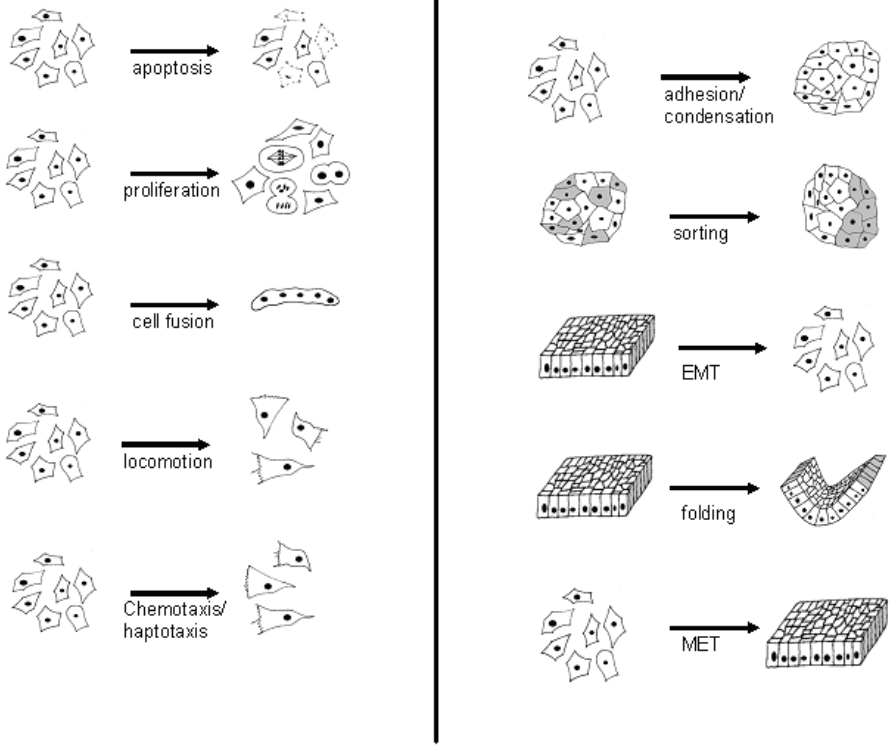
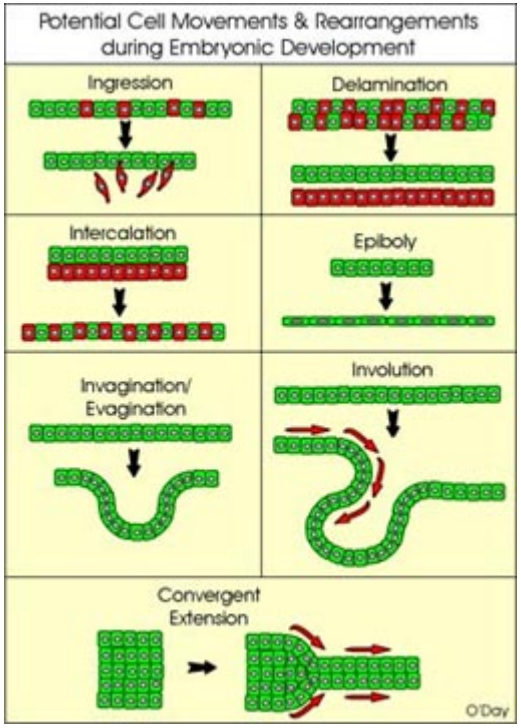
Mechanisms of development: cell movement

Ten basic mechanisms of animal morphogenesis:





