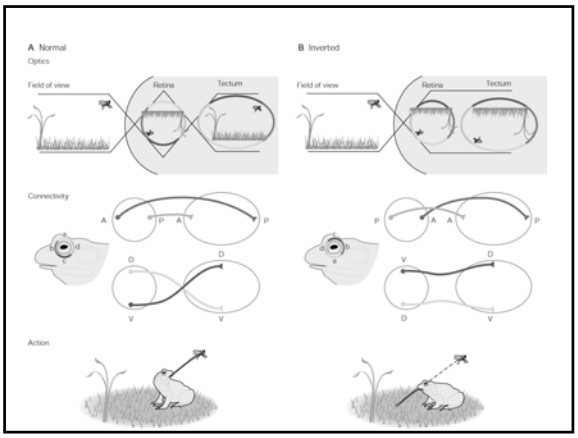
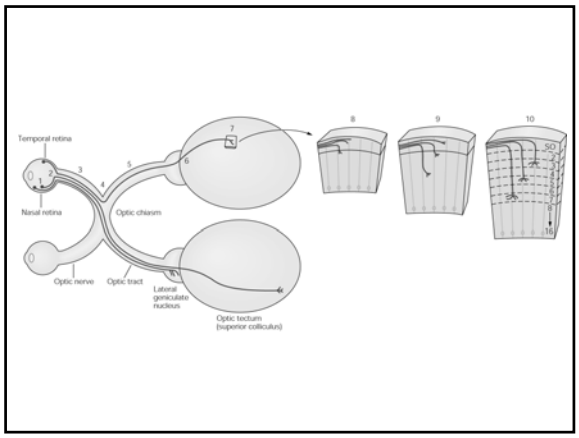
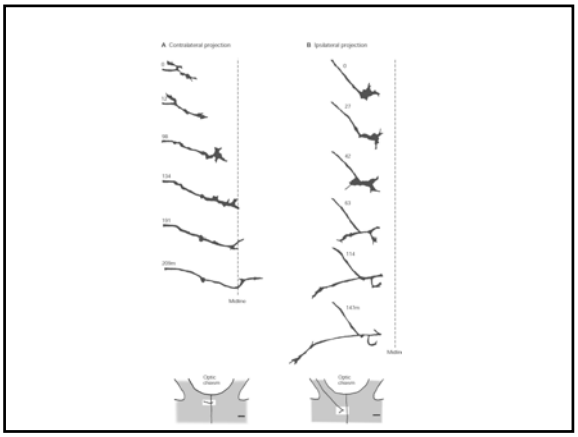
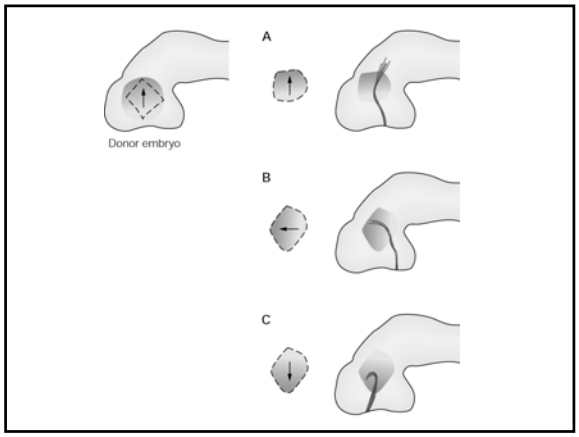
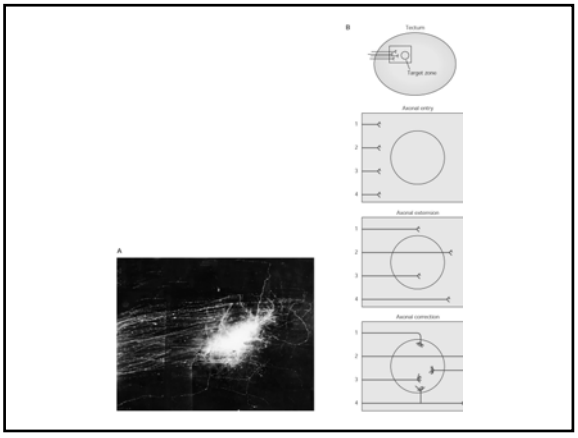
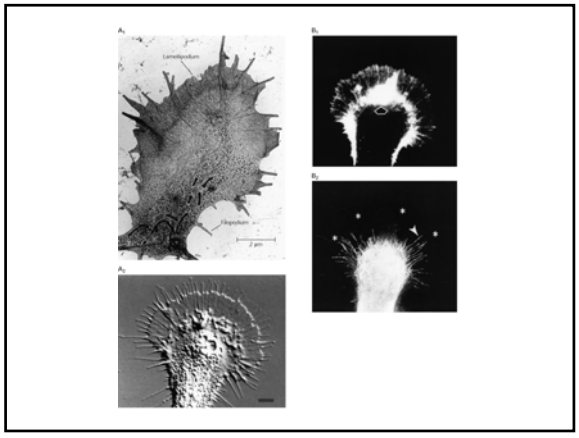

