. 158, 632b, 633f, 634t

Syndecan. A large complex proteoglycan broadly distributed within and across tissue space. 160

Syndetome. A compartment at the rostral and caudal ends of the somite, characterized by Scleraxis expression and containing the tendon progenitors. 234b

Syndromes. Nonrandom patterns of developmental abnormalities. 133b, 135. See also specific syndromes.

Synostosis. A disorder resulting in the fusion of bones or intervening soft tissue. 634t

Synovial cavity. The joint space formed by vacuoles that coalesces within connective tissue. 237

Synovial tissue. Tissue that will line the future joint cavity, formed by condensation of the connective tissue of the central region. 237

Synpolydactyly. A syndrome caused by mutations of HoxD13, resulting in synostotic syndactyly, polydactyly of the fourth and fifth digits, and ectrodactyly. 635t, 637b, 638f

Syphilis. A disease caused by *Treponema pallidum*, which can cross the placenta to infect the fetus. Congenital syphilis can result in fetal anomalies or death. 176

Syringomyelia. A fluid-filled cyst of the spinal cord. 250b

T

Tactile pads. Distal swellings that develop on the fingers by day 52 and on the toes by day 56. 628, 628f

Tail, of spermatozoon. A structure containing microtubules that form part of the spermatozoon's propulsion system. Its tail is 7 to 15 times longer than the head. 25, 27f

Tail bud. Also called caudal eminence. A caudal midline mass of mesoderm formed from remnants of the primitive streak that will give rise to the most caudal structures of the body. 97–98

Talin. A linker protein that transduces signaling from the arginine-glycine-aspartate sequence to cytoplasmic microfilaments. 161

Talipes equinovarus. Club foot deformity. 639b, 639f

Tbx1. A T-box transcription factor located within the 22q11.2 region and expressed in the secondary heart field that interacts genetically with Fgf8. It is also expressed in the pharyngeal endoderm and mesoderm, but not in neural crest cells. 349b, 376b, 383b, 407b, 581b

Tbx3. A T-box transcription factor that regulates the expression of Wnt10b and Lef1. Mutations result in ulnar-mammary syndrome. 636t

Tbx4. A T-box transcription factor expressed in the hindlimb. Mutations result in small patella syndrome. 638b

Tbx5. A T-box transcription factor linked to atrial lineage determination. Initially expressed in the entire cardiac crescent, its expression becomes limited to the sinus venosus and atria with some expression in the left ventricle; it is also expressed in the forelimb. Mutations result in Holt-Oram syndrome. 276b, 349b, 355b, 356f, 382b, 636t, 638b

Tbx6. A T-box-containing transcription factor gene closely related to the prototypical T-box gene Brachyury. 83b

Tbx18. A T-box transcription factor expressed in the cranial half of each sclerotome. 222b

Tcf4. A component of the Wnt signaling pathway. 466f, 467b

Tcof1. The gene for Treacher Collins syndrome, which encodes the nucleolar phosphoprotein Treacle. 580b

Tdgf1/Cripto (Teratocarcinoma-derived growth factor1). One of several genes whose mutation can cause holoprosencephaly. 549b

Tectorial membrane. An acellular gelatinous matrix consisting of collagens and ear-specific noncollagenous proteins. Auditory hair cell function requires contact of the stereocilia with the tectorial membrane. 593, 597b

Tela choroidea. A well-vascularized layer of pia mater covering the thin rhombencephalic roof plate. 263

Telangiectasia, ocular. Permanent dilation of capillaries of the sclera. 613b

Telencephalon. Also called "endbrain." The cranial subdivision of the prosencephalon, which itself subdivides into a dorsal pallium and ventral subpallium. The pallium later gives rise to the cerebral hemispheres and the commissures and structures that join them, along with the olfactory bulbs and tracts. The subpallium bulge into the neural canal to form the ganglion eminences that later make up the basal ganglia. 247b, 251, 252f, 282, 284–285, 284f–286f

Telogen. The resting phase of hair growth. 204

Telogen effluvium. Excessive hair shedding caused when one of a variety of stressors or illnesses shifts the hair cycle toward the telogen phase. 207b

Telophase. The final stage of mitosis and meiosis, following metaphase and immediately preceding cytokinesis, in which the daughter chromatids separate from the kinetochore microtubules and the nuclear membrane reforms.* 22f, 23t

Temporal and spatial colinearity. The temporal and nested expression of the most 5′ members of the Hoxd and Hoxa clusters in cranial-caudal and proximal-distal domains within the growing limb bud. 623b, 625f

Temporal bone. One of two irregular bones forming part of the lateral surfaces and base of the skull, which contains the organs of hearing. It is divided into petrous, squamous, and tympanic parts.* 593, 595f

Temporal lobe. A long tongue-shaped process that is the lower lateral portion of each cerebral hemisphere.* It is formed when the caudal end of each lengthening cerebral hemisphere curves ventrally and then grows forward across the lateral cerebral fossa. 284

Temporalis muscle. One of the muscles of mastication, formed from paraxial mesoderm originating beside the metencephalon. 559

Temporomandibular joint (TMJ). A jaw articulation that develops between the temporal bone and the mandible, consisting of a synovial joint between the mandibular condyle and glenoid blastema, which are separated by an interarticular disc. 554, 556

Tenascin. A basement membrane protein required for primordial germ cell migration. It is also a component of the extracellular matrix, thought to play a permissive or stimulatory role in the branching of the bronchial buds. 121b, 328b

Tensor tympani muscles. A muscle associated with the ossicles. It forms from first pharyngeal arch mesoderm and is innervated by the trigeminal nerve (cranial nerve V). 559, 599

Tensor veli palatini muscles. Muscles that originate from the scaphoid fossa at base of medial pterygoid plate, wall of auditory tube, and spine of sphenoid, which insert on the aponeurosis of soft palate and horizontal part of palatine bone. They are innervated by the mandibular nerve and function to tense the soft palate and open the auditory tube.* 559

Teratocarcinoma-derived growth factor1 (Tdgf1/Cripto). One of several genes whose mutation can cause holoprosencephaly. 549b

Teratogen(s). A substance that causes malformation of the fetus embryo. 92b–93b, 116b–117b, 134, 176–178, 619b, 638b

Teratogenesis. The production of deformity in the developing embryo.* 92b–93b

Teratology. The study of the role of environmental factors in disrupting development. 177

Teratomas. Tumors composed of tissues derived from all three germ layers. They can be extragonadal or gonadal. 17, 18f, 187

Teratospermia. Having an excessive number of abnormal spermatozoa. 25b

Terminal ganglia. Also called parasympathetic ganglia. Aggregations of cell bodies that contain the peripheral (postganglionic) neurons of the two-neuron parasympathetic division of the autonomic nervous system. They may be associated either with the Vagus nerve or with cranial nerves III, VII, and IX, innervating the visceral organs or structures of the head, respectively.* 126