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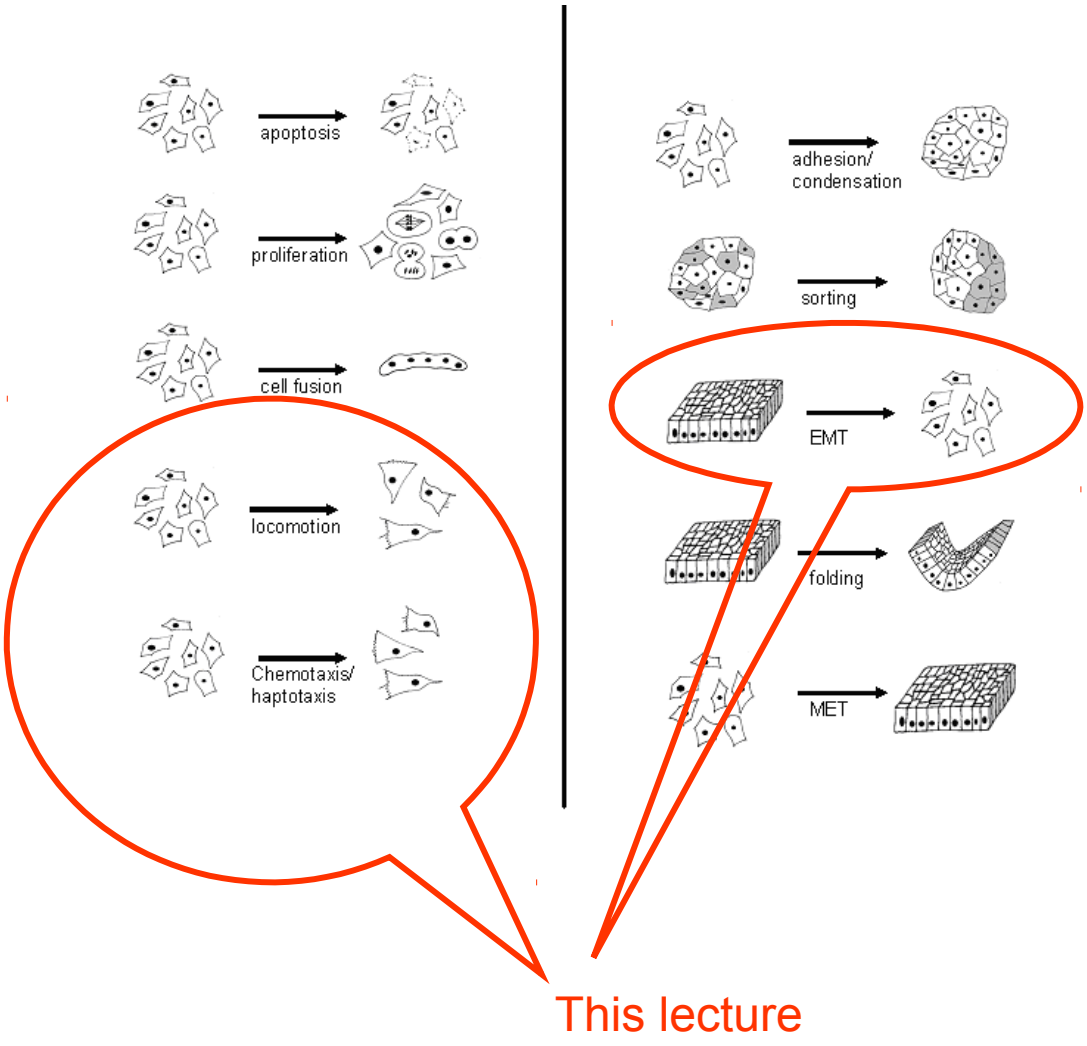
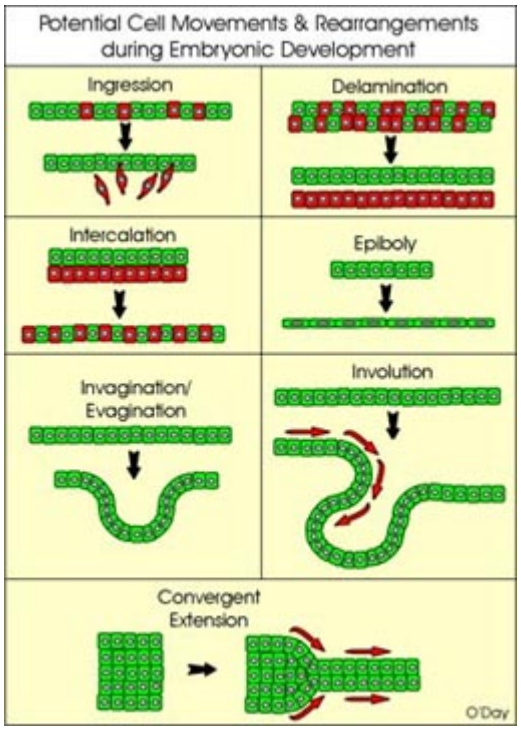
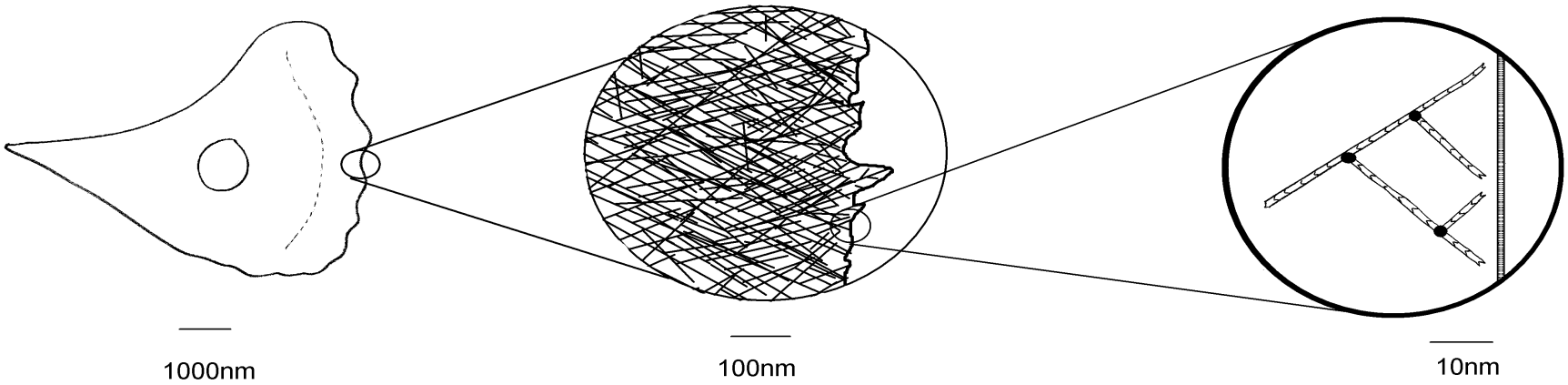
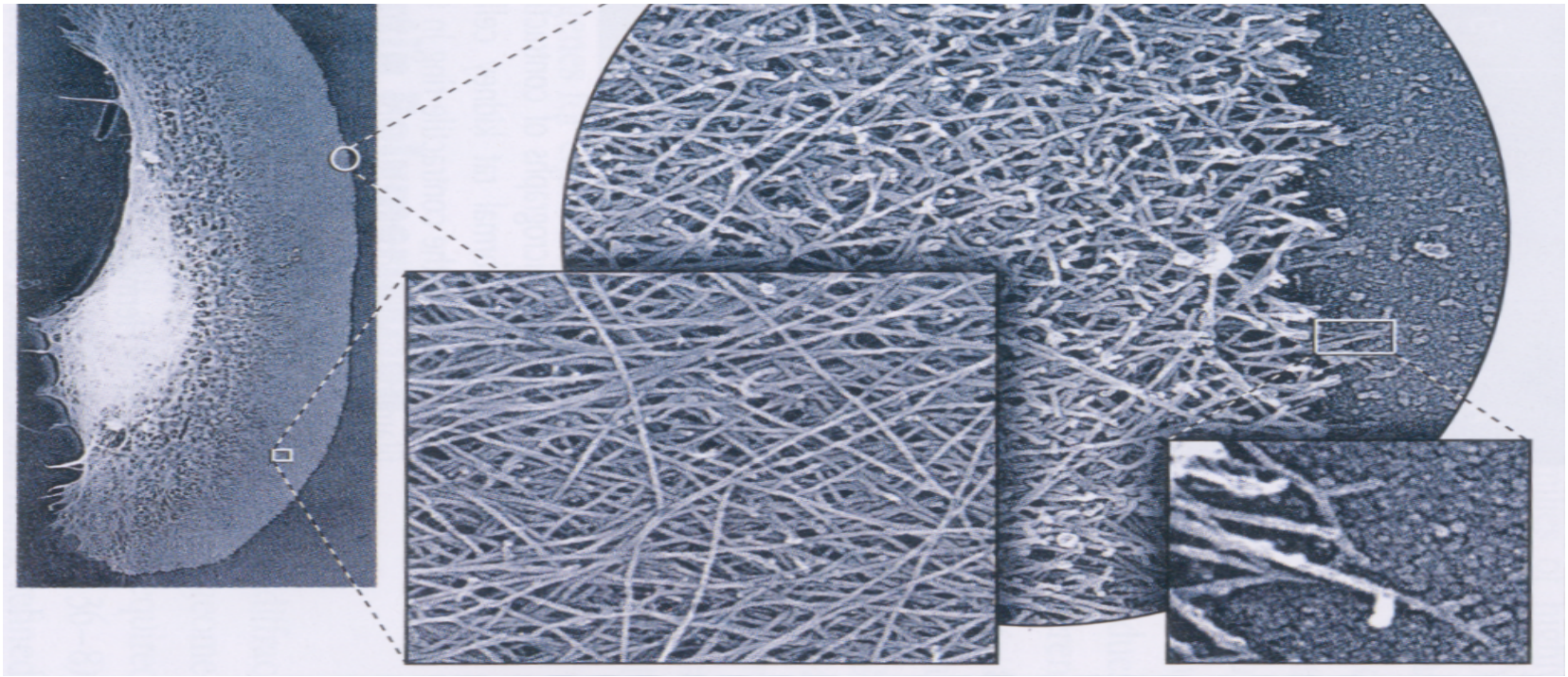