A Normal
B Inverted
Optics
Field of view
Retina
Tectum
Connectivity
Action

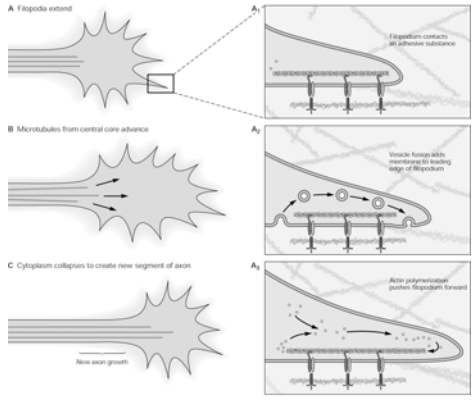

Temporal retina
Nasal retina
Optic chiasm
Optic nerve
Optic tract
Lateral geniculate nucleus
Optic tectum (superior colliculus)

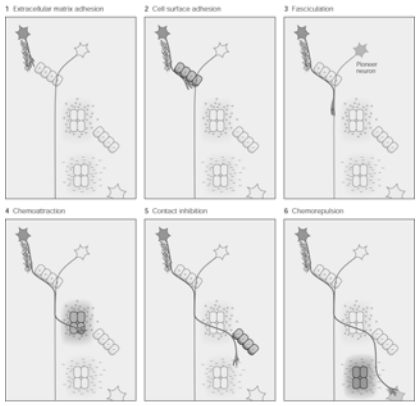

A Contralateral projection
B Ipsilateral projection
Midline
Optic chiasm

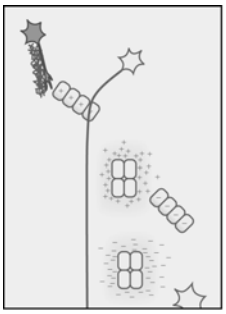

A
B
C
Donor embryo

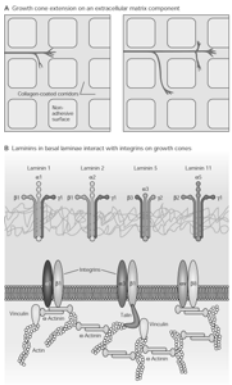

A
B
Tectum
Target zone
Axonal entry
Axonal extension
Axonal correction

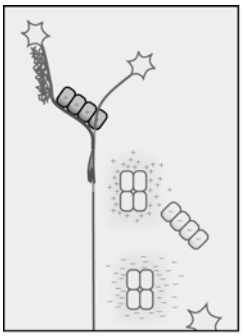

Lamellipodium
Filopodium
2 µm

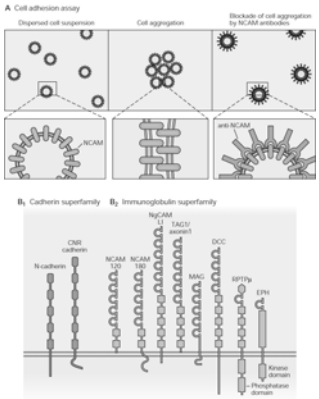

A Filopodia extend
A1
Filopodium contacts an adhesive substance
B Microtubules from central core advance
A2
Vesicle fusion adds membrane to leading edge of filopodium
C Cytoplasm collapses to create new segment of axon
A3
Actin polymerization pushes filopodium forward