Terminal hairs. Pigmented hairs that penetrate into the fatty dermal tissues. 205

Terminal sacs. Also called primitive alveoli. The sacs formed in lung tissue when the respiratory bronchioles become invested with capillaries. 319b, 323

Terminal sulcus. The transverse groove that forms the boundary between the first-arch and third-arch contributions of the tongue. 574, 575, 575f

Terminal villi. Small, nodule-like secondary branches produced by the mature intermediate villi. The terminal villi complete the structure of the placental villous tree. 171

Termination zone. A point in the tectum/superior colliculi where retinal axons arborize and synapse to form a rough map. 280b

Tertiary stem villi. The outgrowths that project into the trophoblastic lucunae, eventually covering the entire chorion. They are formed by the proliferation of the extraembryonic mesoderm lining the chorionic cavity. 171

Testes. The male gonad; either of the paired, egg-shaped glands normally found in the scrotum. The testes produce the spermatozoa and also testosterone, which is responsible for the secondary sex characters of the male.* 505b–508b, 507f, 526, 526b, 529f, 529b–530b, 530f

Testicular feminization syndrome. Also called androgen insensitivity syndrome. A condition in which the androgen receptors are disabled or absent, so that although the male fetus may have normal or high levels of male steroid hormones, the target tissues do not respond. Testes are present and anti-Müllerian hormone is produced, so the Müllerian ducts regress, although a blind-ending vagina may form. The phenotype is usually female, but can range from complete female genital morphology to an ambiguous type to a male phenotype with infertility. 482b, 518, 535b, 535f

Testis cords. The cords formed in the 7th week by differentiating Sertoli cells and interstitial cells of the gonad, which enclose germ cells in the center of the cords. At puberty, the testis cords become canalized and differentiate into a system of seminiferous tubules. 482b, 505

Testosterone. A steroid hormone produced by the testes. It stimulates the development of many secondary sex characteristics and triggers growth of the testes, maturation of seminiferous tubules, and commencement of spermatogenesis. 25, 510, 513b, 532b

Tethered cord. An abnormal attachment of the spinal cord to the sacrum. 250b

Tethered cord syndrome (TCS). A congenital anomaly of the spinal cord that can lead to progressive neurologic dysfunction. 250b

Tetra-amelia. The condition in which all four limbs are absent. 619b, 619f, 634b

Tetralogy of Fallot. A congenital syndrome involving four classic cardiac malformations: pulmonary stenosis, ventricular septal defect, rightward displacement of the aorta, and right ventricular hypertrophy. 382b, 382f

Tetraploidy. The condition in which multiple copies of the entire genome are present, which can arise from errors in fertilization. 34b

Tg737/Polaris. A gene with ties to ciliary assembly and function. It is also associated with polycystic kidney disease. 495b

Thalamic swelling. A swelling dorsal to the hypothalamic sulcus that gives rise to the thalamus. 250b

Thalamus. The largest diencephalic structure that is mainly the relay center for the cerebral cortex. It receives all the information projecting to the cortex from subcortical structures, processes it as necessary, and relays it to the appropriate cortical areas. 250b, 272, 274, 373f

Thalidomide. A potent teratogen originally prescribed to treat morning sickness during pregnancy, and now used to treat leprosy, AIDS, and certain cancers. It can cause defects such as amelia and phocomelia at single exposures as low as 100 mg. 619b, 638b

Thanatophoric dysplasia. An Fgfr3 mutation that results in severe skeletal dysplasia. It is usually lethal at birth. 158, 239b

Theca externa. The inner layer of connective tissue of the ovarian stroma surrounding the vesicular follicles. 29

Theca interna. The outer layer of connective tissue of the ovarian stroma surrounding the vesicular follicles. 29

Thecal cells. The Leydig cell homolog in females. 518

Therapeutic cloning. A procedure in which embryonic stem cells are derived from the inner cell mass of a blastocyst and then transplanted into a tissue of the donor adult to replace a defective cell type (such as beta cells of the pancreatic islets in a diabetic mouse). Because the nucleus used for somatic cell nuclear transfer was obtained from the same animal that receives the embryonic stem cells, both the cells and the animal are genetically identical, eliminating the problem of tissue rejection. 162

Thoracic arteries, internal. The artery that originates in the subclavian artery and distributes to the anterior thoracic wall, mediastinal structures, and diaphragm.* 411

Thoracic cysts. Cystic disease affecting the thorax, such as congenital cystic adenomatoid malformation. 186

Thoracic duct. The passage that drains the cisterna chyli and the posterior thoracic wall, which is derived from the caudal portion of the right thoracic lymphatic duct, the cranial portion of the left thoracic lymphatic duct, and a median anastomosis. 425, 426f

Thoracolumbar system. The sympathetic division (central and peripheral) of the nervous system, called a thoracolumbar system because the central sympathetic motoneurons are located at all 12 thoracic levels and the first 3 lumbar levels. 125

Thymus gland. A gland located inferior and ventral to the developing thyroid and just dorsal to the sternum, which is formed from the third pharyngeal pouch. The thymus is highly active during the perinatal period and continues to grow throughout childhood, reaching its maximum size at puberty, after which it involutes rapidly. 545b

Thyroarytenoid muscles. Part of the intrinsic laryngeal musculature, mainly devoted to vocalization. 559

Thyroglossal cyst. An enclosed cyst that may be formed when a portion of the thyroglossal duct persists. 576

Thyroglossal duct. The passage that connects the thyroid to the foramen cecum until the 5th week of development, when it breaks down. 576

Thyroglossal sinus. A cavity communicating with the surface of the neck that may be formed by the persistence of the thyroglossal duct. 576

Thyroid gland. The largest of the endocrine glands, consisting of two lateral lobes connected by an isthmus, with a third pyramidal lobe sometimes extending up from the isthmus. The gland is located in the front and sides of the neck just below the thyroid cartilage. It produces hormones that are vital in maintaining normal growth and metabolism, and it also serves as a storehouse for iodine.* It forms as a midline, ventral endodermal evagination of the pharynx. 123, 545b, 576, 577f

Thyroid transcription factor1 (Ttf1). A homeodomain-containing transcription factor required for the regulation of lung cell genes, including surfactant synthesis. 327b

Tight junctions. An intercellular connection point at which adjacent plasma membranes are joined tightly together, separated by only 1 to 2 nm. These junctions variably occlude the intercellular space and limit or eliminate the intercellular passage of molecules.* 43

Tissue-specific promoters. Genetic promoters that can drive expression of a transgene or knock out a gene in specific tissues only. 149

Tobramycin. An aminoglycoside antibiotic. Neonatal exposure to tobramycin can cause hearing loss. 596b

Toe rays. Thickenings that form on the digital plate of the foot. A process of programmed cell death occurs between the rays to free the toes. 626

Toluene. An aromatic solvent similar to xylene. Found in many paints and removers, it is considered to be a neurotoxin.* 579b