This lecture



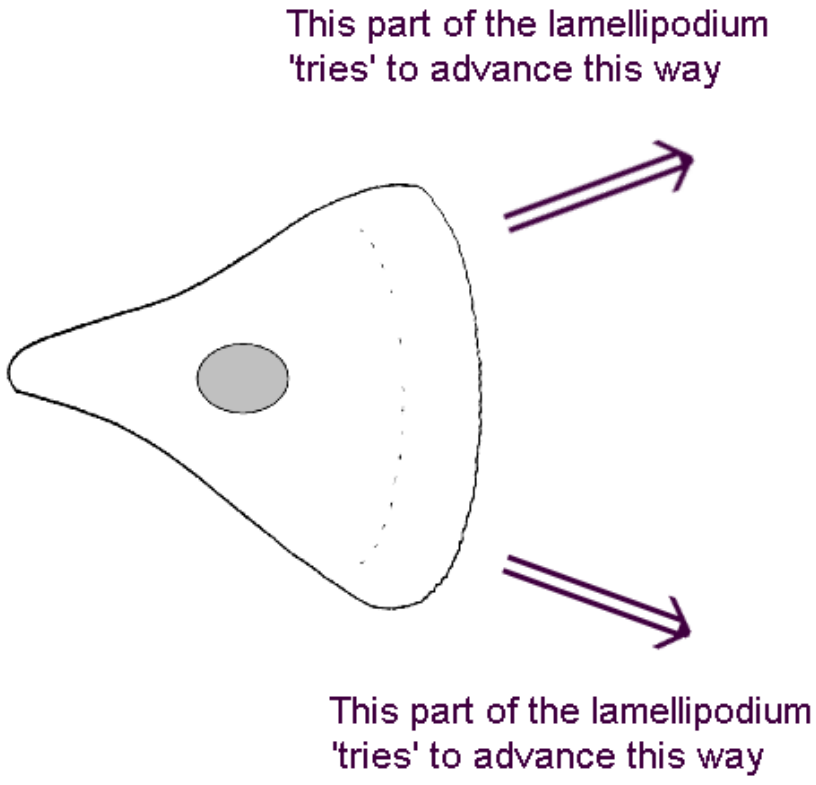
With rare exceptions (eg sperm), mammalian cells move by crawling