New axon growth

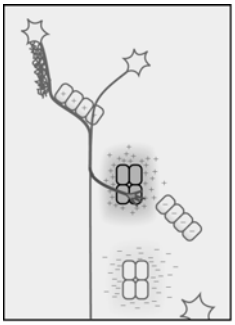

1 Extracellular matrix adhesion
2 Cell surface adhesion
3 Fasciculation
Pioneer neuron
4 Chemoattraction
5 Contact inhibition
6 Chemorepulsion

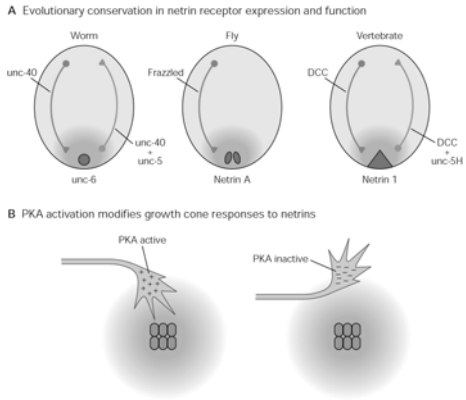


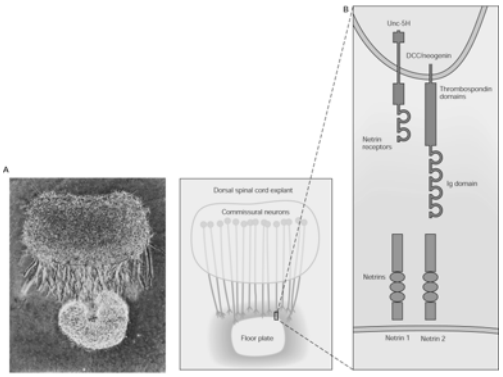

A Growth cone extension on an extracellular matrix component
Collagen-coated corridors
Non-adhesive surface
B Laminins in basal laminae interact with integrins on growth cones
Laminin 1
Laminin 2
Laminin 5
Laminin 11
Integrins
Vinculin
α-Actinin
Talin
Actin

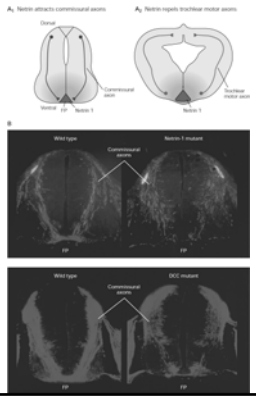


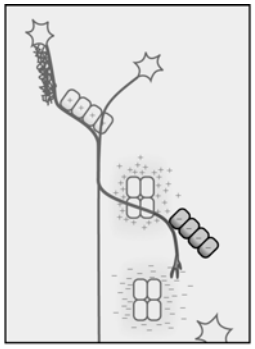

A Cell adhesion assay
Dispersed cell suspension
Cell aggregation
Blockade of cell aggregation by NCAM antibodies
NCAM
anti-NCAM
B1 Cadherin superfamily
B2 Immunoglobulin superfamily
N-cadherin
CNR cadherin
NCAM 120
NCAM 180
NgCAM L1
TAG1/ axonin1
MAG
DCC
RPTPρ
EPH
Kinase domain
Phosphatase domain