Tongue buds. Swellings (median, distal, and lateral) that grow from the first pharyngeal arch throughout embryonic and fetal life to form the anterior two thirds of the tongue. 574, 575f

Tongue-tie. Also called ankyloglossia. A defect that results when the attachment between the ventral surface of the tongue and the floor of the mouth fails to regress. 574

Tonsil(s). Any of several fleshy masses of lymphoid tissue at the back of the throat, found in three pairs: the palatine, lingual, and pharyngeal tonsils. Tonsils are part of the lymphatic system and help to filter the circulating lymph of bacteria and any other foreign material that may enter the body, especially through the mouth and nose.* 545b, 573, 576

Tonsillar crypts. Hollow invaginations of the tonsils, infiltrated by lymphoid tissue. 576

Tooth buds. Structures occurring in two forms: primary tooth buds, 20 composite structures, which consist of the dental lamina ingrowth and underlying mesenchymal condensation that give rise to the primary teeth; and secondary tooth buds, which sprout from the primary buds and form the secondary, permanent teeth. 193b, 210, 212f, 213f

Topographic neural connections. Nerve connection between different regions within the CNS. For example, the point-to-point mapping of retinal cells to the higher brain centers. 274b

Totipotency. The ability to form all cell types. 18b, 148, 162

Tourneux fold. A cranial fold growing toward the cloacal membrane. It is one of two integrated mesodermal septal systems that form the urorectal septum. 473

Townes-Brocks syndrome. A syndrome caused by a mutation in Sall1 that causes preaxial polydactyly and bifid or finger-like thumb. 636t

Toxoplasma virus. A virus that can be transmitted to humans from cat litter and soil and can pass through the placenta to infect the fetus. 176

Trabeculae. Myocardial ridges that form on the inner wall of both ventricles, beginning in the greater curvature of the heart. 368, 369b, 369f

Trabeculae cranii. Also called prechordal cartilages. One of three pairs of cartilaginous precursors that contribute to the cranial base. 547

Trabecular layer. The inner of the two basic layers of myocardium. 369b, 369f

Trabecular network. A Network of bone formed as ossification spreads from the primary ossification center toward the epiphyses of the anlage. 235

Trachea. The air passage that extends from the throat and larynx to the main bronchi, which is reinforced at the front and sides by a series of C-shaped rings of cartilage that keep the passage uniformly open. The trachea is lined with mucous membrane covered with small hairlike processes called cilia that continuously sweep foreign material out of the breathing passages toward the mouth, a process slowed down by cold but speeded up by heat.* 321, 328b, 413b, 415b, 415f–417f

Tracheoesophageal fistula. Also called esophagotracheal fistula. An abnormal connection between the tracheal and esophageal lumina that results from a failure of the foregut to separate completely into the trachea and esophagus. 157, 324b–325b, 325f

Tractus solitarius, nucleus of. Part of the first special afferent column, which receives taste impulses via the facial (VII), glossopharyngeal (IX), and vagal (X) nerves. 260f, 261

Tragus. The ventral hillock of the first pharyngeal arch, one of the six auricular hillocks that give rise to the auricle. 601

Transcription factors. Nuclear proteins that switch other genes on or off by binding to regulatory regions of their DNA. 151

Transcriptional control genes. Genes whose expression in distinct domains on the craniocaudal axis dictates the direction of subsequent development. 253b

Transforming growth factor α (Tgfα), skin diseases and. A protein, excessive levels of which can cause psoriasis and other hyperproliferative skin diseases. 198b

Transforming growth factor β (Tgfβ). A superfamily of proteins that signals through receptors and has a cytoplasmic serine/threonine kinase domain. 72b, 73b–74b, 157, 157f, 205b, 328b, 340b, 341f, 362b, 376b, 393b, 396b, 408b, 449b, 608b, 609f

Transforming growth factor interacting factor (Tgif), holoprosencephaly and. One of several genes identified in which mutations cause holoprosencephaly. 549b, 550b

Transgene. A segment of recombinant DNA that has been transferred from one genome to another. The term is sometimes used specifically to denote one that has been integrated into the germline of the recipient and is transmissible to future generations.* 327b, 329f

Transgenic animals. Animals whose genome contains a foreign DNA sequence. 139, 142, 147–148, 148f, 149, 150, 153–154, 393b, 394f

Transglutaminase. An enzyme that crosslinks the envelope proteins, which is produced by cells in the stratum granulosum. 200

Translocation. An event in which a copy of one chromosome in a developing gamete becomes attached to the end of another chromosome during the first or second division of meiosis. 32b, 34f

Transposition of the great vessels. The defect in which the left ventricle empties into the pulmonary circulation and the right ventricle empties into the systemic circulation. 380b

Transverse foramen. Also called foramina transversaria. The passage in either transverse process of a cervical vertebra that, in the upper six vertebrae, transmits the vertebral vessels. 227

Transversospinalis muscles. Part of the deep epaxial muscles of the back, formed by the epimeres and innervated by the dorsal ramus of the spinal nerve. 231

Transversus abdominis muscle. One of the three homologous layers of the abdominal musculature. 234

Trapezius muscle. One of the neck muscles innervated by cranial nerve XI. 559

Treacher Collins syndrome. An autosomal-dominant syndrome that involves generalized underdevelopment of the first pharyngeal arches and results in defects of the eye, ear, midface, palate, and jaw. It is caused by the Tcof1 gene, which encodes Treacle. 571, 579b, 580b, 602b

Treacle. A nucleolar phosphoprotein encoded by Tcof1. Treacle is expressed in the neural folds as neural crest cells are forming and emerging, and later in the pharyngeal arches. It is thought to regulate microtubule dynamics and to function in ribosomal DNA gene transcription. 580b–581b

Tricho-dento-osseous syndrome. A syndrome caused by a mutation in Dlx3 that affects the hair and teeth. Additionally, the skull bones of those affected by this syndrome have an abnormally high density. 203b

Tricuspid atrioventricular valve. Also called tricuspid valve. The structure between the right atrium and left ventricle of the heart,* which develops from atrioventricular cushion tissue during the 5th and 6th weeks. 337b, 370, 372f

Tricuspid valve. The right atrioventricular structure between the right atrium and left ventricle of the heart,* which develops from atrioventricular cushion tissue during the 5th and 6th weeks. 337b, 370, 372f

Tricuspid valve atresia. An atrioventricular valve defect in which the right atrium is cut off from the right ventricle due to abnormal development of the tricuspid valve. 379b–380b

Trigeminal ganglion. Also called semilunar ganglion. The general afferent ganglion of cranial nerve V. 314

Trigeminal nerve. Cranial nerve V, which arises in the pons and is composed of both sensory and motor fibers. It has three divisions: the ophthalmic division carries sensory impulses from the skin of the upper eyelid, side of the nose, forehead, and front part of the scalp. The maxillary division carries sensory impulses from the mucous membranes of the nose, the skin of the cheek and side of the forehead, the upper lip, and the upper teeth. The

mandibular division carries sensory impulses from the side of the head, the chin, the mucous membrane of the mouth, the lower teeth, and the front two thirds of the tongue.* 260f, 559