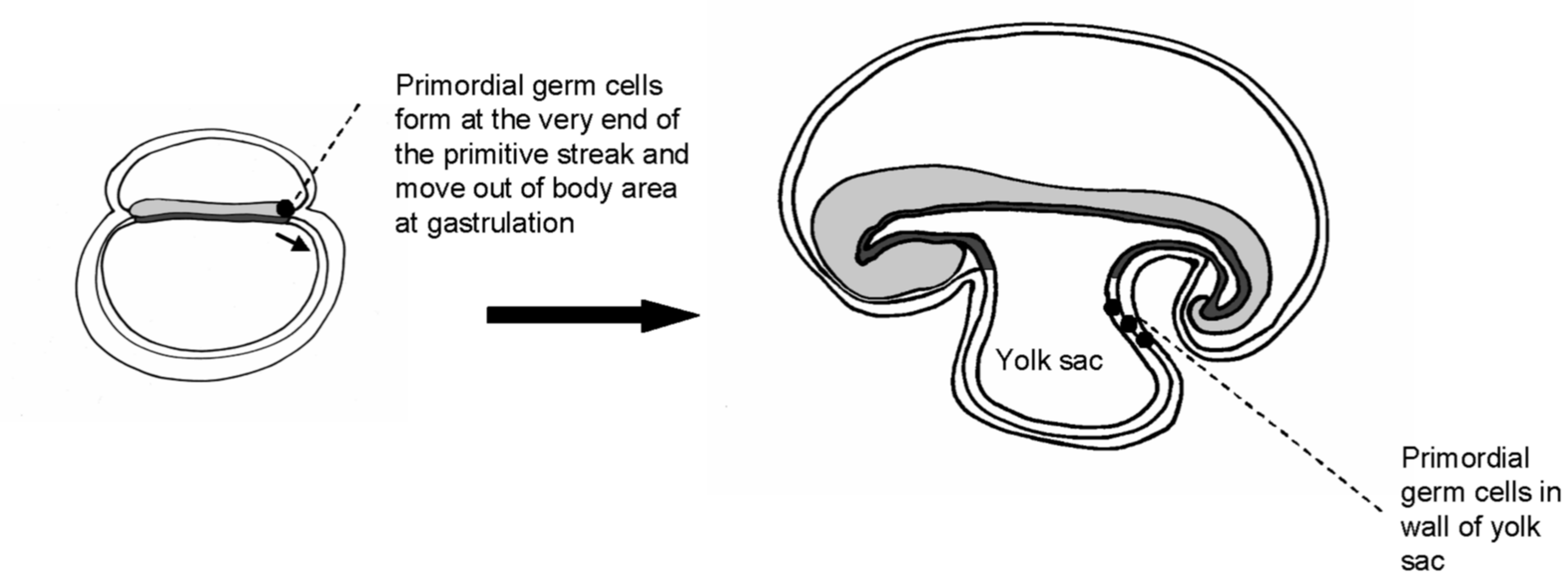

1000nm
100nm
10nm



The leading edge is autonomous

The direction in which a cell moves is determined partly by a tug-of-war

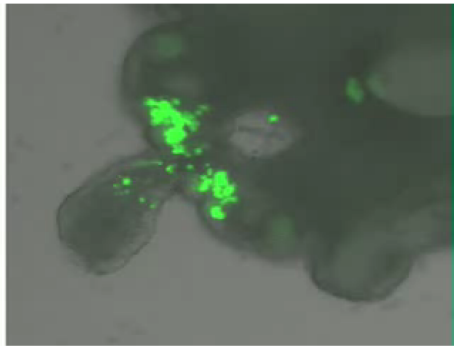



Primordial germ cells form at the very end of the primitive streak and move out of body area at gastrulation
Yolk sac
Primordial germ cells in wall of yolk sac

Real images (GFP-expressing PGCs).

Leaving the gut

and congregating in the gonad



http://embryology.med.unsw.edu.au/Movies/genital/germcell.htm

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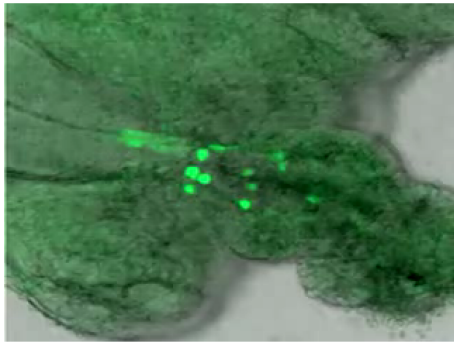

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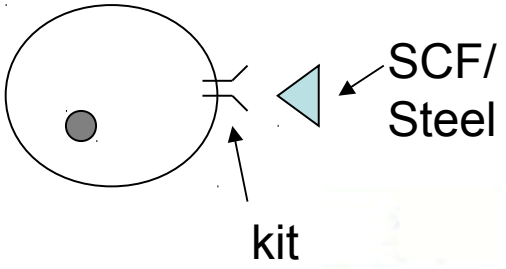
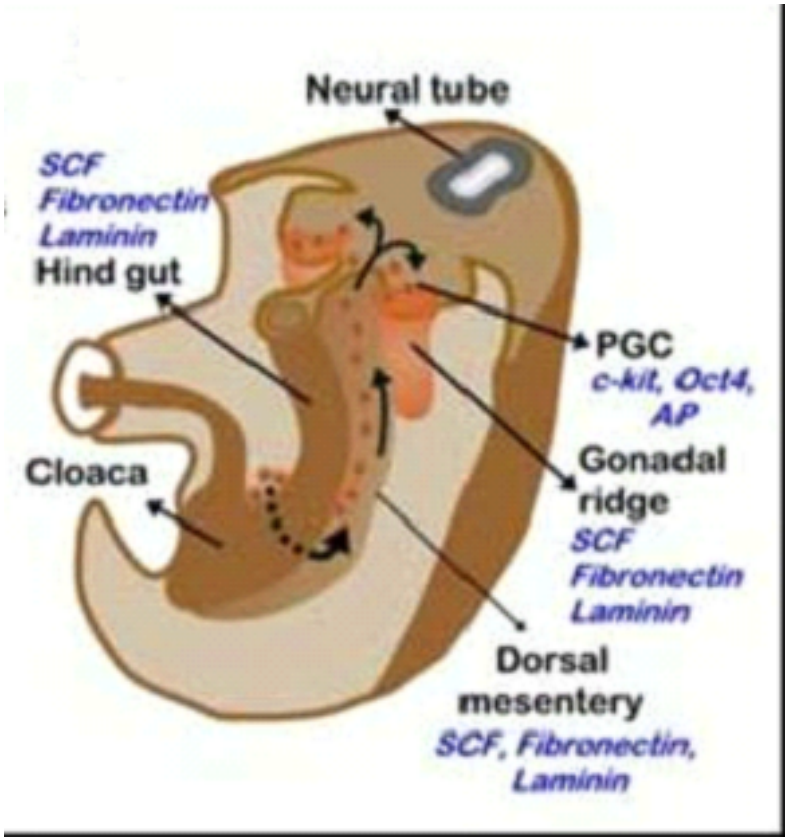
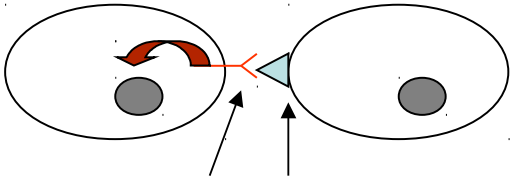
Guidance cues for primordial germ cells:





http://www.endotext.org/pediatrics/pediatrics7/pediatrics7.html

Kit is also used for getting pigment into the skin:



