CELL DEATH DURING DEVELOPMENT

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JANUARY 31, 2005

KEY DEVELOPMENTAL PROCESSES

CELL PROLIFERATION

CELL MIGRATION

CELL DIFFERENTIATION

CELL DEATH

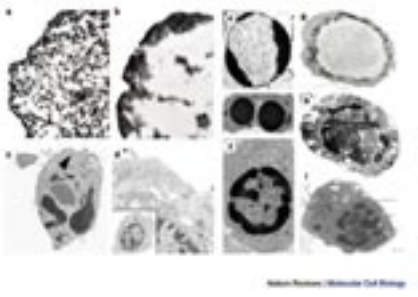
WHAT ARE THE MECHANISMS BY WHICH CELLS DIE DURING DEVELOPMENT?

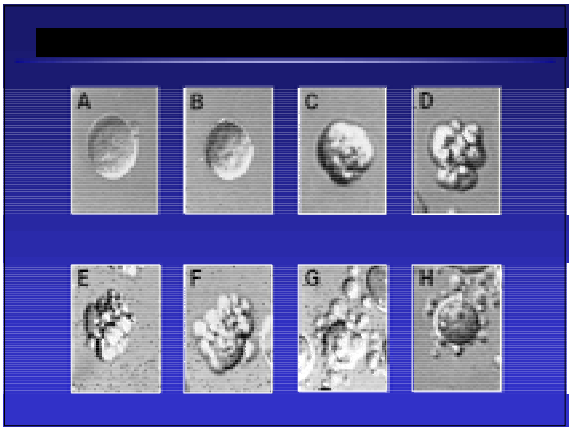
THERE ARE EVOLUTIONARILY CONSERVED MECHANISM

THAT GOVERN DEVELOPMENTAL CELL DEATH

APOPTOTIC DEATH	vs	NECROTIC DEATH
PRESENT IN DEVELOPING TISSUES		RESPONSE TO CELL INJURY, TOXINS
CYTOPLASMIC BLEBBING		
CELLULAR & NUCLEAR PYKNOSIS		CELL & NUCLEAR SWELLING
CHROMATIN CONDENSATION		
DNA DEGRADATION BY ENDONUCLEASES DEGRADATION (FORMATION OF DNA LADDER)		RANDOM DNA
FORMATION OF MEMBRANE-LIMITED APOPTOTIC BODIES		LOSS OF MEMBRANE INTEGRITY & LOSS OF CYTOPLASMIC CONTENTS
PHAGOCYTOSIS OF APOPTOTIC BODIES		

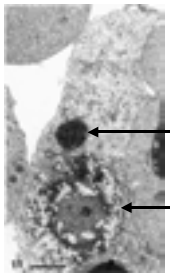
ELECTRON MICROSCOPIC VIEWS OF NORMAL (a) AND APOPTOTIC (b-i) NUCLEI





APOPTOTIC BODIES AND NUCLEI ARE CLEARED BY PHAGOCYTOSIS

EM OF A MACROPHAGE ENGULFING AN APOPTOTIC BODY AND APOPTOTIC NUCLEUS IN THE VENTRICULAR WALL OF THE DEVELOPING MOUSE HEART

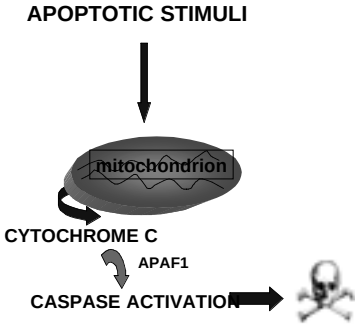


From: Abdelwahid et al. Anat. Rec. 256:208 (1999)

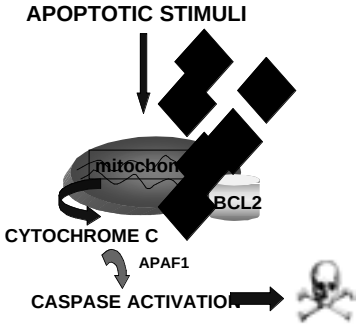
CASPASES

- FAMILY OF EXECUTORS OF APOPTOTIC DEATH
- CYSTEINE PROTEASES THAT CLEAVE AFTER ASP
- CONSTITUTIVELY PRESENT AS INACTIVE FORMS
- ACTIVATED BY CLEAVAGE OR BY INTERACTION WITH COFACTORS SUCH AS APAF1 AND CYTOCHROME C
- WHEN ACTIVATED, CLEAVE CELLULAR SUBSTRATES, LEADING TO APOPTOTIC DEATH