Trigeminal placode. A placode that develops in the area between the epipharyngeal placodes and the lens placode. 313, 315f

Trigone, of bladder. The triangular area of exstrophied mesonephric duct on the posteroinferior wall of the bladder. 497

Trigonum habenulae. A neural structure formed by the epithalamus, which includes the nucleus habenulae. 274

Trimesters. Three-month periods beginning with the date of onset of the last menstrual period and ending at birth. These subdivisions of human prenatal development are used by prospective parents and physicians. 167b

Trinucleotide repeat tracts. Unstable CAG tracts within the coding regions of certain genes. The trinucleotide CAG codes for the amino acid glutamine, and polyglutamine disorders occur when the tracts expand to reach a disease-causing threshold. 269b

Triphalangeal thumb. The duplication defect in which the thumb develops with three rather than two phalanges. 632b, 633f, 634b, 634t

Triploidy. The condition caused by errors in fertilization in which multiple copies of the entire genome are present. 34b

Trisomy. The presence of two of the same kind of chromosome in one of the gametes that forms a zygote. 32b, 33f, 34b

Trisomy 21. Also known as Down syndrome. A disorder most frequently caused by an error during meiosis. If the two copies of chromosome 21 fail to separate during the first or second meiotic anaphase of gametogenesis in either parent (a phenomenon called nondisjunction), half the resulting gametes will lack chromosome 21 altogether and the other half will have two copies. In addition to recognizable facial characteristics, mental retardation, and short stature, individuals with Down syndrome may exhibit congenital heart defects (atrioventricular septal defect being most common, that is, a failure to form both the atrial and ventricular septae), hearing loss, duodenal obstruction, a propensity to develop leukemia, and immune system defects. 32b, 33f, 34b, 34f, 114b, 135, 182, 379b

Tritanopes. Individuals who are color blind due to the absence of S-cones. 608

Trochlear nerve. Cranial nerve IV, which originates from the hindbrain and innervates the superior oblique muscle. 260f, 559

Trophic factors. Factors that promote cell growth and survival. 277b

Trophinin-tastin-bystin. A cell adhesion complex. 55b

Trophoblast. The outer cell mass of the cleaving embryo, which forms the fetal component of the placenta and associated extraembryonic membranes. 15b, 41, 42f, 43, 43b, 64b-65b

Trophoblastic disease, persistent. A condition caused by residual trophoblastic tissue remaining in the uterus after spontaneous abortion or surgical removal of a hydatidiform mole in which the mole remnant grows to form a tumor. 64b

Trophoblastic lacunae. Cavities that form in the syncytiotrophoblast of the chorion and anastomose with maternal capillaries. 55f, 59, 62f, 171

Trophoblastic sprouts. Sprouts of the syncytiotrophoblast, which become terminal mesenchymal villi. 171, 174f

Truncus arteriosus. The artery connected to the heart and the aortic sac. Formed by the conotruncus, it eventually splits to form the ascending aorta and pulmonary artery. 337b, 346

Tuberculum impar. Also called median tongue bud. A median swelling formed by the first pharyngeal arch that begins development of the tongue. 574, 575f

Tube-within-a-tube body plan. A three-dimensional body plan consisting of an outer tube (formed from the ectodermal germ layer) and an inner tube (formed from the endodermal germ layer), with the two tubes separated by the mesoderm. 69b, 101b, 103, 104f, 105f, 105–107, 319b

Tubotympanic recess. A cavity formed by the expansion of the first pharyngeal pouch that differentiates to become the tympanic cavity of the middle ear and the auditory (eustachian) tube. 572–573, 583b, 598

Tubulobulbar complexes. Unique cytoplasmic processes that extend into the Sertoli cells, which connect them to the maturing spermatocytes and spermatids. They are thought to provide a mechanism by which the excess cytoplasm is transferred to Sertoli cells. 25

Tumor protein p73-like (Tp73l). Also known as p63. A transcription factor expressed in the stratum germinativum that regulates cell proliferation, expression of cell-adhesion molecules, and differentiation. 197b, 199f, 202, 203b, 636t

Tumor suppressor gene. A gene whose function is to limit cell proliferation, and loss of whose function leads to cell transformation and tumor growth.* 302b

Tunica albuginea. A layer of connective tissue that separates the coelomic epithelium from the testis cords in males. 505

Tunica vaginalis. A distal remnant sac left in males by the cranial portion of the vaginal process, which lies ventral to the testis. During infancy, this sac wraps around most of the testis. Its lumen is normally collapsed, but under pathologic conditions, it may fill with serous secretions, forming a testicular hydrocele. 526, 529f, 530f

Tunica vasculosa lentis. Branches of the hyaloid artery that extend over the lens. 611

Turner syndrome. A condition caused by a 45,X karyotype or 45,X/46,XX mosaicism. It is characterized by the failure of normal sexual maturation at puberty, as well as a range of anomalies that include short stature, webbed neck, coarctation of the aorta, and cervical lymphatic cysts. 34b, 416b, 428b

Twin(s). Offspring produced in the same pregnancy.* Twins that form by the splitting of a single embryo are called monozygotic, or identical, twins. Twins arising from separate oocytes produced during the same menstrual cycle are called dizygotic, or fraternal, twins. Dizygotic twin embryos implant separately and develop separate fetal membranes (amnion, chorion, and placenta). Monozygotic twins, in contrast, may share none, some, or all of their fetal membranes, depending on how late in development the original embryo splits to form twins. 179–180, 181f

Twin-reversed arterial perfusion (TRAP) sequence. A condition in which one twin (the so-called pump twin) provides all of the blood flow to a second acardiac/acephalic twin through placental vascular anastomoses. Because of the additional stress placed on the pump twin's heart, cardiac failure and the pump twin's subsequent demise occur in 50% to 75% of the cases (the acardiac twin cannot survive without the pump twin, and it dies either with the death of the pump twin or at birth). 180, 187

Twin-twin transfusion syndrome (TTTS). A condition in which vascular anastomoses occur between vessels in the two placentae that result in unbalanced blood flow between the twins. One twin, the so-called donor twin, exhibits oligohydramnios and growth restriction, whereas the other, the so-called recipient twin, exhibits polyhydramnios and cardiac enlargement and eventually cardiac failure. 180, 187

Twist. A transcription factor, mutations in which may cause craniosynostosis and Saethre-Chotzen syndrome. 550b, 636t

Two-hit hypothesis, of neurofibromatosis-type 1. A hypothesis based on evidence that the second wild-type allele is lost in NF-1 patients through a subsequent somatic deletion, which leads to certain types of tumors. However, because of the infrequency of somatic deletion and frequency of neurofibromas developing in NF-1 patients, second mutations are likely not required for neurofibroma formation. 302b