Also called Kit-ligand, Kitl

1. Dermatome cells (part of somite) make Steel (the membrane-bound ligand for Kit)
2. Some Neural Crest cells express the Kit receptor tyrosine kinase before leaving the neural tube
3. These cells migrate along the Steel expressed by the dematome-derived dermal fibroblasts.
4. Dermal fibroblasts stop making Steel, and epidermis starts to
5. Crest-derived cells now migrate into the epidermis, following Steel, and disperse in that tissue
6. Crest-derived cells differentiate into melanocytes
7. Steel is needed for survival of melanocytes (except in nevi or melanoma

Ref: http://www.blackwell-synergy.com/doi/full/10.1034/j.1600-0749.2003.00055.x?cookieSet=1

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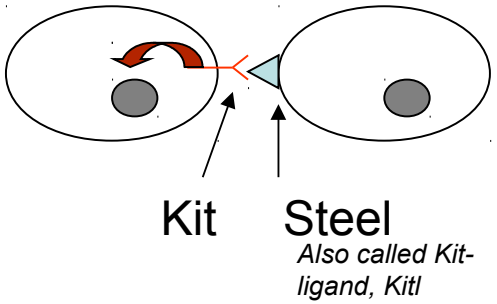

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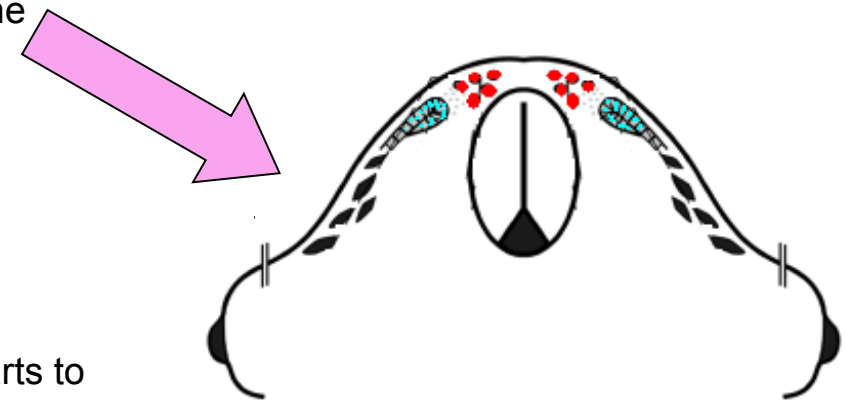

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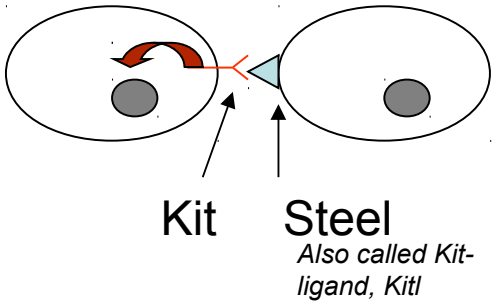

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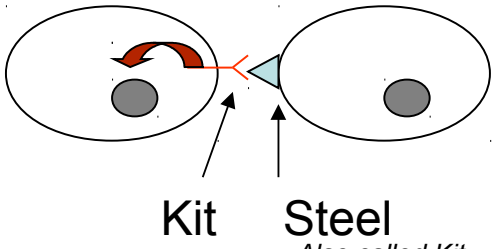

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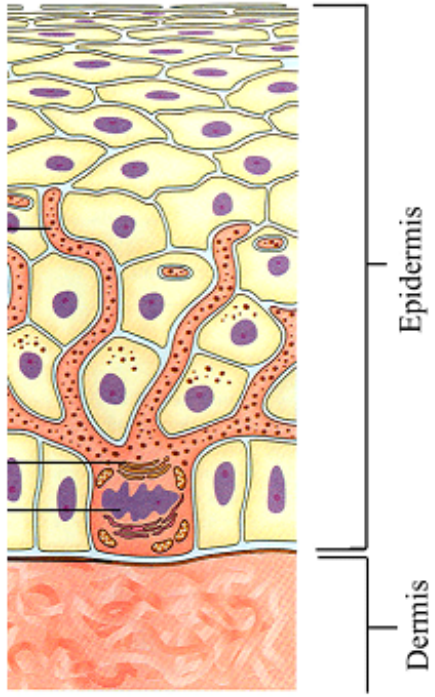

Pic: http://www.freethought-forum.com/forum/showthread.php?t=11578&garpg=2

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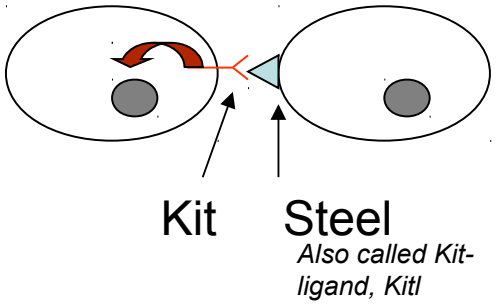