THE MITOCHONDRIAL PATHWAY OF APOPTOTIC DEATH -



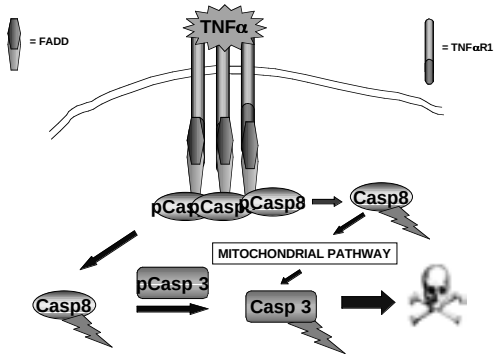
THE MITOCHONDRIAL PATHWAY OF APOPTOTIC DEATH -



DEATH PROMOTING RECEPTORS AND LIGANDS

LIGAND	RECEPTOR
TNFα	TNFαR1
FAS ligand	FAS
TRAIL	TRAIL-R

THE RECEPTOR-MEDIATED PATHWAY OF APOPTOTIC DEA



FUNCTIONS OF DEVELOPMENTAL CELL DEATH

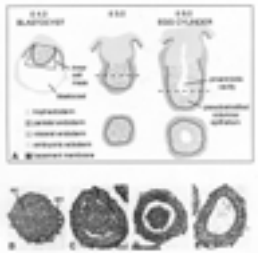
A. **MORPHOGENESIS**: SCULPTING/SHAPING STRUCTU

CREATION OF CAVITIES AND TUBES

FUSION OF TISSUE MASSES (PALATE/NEURAL TUBE)

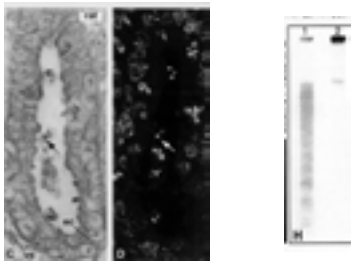
CREATION OF FORM (DIGITS, SEMICIRCULAR CANALS

CELL DEATH AND FORMATION OF THE PROAMNIC CAVITY FROM THE BLASTOCYST 1



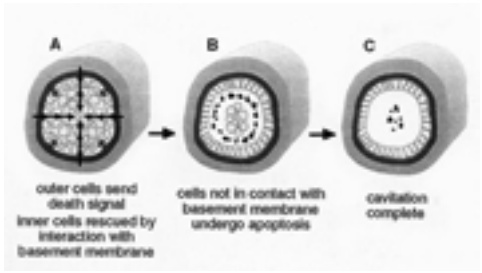
FROM: Coucouvanis and Martin. Cell 83: 279-287 (1995)

CELL DEATH AND FORMATION OF THE PROAMNIC CAVITY FROM THE BLASTOCYST 2



FROM: Coucouvanis and Martin. Cell 83: 279-287 (1995)

CELL DEATH AND FORMATION OF THE PROAMNIC CAVITY FROM THE BLASTOCYST 3



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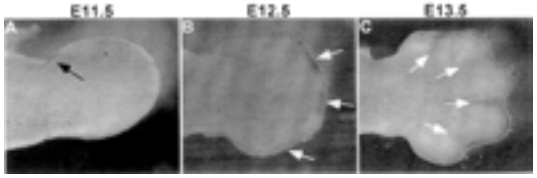
CREATION OF FORM (DIGITS)

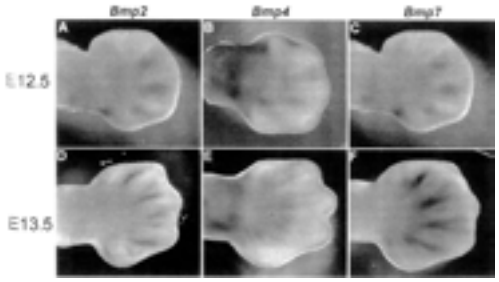
CELL DEATH AND FORMATION OF DIGITS 1



DYING CELLS ARE VISUALIZED BY NILE BLUE STAINING

FROM: Chen and Zhao, J. Exp. Zool. 282:691 (1998).