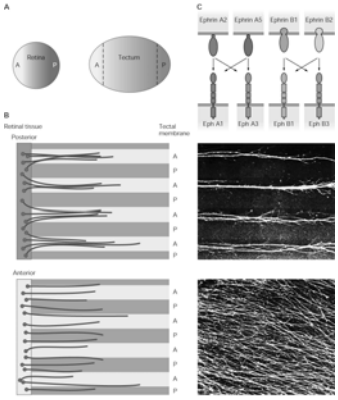


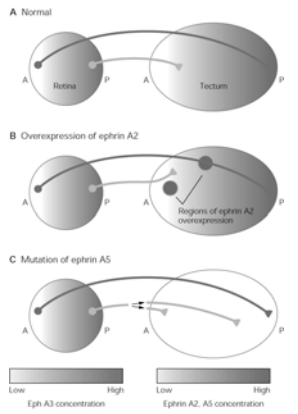

A Evolutionary conservation in netrin receptor expression and function
Worm
Fly
Vertebrate
unc-40
Frazzled
DCC
unc-40
+
unc-5
DCC
+
unc-5H
unc-6
Netrin A
Netrin 1
B PKA activation modifies growth cone responses to netrins
PKA active
PKA inactive

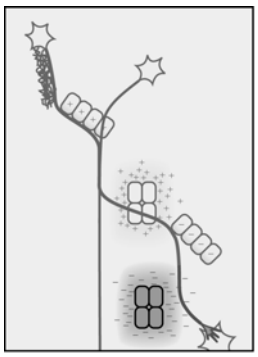

A
B
Dorsal spinal cord explant
Commissural neurons
Floor plate
Unc-5H
DCC/neogenin
Thrombospondin domains
Netrin receptors
Ig domain
Netrins
Netrin 1
Netrin 2

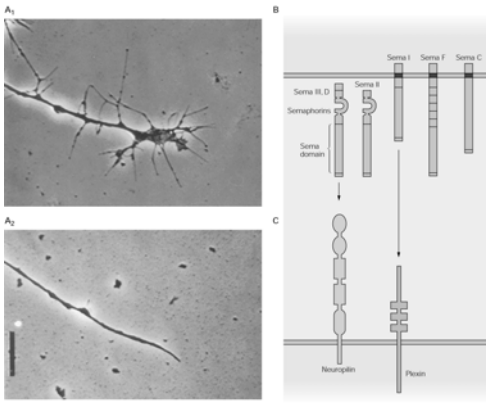

Wild type
Netrin-1 mutant
Commissural axons
FP
Wild type
DCC mutant
Commissural axons
FP

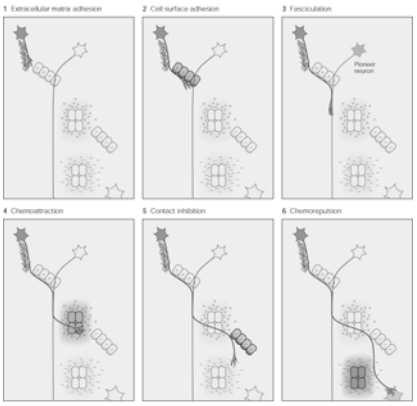


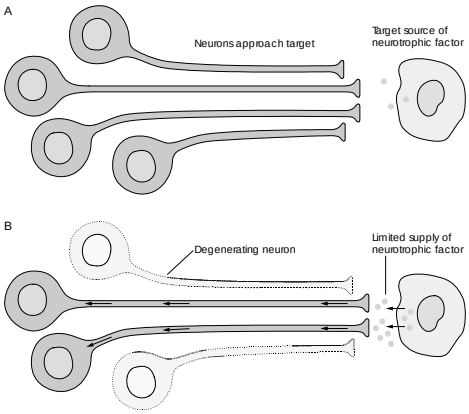

A
Retina
Tectum
C
Ephrin A2
Ephrin A5
Ephrin B1
Ephrin B2
Eph A1
Eph A3
Eph B1
Eph B3
B
Retinal tissue
Tectal membrane
Posterior
Anterior