Tympanic cavity. The cavity in the middle ear in which the malleus, incus, and stapes are arranged in a chain. It is formed by the differentiation of the tubotympanic recess. 545b, 573, 588, 598

Tympanic membrane. Also called eardrum. The obliquely placed thin membranous partition between the external acoustic meatus and the tympanic cavity. The greater portion, the pars tensa, is attached by a fibrocartilaginous ring to the tympanic plate of the temporal bone; the much smaller triangular portion, the pars flaccida, is situated anterosuperiorly between the two mallear folds.* 572, 584f, 590f, 599

Tyrosine kinase signaling. The signaling of growth factors, such as Fgfs and Ephrins, that bind to receptors that have a cytoplasmic Tyrosine kinase domain. 157–158, 158f

Tyrosine kinase with immunoglobulin-like and EGF-like domains receptor (Tie). A group of Tyrosine kinase receptors and ligands that act in parallel to promote proper angiogenesis. 396b

U

Ubiquitin fusion degradation 1 (Ufd1). A gene regulated by Hand2 that may be involved in 22q11.2 deletion syndrome. 383b

uE3 (Estriol). A serum component produced by the placenta and measured as part of maternal serum screening. It is used in a treatment method for diagnosing fetal malformations and genetic diseases. When carrying a fetus with Down syndrome, maternal estriol levels are low. 182

Ulnar artery. An artery of the upper limb that distributes to the forearm, wrist, and hand.* It develops partly as a sprout of the axis artery. 411, 413f

Ulnar-mammary syndrome. An autosomal dominant disorder resulting from mutations in Tbx3. This syndrome affects the caudal side of the limb, with reduction or complete loss of the ulna and posterior digits, and causes mammary gland defects. 209b, 636t, 637b–638b

Ultimobranchial bodies. Embryonic derivatives of the fifth pharyngeal pouches, which migrate along with the parathyroid glands and are incorporated in the thyroid gland.* 578

Ultrabithorax. A gene in which mutation in Drosophila results in homeotic transformation of the third thoracic segment into an additional second thoracic segment, giving a fruitfly four wings instead of the normal two. 153

Ultrasonography. A method for scanning the inside of the body with a beam of ultrasound (sound with a frequency of 3 to 10 MHz), and using a computer to analyze the pattern of the returning echoes. Because tissues of varying densities reflect sound differently, revealing tissue interfaces, the pattern of echoes can be used to decipher the inner structure of the body, making it possible to visualize the structure of the developing fetus and to identify many malformations. 114b, 169b, 182, 183f, 184, 184f

Umbilical arteries. Arteries that develop in the umbilical cord to circulate blood between the embryo and the placenta. 385b, 409f, 411, 414f

Umbilical cord. A composite structure formed when the amnion expands, enclosing the connecting stalk and yolk sac neck in a sheath of amniotic membrane. Its main function is to circulate blood between the embryo and the placenta. 167b, 171, 173, 175f, 319b

Umbilical hernia. A small protrusion of bowel through the umbilical ring, which is covered by skin. An umbilical hernia can occur as an isolated defect but is commonly associated with syndromes such as Beckwith-Wiedemann syndrome. 461b

Umbilical ligament, median. Also called urachus. A ligamentous band formed by the allantois and the constricted bladder apex, which runs through the subperitoneal fat from the bladder to the umbilicus. 475b

Umbilical region. The area in which the yolk sac and connecting stalk emerge. 105

Umbilical ring. The aperture in the abdominal wall through which the umbilical cord communicates with the fetus. After birth it is felt for some time as a distinct fibrous ring surrounding the umbilicus; these fibers later shrink progressively.* 171, 173, 319b

Umbilical urachal sinus. Dilation of part of the urachus at the umbilical end, either congenitally or as a result of a urachal cyst that has begun to drain to the surface.* 475b, 476f

Umbilical veins. A pair of veins that deliver oxygenated blood from the placenta to the heart. 385b, 421

Umbilicus. The cicatrix that marks the site of attachment of the umbilical cord in the fetus.* 104f, 105

Uncinate process. A hook-like process formed by the ventral pancreatic bud. 451

Uncx4.1. A homeobox-containing transcription factor expressed in the caudal half of each sclerotome. 222b, 226b

Urachal cyst. A vesicle that results when part or all of the allantois and bladder apex remains patent. 475b, 476f

Urachus. Also called median umbilical ligament. A ligamentous band formed by the allantois and the constricted bladder apex, which runs through the subperitoneal fat from the bladder to the umbilicus. 475b, 476f

Ureter. The fibromuscular tube that conveys urine from the kidney to the bladder. Formed by the differentiation of the ureteric bud, it begins with the renal pelvis and empties into the base of the bladder.* 497b, 498f, 499b

Ureteric buds. Structures that form within the intermediate mesoderm of the sacral region. The ureteric buds eventually form the definitive kidney and ureters. 485f, 486, 487–488, 487f, 488f, 490, 490b–493b, 491f, 492f

Urethra. The membranous canal that conveys urine from the bladder to the exterior of the body.* 479b, 495, 496f, 497, 521, 523f

Urethral fistulas, rectoprostatic. An abnormal fistula that occurs in males, which connects the rectum to the prostatic urethra. 536b, 537f, 538b

Urethral plate. Also called urethral membrane. A plate of endodermal cells formed by the roof of the phallic segment after rupture of the cloacal membrane. The urethral plate lengthens as the genital tubercle grows, and is bordered by the genital tubercle ventrally and the urethral folds laterally. 474, 474f, 482b, 521, 523f

Urinary system. The organ system formed from the intermediate mesoderm; it maintains the electrolyte and water balance of the body fluids that bathe the tissues in a salty, aqueous environment. 479b, 479–500. See also the specific organs.

Uriniferous tubule. The structure formed when the lumina of the S-shaped tubule becomes continuous with the ureteric duct. 489

Urogenital folds. Also called cloacal folds. A pair of swellings that develop on either side of the urethral plate through an expansion of mesoderm underlying the ectoderm. Inferiorly, these folds meet and join the genital tubercle, and eventually help to form the external genitalia. 474, 482b

Urogenital ridge. A longitudinal ridge in the embryo, lateral to the mesentery.* 485

Urogenital sinus. A part of the cloaca partitioned by the urorectal septum. It gives rise to the bladder, pelvic urethra, and phallic segment. 435b, 472, 473f, 474f, 495, 496f, 521, 522f

Urorectal septum. A coronal partition that separates the urogenital sinus and the anorectal canal in the cloaca. Its tip forms the future perineum. 435b, 472, 473f

Usher syndrome type 1. An autosomal recessive disorder that is characterized by sensorineural hearing loss and retinitis pigmentosa. 596b, 597b

Uteroplacental circulation. The system that begins to form on day 9 by which maternal and fetal blood flowing through the placenta come into close proximity and exchange gases and metabolites by diffusion. 58–60, 62f