CELL DEATH AND FORMATION OF DIGITS 2



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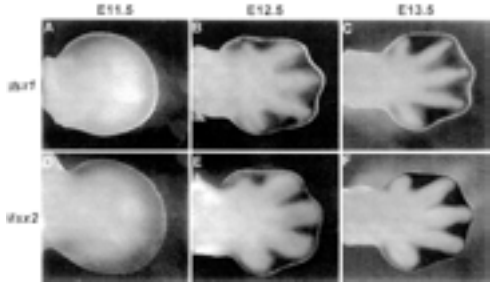

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FUNCTIONS OF DEVELOPMENTAL CELL DEATH

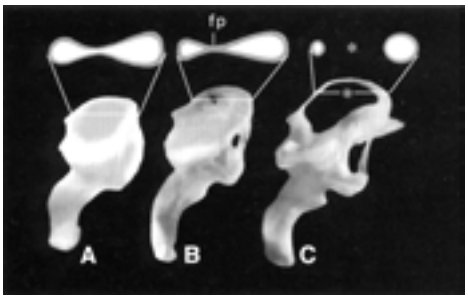
A. **MORPHOGENESIS**: SCULPTING/SHAPING STRUCTU

CREATION OF CAVITIES AND TUBES

FUSION OF TISSUE MASSES

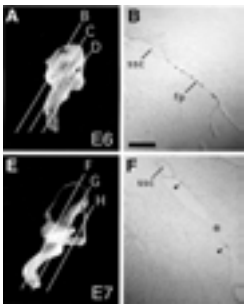
CREATION OF FORM (SEMICIRCULAR CANALS

CELL DEATH AND FORMATION OF THE SEMICIRCULAR CANALS 1



FROM: Fekete et al., Development 124: 2451 (1997)

CELL DEATH AND FORMATION OF THE SEMICIRCULAR CANALS 2

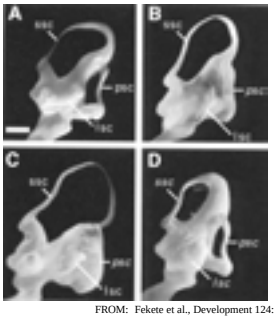


fp = fusion plate

B. Dying cells are indicated By TUNEL staining

FROM: Fekete et al., Development 124: 2451 (1997)

CELL DEATH AND FORMATION OF THE SEMICIRCULAR CANALS 3

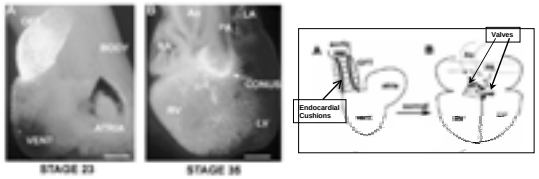


A: NORMAL

B-D: CELL DEATH PARTIALLY BLOCKED

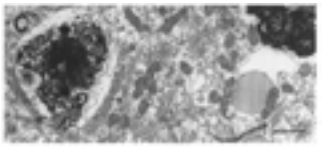
FROM: Fekete et al., Development 124: 2451 (1997)

CELL DEATH AND CARDIAC MORPHOGENESIS



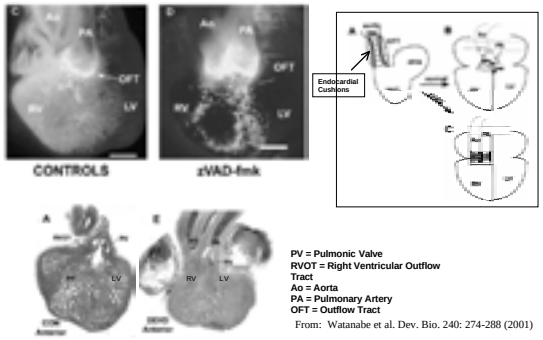
OTF = Outflow Tract
RA = Right Auricle
RV = Right Ventricle
LA = Left Auricle
LV = Left Ventricle
PA = Pulmonary Artery
Ao = Aorta

a = Apoptotic Cardiomyocyte



From: Watanabe et al. Dev. Bio. 240: 274-288 (2001)

BLOCKADE OF DEATH IN DEVELOPING HEART OFT LEADS TO DOUBLE OUTLET RIGHT VENTRICLE (DORV)



PV = Pulmonic Valve
RVOT = Right Ventricular Outflow Tract
Ao = Aorta
PA = Pulmonary Artery
OFT = Outflow Tract

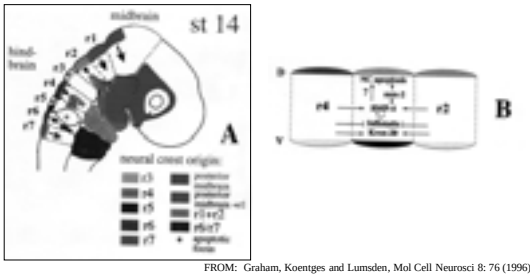
From: Watanabe et al. Dev. Bio. 240: 274-288 (2001)