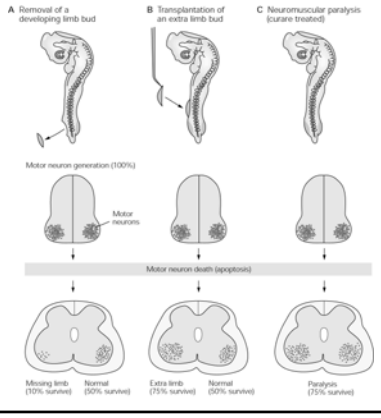

A Normal
Retina
Tectum
A
P
B Overexpression of ephrin A2
Regions of ephrin A2 overexpression
C Mutation of ephrin A5
Low
High
Eph A3 concentration
Ephrin A2, A5 concentration

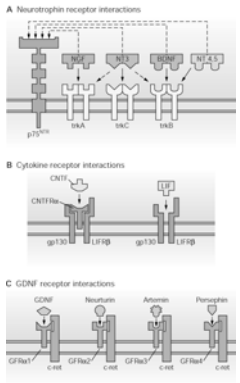


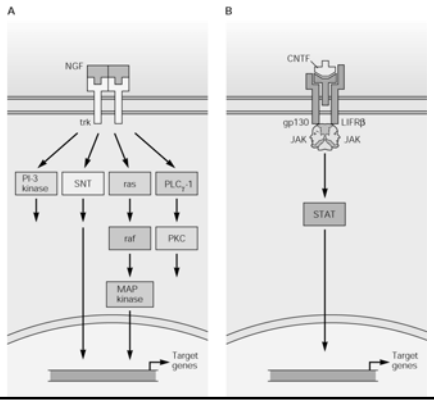

A1
A2
B
C
Sema I
Sema F
Sema C
Sema II
Sema III, D
Semaphorins
Sema domain
Neuropilin
Plexin

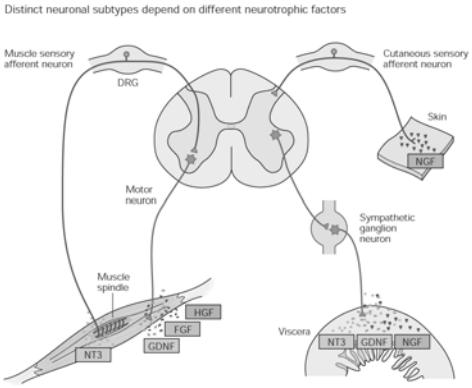

1 Extracellular matrix adhesion
2 Cell surface adhesion
3 Fasciculation
Pioneer neuron
4 Chemoattraction
5 Contact inhibition
6 Chemorepulsion

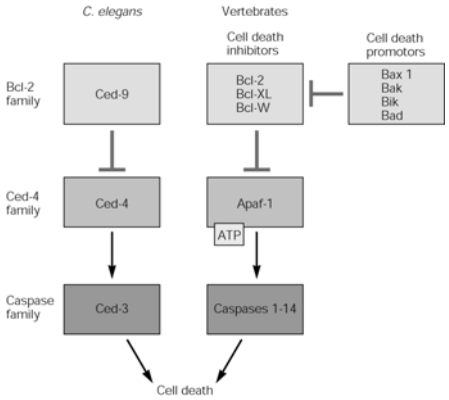

A
Neurons approach target
Target source of neurotrophic factor
B
Degenerating neuron
Limited supply of neurotrophic factor