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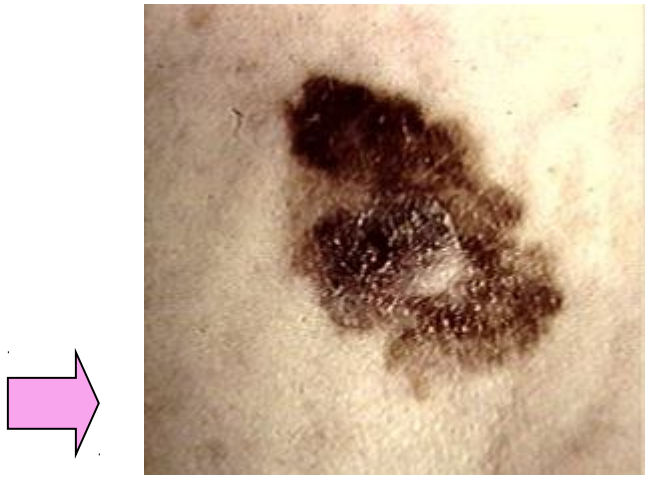

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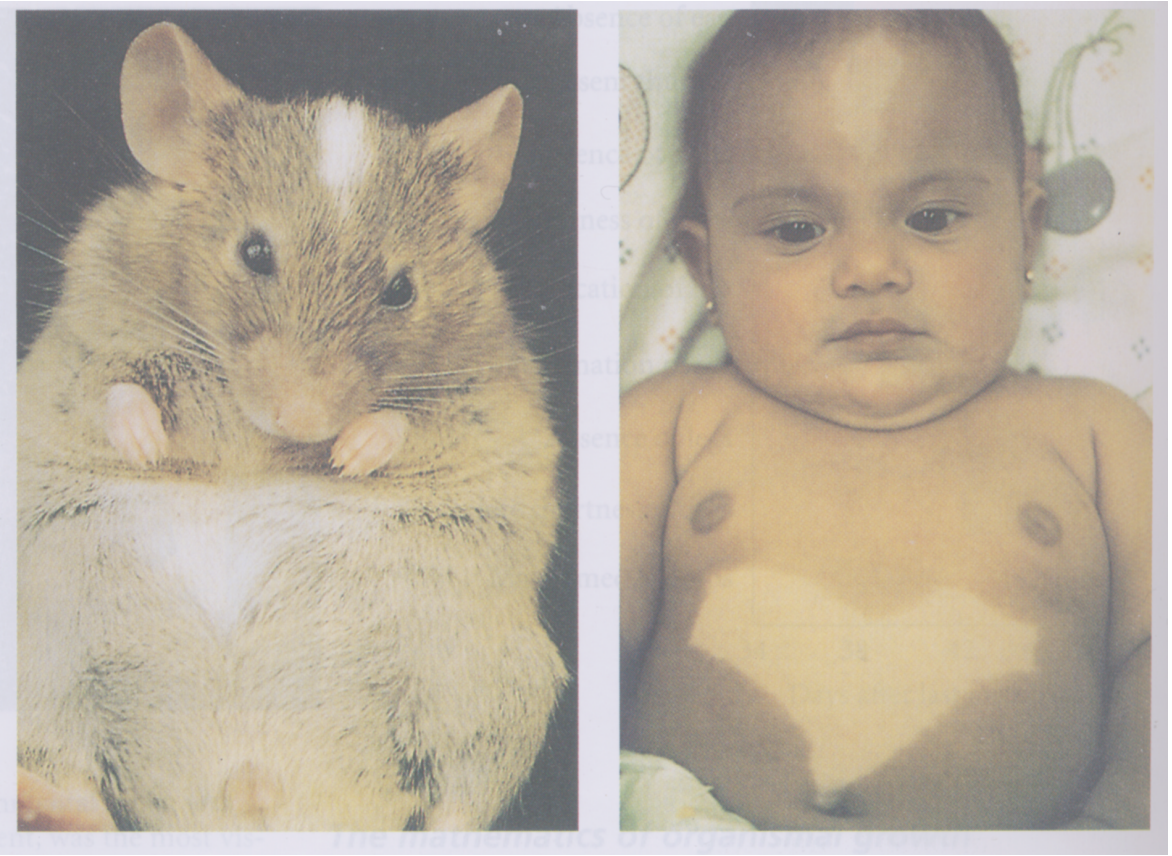
Kit mutations cause defects in neural crest (->melanocyte) migration in mice

Pic: RA Fleischman (also in Gilbert)

Kit mutations cause defects in neural crest (->melanocyte) migration in mice

… and in humans.