Uterovaginal canal. A short tube with a single lumen formed by fusion of the Müllerian ducts. It eventually becomes the uterus. 518, 519f

Uterus. The hollow muscular organ in females, formed from the uterovaginal canal, in which the blastocyst can become embedded and in which the developing embryo and fetus can be nourished.* 28, 29f, 482b, 520b, 520f, 530, 531f–532f

Utricle. The major organ of the vestibular system, which gives information about the position and movements of the head. It is the larger of the two divisions of the membranous labyrinth of the inner ear.* 583b, 588

V

αvβ3. A transmembrane glycoprotein involved in adhesion and cell signaling. 55b

αvβ5. A transmembrane glycoprotein involved in adhesion and cell signaling. 55b

VACTERL association. An extension of the VATER association that includes some or all of the following abnormalities: **v**ertebral defects, **a**nal atresia, **c**ardiovascular anomalies, **t**racheo**e**sophageal fistula, and **r**enal and **l**imb defects. 92b, 230b, 324b

Vagina. The canal in females that extends from the external genitalia to the cervix uteri. The vagina receives the erect penis in coitus; spermatozoa are discharged into it, swim through the cervical canal, and enter the uterus. The vagina is also the passage for menstrual discharge, and it functions as the birth canal. Its interior lining is mucous membrane, and muscles and fibrous tissue form its walls. In pregnancy, changes occur in these tissues, enabling the vagina to stretch to many times its usual size for childbirth.* 479b, 482b, 497, 518, 520b, 521

Vaginal adenosis. A condition in which stratified squamous epithelium is transformed to a columnar type, a possible precursor step toward development of adenocarcinoma. 520b–521b

Vaginal plate. A solid block of tissue formed by the fusion of the sinuvaginal bulbs. It eventually canalizes to form the vaginal lumen, and is thought to give rise to the inferior portion of the vagina. 518, 519f

Vaginal process. A slight evagination of the peritoneum that develops on three sides of each gubernaculum, forming a nearly annular, blind-end cavity. As it elongates, it hollows out the inguinal canals and labioscrotal swellings, providing a cavity into which, in males, the testes descend. In females, it remains rudimentary and normally degenerates during development. 526, 527f

Vaginal rings. A form of birth control that can be inserted and removed by the user. When in place around the cervix, the rings release progestins continuously for 3 months. 45b

Vagus nerve. The nerve formed when the preganglionic parasympathetic fibers associated with cranial nerve X join with somatic motor and sensory fibers to form the vagus nerve. Some branches serve structures in the head and neck, but other fibers within the nerve continue into the thorax and abdomen. 260f, 314t, 316, 559, 575-576

Valproic acid. An anticonvulsant and known teratogen. 117b, 638b

Valve atresia. An abnormality in the heart in which the valvular orifice is completely obliterated. 379b

Van der Woude syndrome. The most common combined cleft lip and palate syndrome, caused by mutations in Irf6. 571b

Varicella infection. A potentially congenital infection associated with limb defects. 639b

Varicella-zoster virus. The agent of varicella or chickenpox, which can cross the placenta and infect the fetus. 176

Vas deferens. The excretory duct of the testis, which joins the excretory duct of the seminal vesicle to form the ejaculatory duct.* It is formed from the mesonephric duct. 28, 482b, 504f, 505, 511, 511f, 512b

Vasa. An RNA-binding protein of the DEAD box family, which is segregated to germ cells in Drosophila. Its possible role is to bind mRNAs involved in germ line determination and to control the onset of their translation. 19b

Vascular rings. A malformation in which a double aortic arch encloses the trachea and esophagus. The resulting ring may constrict the trachea and esophagus, interfering with both breathing and swallowing. 413b, 415b, 415f–417f

Vascular supply, of pharyngeal arches. The aortic arch artery system that initially takes the form of a basket-like arrangement of five pairs of arteries arising from the aortic sac and connecting the paired ventral aorta with the paired dorsal aortae. Blood reaches the head via the vertebral arteries and common carotid arteries. These arteries are modified to form the definitive arteries of the upper thorax, neck, and head. 556f, 556–557

Vasculogenesis. The process in which inducing substances secreted by the underlying endoderm cause some cells of the splanchnic mesoderm to differentiate into endothelial precursor cells (EPCs. These develop into flattened endothelial cells and join together to form small vesicular structures, which in turn coalesce into long tubes or vessels. 337b, 342, 385b, 389, 392f, 392–399, 392b–393b, 393f, 394f, 395f, 395b–397b, 396f–399f, 397b–399b, 400f

Vasectomy. The surgical removal of all or part of the vas deferens, done to induce infertility.* 45b

VATER association. An association of caudal and cranial malformations, including some or all of the following: **v**ertebral defects, **a**nal atresia, **t**racheal**e**sophageal fistula, **r**enal defects, and radial forearm anomalies. 92b, 230b, 324b

Vax2. The homeobox gene expressed in the ventral retina. Misexpression results in ventralization. 276b–277b

VE-Cadherin. Vascular endothelial-cadherin cell-to-cell adhesion molecule. 361b

Vegf. Vascular endothelial growth factor, a family of growth factors that binds to receptors having a cytoplasmic Tyrosine kinase domain. It is active in cardiac cushion formation and vascularization. 157, 237b, 342, 393b, 395b, 396b, 397b, 399f,

VegT. A T-box-containing transcription factor that is active in endoderm formation. 56b

Vellus. The nonpigmented hairs that do not project deep into the dermis. 205

Velocardiofacial syndrome. Also called 22q11.2 deletion syndrome or DiGeorge syndrome. Microdeletions within the 22q11.2 region. Those affected exhibit at least one element of abnormal neural crest cell development and manifest congenital heart defects. 128b, 375b, 383b, 545b, 546f, 562b, 581b

Vena cavae. The superior vena cava and the inferior vena cava. The superior vena cava is the venous trunk that drains blood from the head, neck, upper extremities, and chest. The inferior vena cava is the venous trunk for the lower extremities and the pelvic and abdominal viscera. Both empty into the right atrium of the heart.* 337b, 355, 357, 357f, 359f, 419, 421f–423f, 424, 424b–425b, 425f

Venous valves. A pair of tissue flaps that develop on either side of the three ostia. 357

Ventral flexion, of upper limb. The bending of the upper limb toward the ventral side, complete by day 47 of development. 626, 628f

Ventral margin. A separate tail organizer found in zebrafish. 97b

Ventral plates. The unpaired ventral longitudinal zone of the neural tube, forming the floor of that tube,* in which the somatic motor column and visceral motor column form. 247b, 257, 257f

Ventral ramus, of spinal nerve. The ramus formed by fibers of the spinal nerve that grow toward the hypomere. The ventral ramus innervates the hypaxial muscles. 231

Ventral roots. The major divisions of each spinal nerve, which are attached centrally to the spinal cord and join peripherally with the corresponding posterior root to form the nerve before emerging through the intervertebral foramen.* 297b, 303, 304f