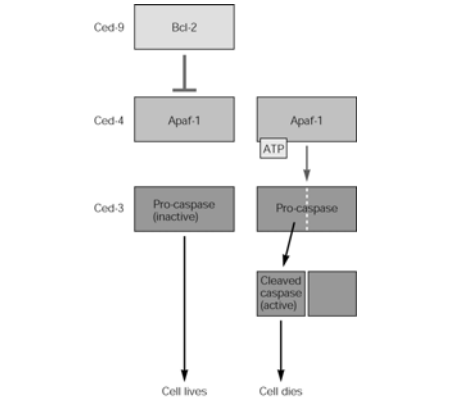

A Removal of a developing limb bud
B Transplantation of an extra limb bud
C Neuromuscular paralysis (curare treated)
Motor neuron generation (100%)
Motor neurons
Motor neuron death (apoptosis)
Missing limb (10% survive)
Normal (50% survive)
Extra limb (75% survive)
Normal (50% survive)
Paralysis (75% survive)

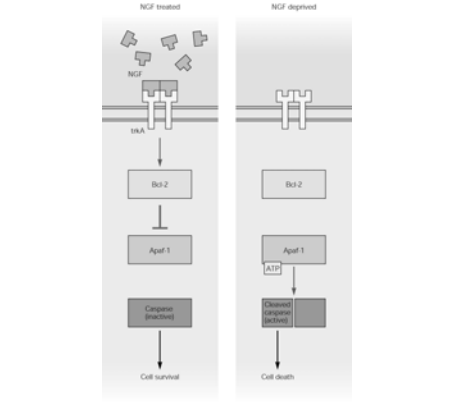

A Neurotrophin receptor interactions
NGF
NT3
BDNF
NT-4/5
trkA
trkC
trkB
p75NTR
B Cytokine receptor interactions
CNTF
CNTFRα
gp130
LIFRβ
IL6
gp130
LIFRβ
C GDNF receptor interactions
GDNF
Neurturin
Artemin
Persephin
GFRα1
GFRα2
GFRα3
GFRα4
c-ret

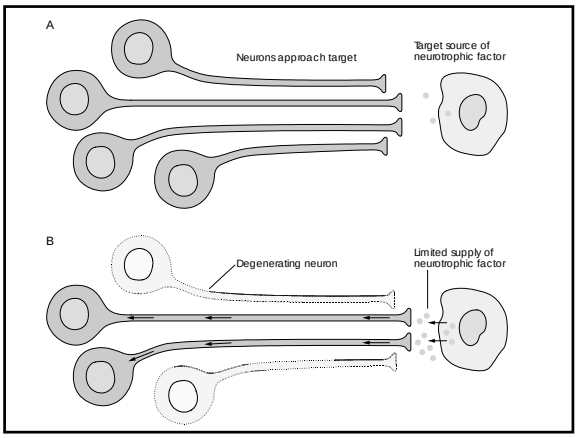

A
B
NGF
trk
PI-3 kinase
SNT
ras
PLCγ-1
raf
PKC
MAP kinase
Target genes
CNTF
gp130
LIFRβ
JAK
JAK
STAT
Target genes


Distinct neuronal subtypes depend on different neurotrophic factors
Muscle sensory afferent neuron
DRG
Cutaneous sensory afferent neuron
Skin
NGF
Motor neuron
Sympathetic ganglion neuron
Muscle spindle
HGF
FGF
GDNF
NT3
Viscera
NT3
GDNF
NGF


C. elegans
Vertebrates
Cell death inhibitors
Cell death promotors
Bcl-2 family
Ced-9
Bcl-2
Bcl-XL
Bcl-W
Bax 1
Bak
Bik
Bad
Ced-4 family
Ced-4
Apaf-1
ATP
Caspase family
Ced-3
Caspases 1-14
Cell death


Ced-9
Bcl-2
Ced-4
Apaf-1
Apaf-1
ATP
Ced-3
Pro-caspase (inactive)
Pro-caspase
Cleaved caspase (active)
Cell lives
Cell dies


NGF treated
NGF deprived
NGF
trkA
Bcl-2
Apaf-1
Caspase (inactive)
Cell survival
Bcl-2
Apaf-1
ATP
Cleaved caspase (active)
Cell death


A
Neurons approach target
Target source of neurotrophic factor
B
Degenerating neuron
Limited supply of neurotrophic factor