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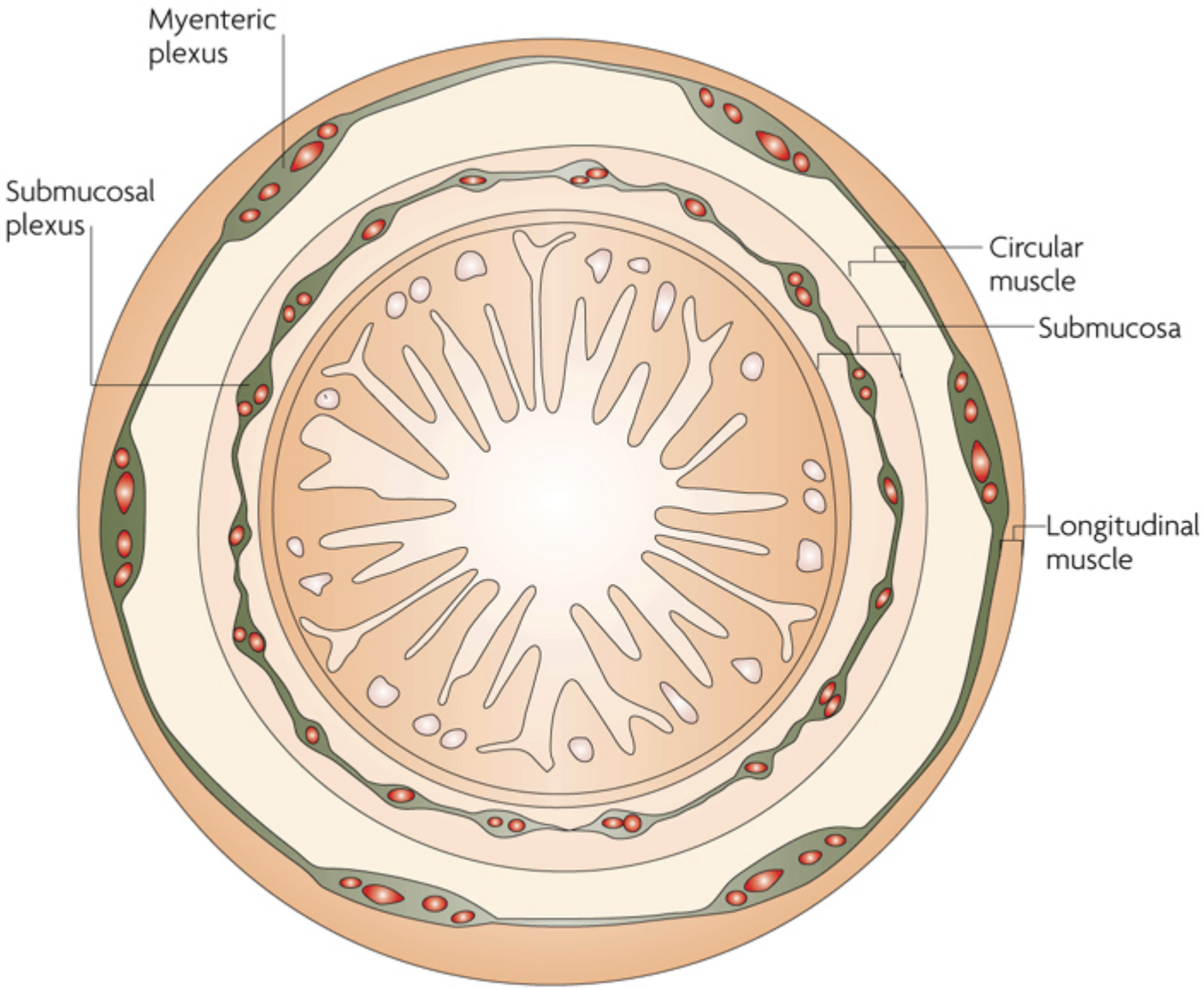
The story of the enteric nervous system (the longest crest migration, and the most complex part of the PNS)



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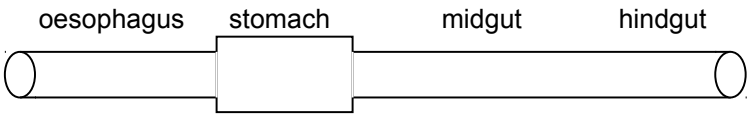

Neural crest cells from the level of somites 1-7

Migrate to foregut

Enteric neural crest-derived cells (ENCCs)

Migrate down gut

ENCCs pause at caecum

Migrate again

Settle and make neurons & glia

Growth cone migration

ENS complete

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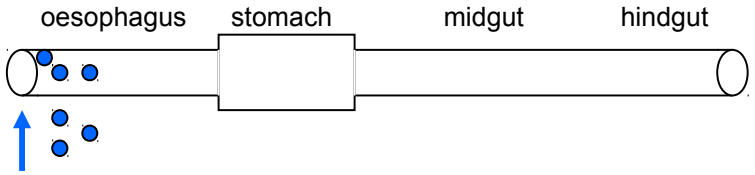

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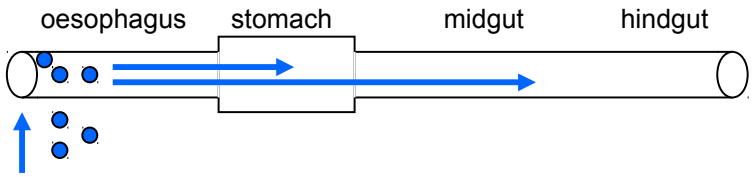

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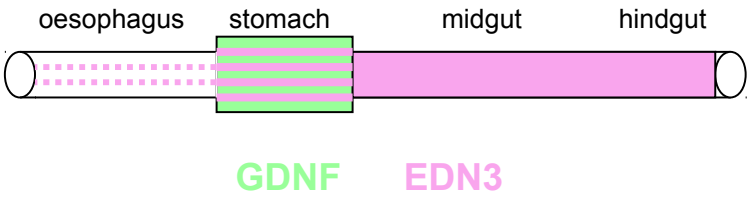

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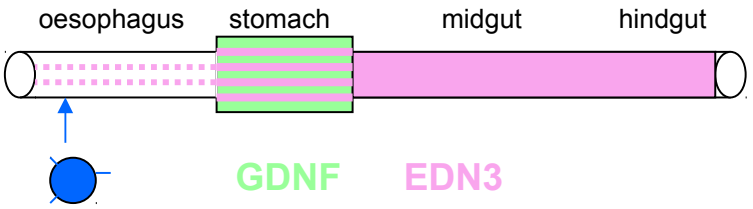

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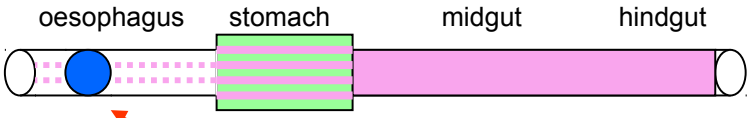

GDNF EDN3

Neural crest cells from the level of somites 1-7

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ENCCs express Ret (binds GDNF)

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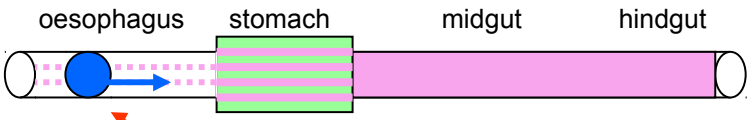

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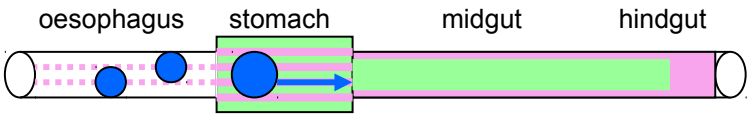