Ventralizing factors. Bmps and Wnts that form gradients involved in mesodermal patterning. 81b

Ventricle (in optic vesicle). The cavity within the optic vesicle that is continuous with the neural canal. 602

Ventricles (of brain). Cavities, formed by expansion of the neural canal in each brain vesicle, that are eventually filled with cerebrospinal fluid. 250b, 251, 253, 282, 284, 285f

Ventricles (of heart). The cavities of the heart. The right ventricle, formed primarily from the bulboventricular sulcus, propels blood through the pulmonary trunk and arteries into the lungs. The left ventricle, formed from the primitive ventricle, propels blood out through the aorta into the systemic arteries.* 337b, 346, 354b–355b, 356b, 368f, 368–369, 370–371, 373f, 374f, 380b

Ventricular fold, primary. The trabeculated ventral portion of the muscular interventricular septum. 368, 368f

Ventricular hypertrophy. Abnormally high blood pressure in the cardiac ventricle. 382b, 382f

Ventricular septal defects. Congenital heart malformations resulting in the left-to-right shunting of blood, which can arise from several causes, These include: (1) deficient development of the proximal conotruncal swellings, (2) failure of the muscular and membranous ventricular septa to fuse, (3) failure of the dorsal and ventral endocardial

cushions to fuse, and (4) insufficient development of the interventricular muscular septum. 379b, 380b, 380f, 382b, 382f

Ventricular septum. The partition that separates the left ventricle from the right ventricle of the heart, consisting of a muscular and a membranous part.* 337b, 371

Ventricular zone. The area of the brain stem containing proliferating neuroepithelial cells that generates young neurons and glioblasts. 247b, 258

Ventroptin. A Bmp antagonist that diffuses from the ventral pole within the dorsal-ventral plane in the neural retina. 276b

Ventrotemporal crescent. A small region of the retina in each eye of the mouse, from which axons intermingle in the optic tract. 278b, 279f

Vermiform appendix. A wormlike diverticulum of the cecum, varying in length from 7 to 15 cm, and measuring about 1 cm in diameter.* 456, 457f

Versican. A myocardial-secreted molecule essential for endocardial cushion tissue formation. 361b

Vertebrae. The 33 bones of the spinal column.* 227b, 229b, 230b–231b, 230f–232f, 233f

Vertebral arch. The bony arch on the dorsal aspect of a vertebra, composed of the laminae and pedicles.* It is formed when the sclerotome expands dorsally to the neural tube. 222

Vertebral arteries. Paired arteries, formed from intersegmental artery anastomoses, that carry arterial blood to the head. 411, 412f

Vertebral body. The body of a vertebra, consisting of the centrum, ossified neurocentral joint and part of the vertebral arches, and facets for the heads of the ribs.* It is formed from the ventral portion of the sclerotome, which surrounds the notochord. 222

Vertebral spine. The rigid bony structure in the midline of the back that is composed of the vertebrae.* It is formed by cells in the dorsal portion of the sclerotome that surround the neural tube. 222

Vertebral transverse process. A process on either side of a vertebra that projects laterally from the junction between the lamina and the pedicle.* It is formed by the laterally located sclerotome. 222

Vestibular apparatus. The part of the inner ear that is composed of the three semicircular canals, the utricle, and the saccule. It perceives orientation, movement, and gravity, and is necessary for balance. 588

Vestibular aqueduct. The bony canal that transmits the endolymphatic duct. 597b, 598f

Vestibular ganglion. The special afferent ganglion of the vestibulocochlear nerve (cranial nerve VIII). 314

Vestibule, of vagina. In females, the space between the labia minora into which the urethra and vagina open.* It is formed from the phallic portion of the urogenital sinus. 479b, 497, 518, 521

Vestibulocochlear dysplasias. Structural malformations or improper functioning of inner ear structures, including the cochlea and vestibular system. 597b

Vestibulocochlear ganglion. Also called statoacoustic ganglion. The ganglion of the vestibulocochlear nerve (cranial nerve VIII) that innervates the sensory regions of the inner ear. 588, 592

Vestibulocochlear nerve. Also called statoacoustic nerve. Cranial nerve VIII, the nerve that arises from the otic placode and innervates the developing inner ear. 260f, 5314t, 583b, 588, 592–593, 596b

Vg1. A Tgfβ family member that induces the epiblast to express the protein Nodal during primitive streak formation. 72b, 157

Vimentin. A cytoskeletal protein. 81b

Vinculin. A linker protein that transduces signaling to cytoplasmic microfilaments. 160

Viscera. The large interior organs in any of the great body cavities, especially those in the abdomen.* 74b

Visceral afferent neurons. Neurons that receive impulses via the vagus nerve from sensory receptors in the walls of the thoracic, abdominal, and pelvic viscera. 259f, 260f, 261

Visceral efferent neurons. Neurons that serve the parasympathetic pathways innervating the sphincter pupillae and ciliary muscles of the eyes (III) and (via the glossopharyngeal, IX, and vagus nerve, X) the smooth muscle and glands of the thoracic, abdominal, and pelvic viscera, including the heart, airways, and salivary glands. 259f, 259–260, 260f, 261

Visceral nervous system. Also called autonomic nervous system. One of the two major functional divisions of the nervous system. It innervates the viscera and smooth muscle and glands in the more peripheral part of the body. 251, 299

Visceral skeleton. The part of the cranial skeleton of fishes that supports the gill bars and jaws. 545

Visceroatrial heterotaxy syndrome. An abnormality in which the abdominal viscera and atrial pole are oriented on opposing sides. It is associated with structural defects including common atrium, malalignment of atrioventricular canal and outflow tract, and abnormal venous and arterial vascular connections. 353b, 383b

Viscerocranium. The bones of the face and pharyngeal arches. 543b, 545, 547

Vision, binocular. The type of vision in which the visual fields of the left and right eyes overlap and information from the visual field is relayed from both eyes to one side of the brain. 278b

Visual cortex, primary. Part of the occipital lobe that receives information from the visual fields. 279b

Visual system. The series of structures by which visual sensations are received from the environment and conveyed as signals to the central nervous system. It consists of photoreceptors in the retina and afferent fibers in the optic nerve, chiasm, and tract.* 274b, 276b–282b, 277f, 278f, 279f. *See also Eye(s).*

Vitamin A. Retinol, from which retinoic acid is derived. 161, 550b

Vitelline arteries. The arteries that develop in the yolk sac and vitelline duct, anastomosing with the paired dorsal aortae to form part of the vasculature of the developing gut and gut derivatives. 385b, 408, 409f, 410

Vitelline duct. A slim stalk derived from the neck of the yolk sac. 101b, 104f, 106, 439

Vitelline system. One of three major embryonic venous systems. The vitelline system drains the gastrointestinal tract and gut derivatives. 387b, 419, 420f–423f