FUNCTIONS OF DEVELOPMENTAL CELL DEATH

B. REGULATION OF CELL MIGRATION AND PATTERNING

EMIGRATION OF CRANIAL NEURAL CREST & FORMATIC
OF SEPARATE MIGRATORY STREAMS

CELL DEATH IN THE NEURAL CREST AND ESTABLISHMENT OF CRANIOFACIAL PATTERN



FROM: Graham, Koentges and Lumsden, Mol Cell Neurosci 8: 76 (1996)

FUNCTIONS OF DEVELOPMENTAL CELL DEATH

C. DELETION OF UNNEEDED STRUCTURES

KIDNEY: PRONEPHROS AND MESONEPHROS

BRAIN: CORTICAL SUBPLATE NEURONS

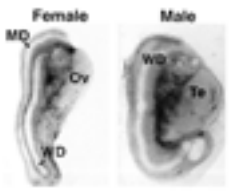
UROGENITAL SYSTEM: WOLFFIAN AND MÜLLE
DUCTS

REGULATION OF REPRODUCTIVE TRACT DEVELOPMENT 1

EMBRYONIC RAT GENITAL RIDGES SHOWING:

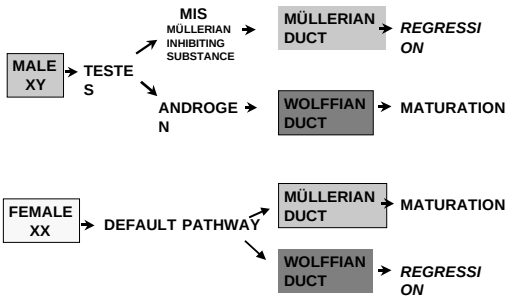
MÜLLERIAN DUCT (MD)
WOLFFIAN DUCT (WD

OVARY (Ov)
TESTES (Te)

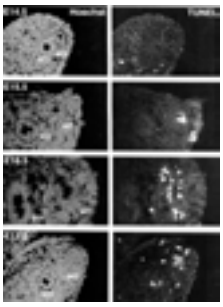


FROM: Roberts et al., Devel. Bio. 208: 110 (1999)

REGULATION OF REPRODUCTIVE TRACT DEVELOPMENT 2



REGULATION OF REPRODUCTIVE TRACT DEVELOPMENT 3
CELL DEATH DURING MÜLLERIAN DUCT REGRESSION



FROM: Roberts et al., Devel. Bio. 208: 110 (1999)

FUNCTIONS OF DEVELOPMENTAL CELL DEATH

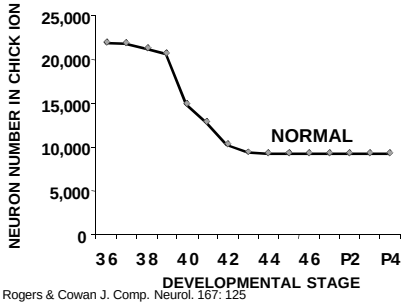
D. CULLING: REGULATION OF CELL NUMBERS

NERVOUS SYSTEM:

MATCHING NEURONS WITH TARGETS

MATCHING SCHWANN CELL AND OLIGODENDROCYTES WITH AXONS

NORMAL DEVELOPMENTAL NEURONAL DEATH OCCURS AND IS REGULATED BY TARGET DERIVED TROPHIC FACTORS



Clarke, Rogers & Cowan J. Comp. Neurol. 167: 125 (1976)

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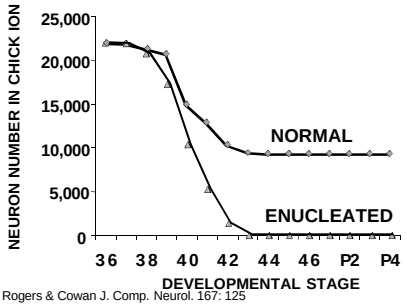
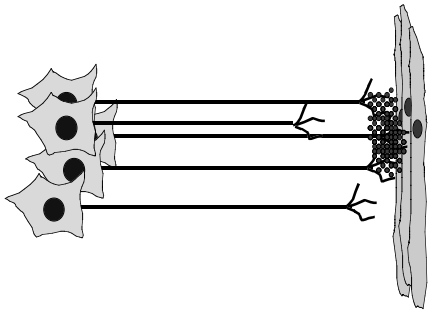