Vitelline veins. The veins that arise from the capillary plexuses of the yolk sac and form part of the vasculature of the developing gut and gut derivatives. 385b, 419, 420f–423f

Vitreous body, primary. A gelatinous matrix secreted by mesodermally derived mesenchymal cells in the lentiretinal space. 604

Viviparity-driven conflict hypothesis. Also called genetic-conflict hypothesis. In polyandrous mammals, the proposal that there is a conflict between males and females over the allocation of maternal resources to offspring. Fathers favor providing maximal resources for their offspring at the expense of mothers and future offspring who may be fathered by other males. Mothers favor providing equal resources among all their litters. The outcome is a compromise occurring in the growth rate. 65b

Vocalis muscles. Part of the intrinsic laryngeal musculature, mainly devoted to vocalization. 559

Volvulus. Torsion of the small intestine. 458b, 460f

Von Ebner's fissure. Also called intrasegmental boundary. A line of transversely arranged cells that divide the cranial and caudal portions of each sclerotome. 222

Von Hippel-Lindau disease. A rare, dominantly inherited, familial cancer syndrome characterized by mutations in a tumor suppressor gene located at chromosome 3p25-26. Affected individuals exhibit life-threatening multiple central nervous system, retinal, and liver hemangioblastomas, renal cell carcinomas, and visceral cysts. 399b, 401b

Von Recklinghausen disease. Also called neurofibromatosis. A prevalent familial tumor disposition with multiple defects, including benign and malignant tumors of the peripheral and central nervous systems. 128b

W

Waardenburg's syndrome. An autosomal dominant disorder characterized by wide bridge of the nose due to lateral displacement of the inner canthi and puncta; pigmentary disturbances, including white forelock, heterochromia iridis, white eyelashes, and leukoderma; and sometimes cochlear hearing loss.* 128b, 472b

WAGR syndrome. A syndrome characterized by **W**ilms' tumor, **a**niridia, **g**enitourinary anomalies, and mental **r**etardation. 614b, 495b

Warfarin. An anticoagulant known to be teratogenic, inducing limb malformations. 638b

Weigert-Meyer rule. The crossing of the normal ureter, which drains the caudal pole of the kidney, and the ectopic ureter, which drains the cranial pole. 498f, 499b

White matter. Massive tracts that connect the forebrain with the hindbrain and spinal cord. So-called because of the whitish color imparted by the fatty myelin sheaths that wrap around many of the axons. 257, 285

White ramus. A branch formed by sympathetic fibers exiting the ventral roots at levels T1 through L2 or L3 and growing ventrally to enter the corresponding sympathetic chain ganglion. 297b, 304

White sponge naevus. A syndrome affecting the oral keratinocytes that is characterized by formation of patches of loose, white epithelium. It is caused by mutations in Krt4 and Krt13. 198b

Whole mounts. Intact whole embryos on which techniques can be used to reveal patterns of gene expression. 145

Wilms' tumor(s). A rapidly developing malignant mixed tumor of the kidneys, made up of embryonal elements and seen mainly in young children. A genetic component is suspected. It may be accompanied by congenital defects such as urinary tract abnormalities, absent iris of the eye, or asymmetry of parts.* 68b, 490b, 494b–495b

Wnt(s). A family of secreted signaling molecules. In the embryo, Wnt signaling controls specification of cell fate. Mutation of members of the Wnt signaling pathway results in malignant transformation (i.e., cancer). 3b, 62b, 81b, 83b, 91b, 111b, 129b, 155f, 155–156,

Wolffian ducts. Also called mesonephric ducts. A pair of passages that drain the mesonephroi, which grow caudally to open into the posterior wall of the primitive urogenital sinus. 479b, 483, 484f, 485f, 485–486, 486b

Wt1. Wilms' tumor suppressor 1. One of the first genes identified as important in ureteric bud branching in humans. Mutations in Wt1 are associated with several renal and gonadal malformations and are the most common cause (although rare) of children's kidney tumors. 490b–491b, 494b–495b

X

X chromosome. One of the two kinds of sex chromosome. Individuals with one X chromosome and one Y chromosome (XY) are genetically male; individuals with two X chromosomes (XX) are genetically female. Nonetheless, one of the X chromosomes in the female genome is randomly inactivated, leaving only one active X chromosome in each cell. 21, 67b

Xiphoid process. The pointed process of cartilage, supported by a core of bone, that is connected with the lower end of the sternum.* 227

X-linked cleft palate plus ankyglossia syndrome. A syndrome that has been linked to T-box transcription factor Tbx22. It involves cleft palate and decreased mobility of the tongue. 571

Y

Yolk sac. A bubble-like extraembryonic membrane attached to the developing gut and enclosing a fluid-filled cavity. 15b, 17, 18f, 51b, 55f, 57–58, 58f–61f, 388, 388f

Z

Z gene. A hypothesized gene that acts as an inhibitor of the male pathway. This gene would normally be expressed in females but is blocked by the Sry protein in males. In XX sex-reversal cases, both copies of the Z would be mutated, leading to activation of male cascade. In XY sex-reversal cases, mutations in Sry or elsewhere in the genome would lead to inappropriate activation of the Z gene, resulting in repression of the male cascade. 508b

Zeugopod. The part of the developing limb that consists of the proximodistal region containing the radius and ulna or the tibia and fibula. 621b

Zic2. A zinc-finger transcription factor that regulates the noncrossing phenotype of ventrotemporal retinal ganglion cells, which is expressed exclusively in these cells. 279b, 549b

Zic3. A zinc-finger gene expressed strongly in the peripheral retina with a decreasing gradient toward the optic disc. It seems to regulate the expression of (thus far unidentified) axon repellent factors. 277b

Zona fasciculata. The thick middle layer of the suprarenal cortex.* 500

Zona glomerulosa. The outermost layer of the suprarenal cortex.* 500

Zona limitans intrathalamica. An area in the middle of the diencephalon where a signaling center develops to evoke formation of the prethalamus and thalamus. 253b

Zona pellucida. A shell of glycoprotein that surrounds the oocyte. 29, 30f, 31f, 39, 40f, 43–44, 44f, 516b

Zona reticularis. The innermost layer of the suprarenal cortex.* 500

Zone of polarizing activity (ZPA). A small region of mesenchyme in the caudal part of the limb. Signaling from the ZPA determines the cranial-caudal axis. 628b, 629f, 630b

ZPA regulatory sequence (ZRS). A highly conserved sequence that regulates Shh expression in the zone of polarizing activity. 634b

Zygote. The first stage of development during the period of the egg, formed at fertilization before the egg becomes multicellular. 15b, 39, 41-43, 42f

Zygote intrafallopian transfer (ZIFT). A form of assisted reproductive technology in which the oocytes are fertilized in vitro, and only fertilized pronuclear zygotes are introduced into the ampulla. 46b, 49b

Zygotic genes. A class of genes in Drosophila expressed after fertilization that involve both maternally and paternally inherited genes. 151