Clarke, Rogers & Cowan J. Comp. Neurol. 167: 125 (1976)

NEURONAL CULLING AS REGULATED BY COMPETITION FOR TARGET-SUPPLIED TROPHIC FACTOR



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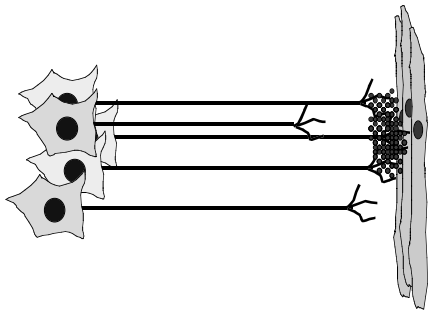

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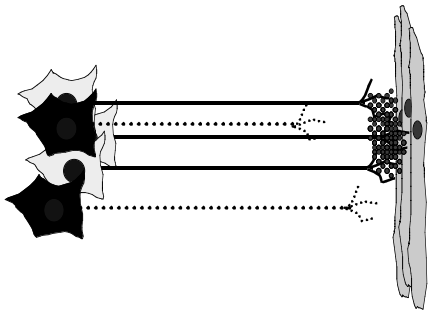
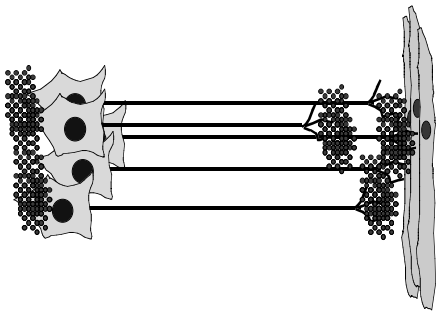
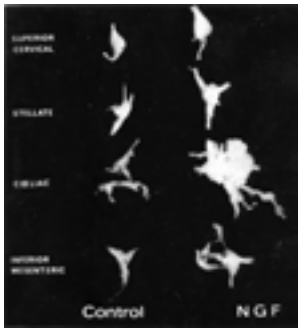


NEURONAL CULLING AS REGULATED BY COMPETITION FOR TARGET-SUPPLIED TROPHIC FACTOR



EXTERNALLY SUPPLIED TROPHIC FACTOR BLOCKS DEVELOPMENTAL NEURONAL CULLING

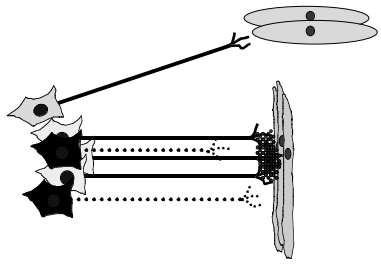


FUNCTIONS OF DEVELOPMENTAL CELL DEATH

E. <u>ELIMINATION OF ECTOPIC, DAMAGED OR UNEE CELLS</u>

ECTOPIC CELLS

ELIMINATION OF ECTOPIC NEURONS



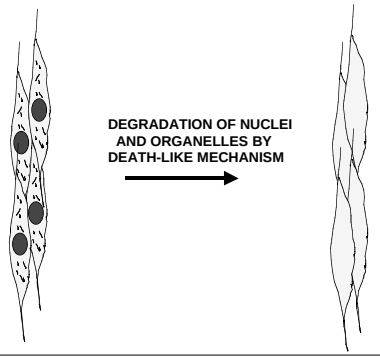
FUNCTIONS OF DEVELOPMENTAL CELL DEATH

F. PRODUCTION OF STRUCTURES WITHOUT ORGANELLES

SQUAMOUS EPITHELIUM FROM KERATINOCYTES

FORMATION OF LENS FROM LENS FIBER CELLS

FORMATION OF CLEAR LENS FROM LENS FIBER CELLS



CONSEQUENCES OF FAULTY CELL DEATH MECHANISM

- **EMBRYONIC LETHALITY**

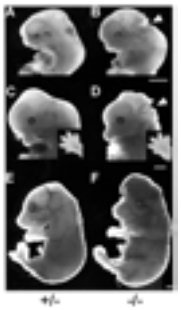
  EXCESSIVE DEATH

- **SPINAL MUSCULAR ATROPHY**
- **SEVERE CONGENITAL NEUTROPENIA**

  IMPAIRED DEATH

- **SYNDACTYLY - WEBBED FINGERS/TOES**
- **CONGENITAL HEART DEFECTS**

EMBRYOGENIC DEFECTS IN A MOUSE LACKING CASPASE



From: Kuida et a Cell:94: 325-337, 1998