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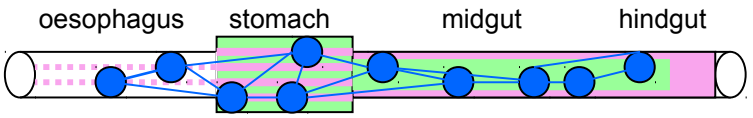

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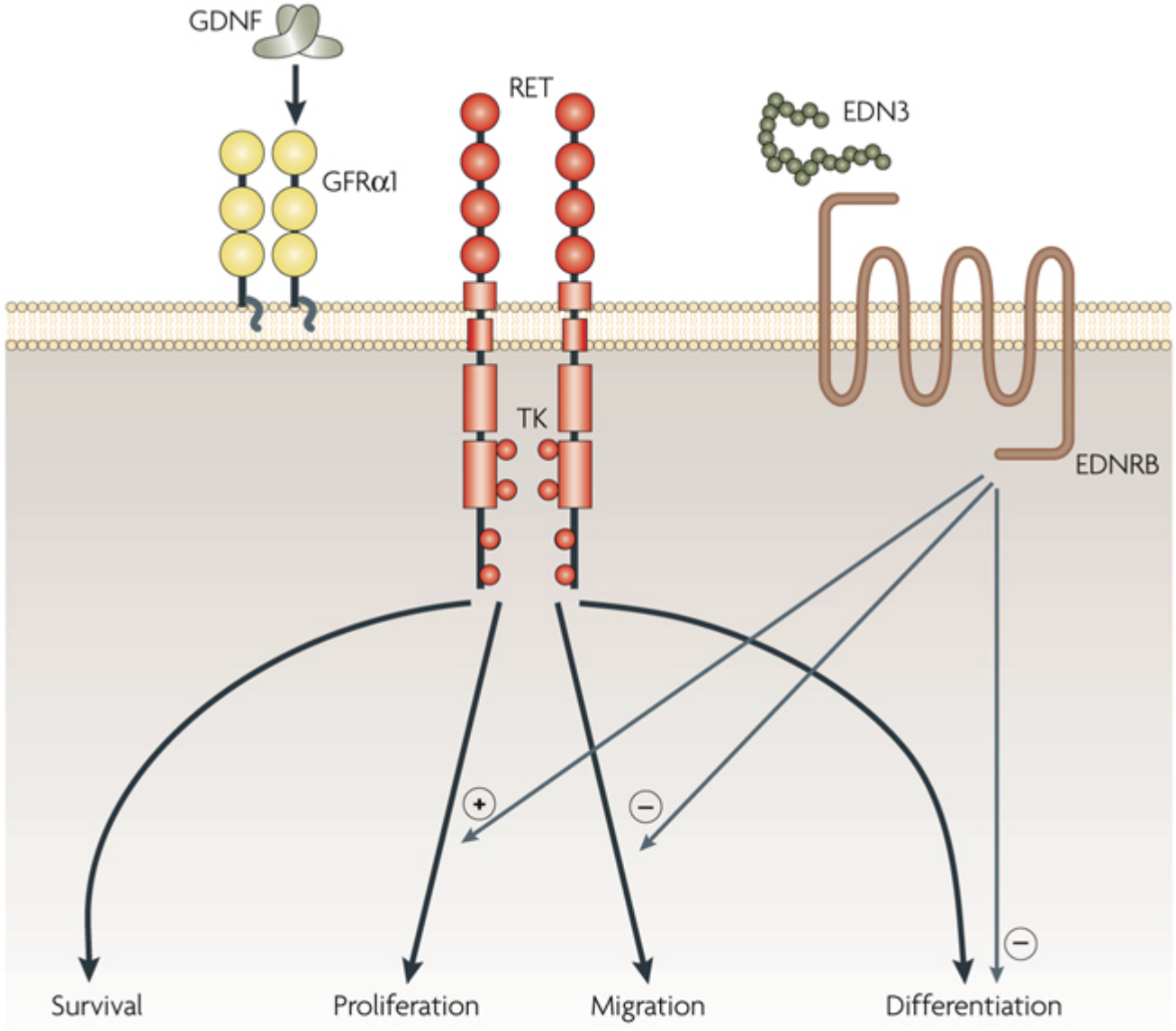
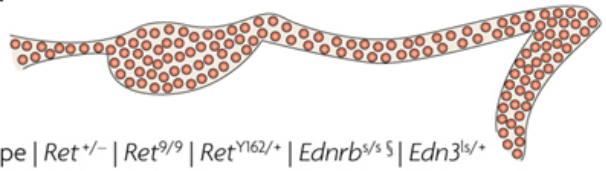

GDNF
GFRα1
RET
TK
EDN3
EDNRB
+
−
−
Survival
Proliferation
Migration
Differentiation

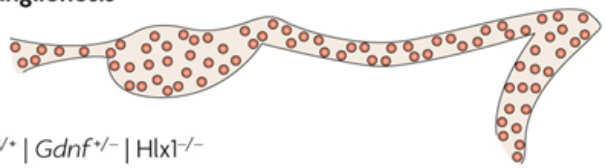
Mutants:

Normal



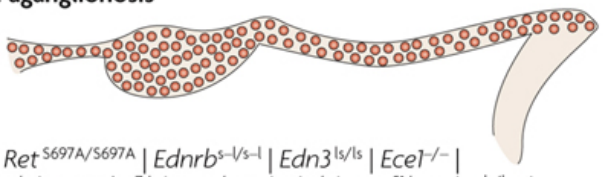
Wild type | *Ret*$^{+/-}$ | *Ret*$^{9/9}$ | *Ret*$^{Y1162/+}$ | *Ednrb*$^{s/s}$ § | *Edn3*$^{ls/+}$

Hypoganglionosis



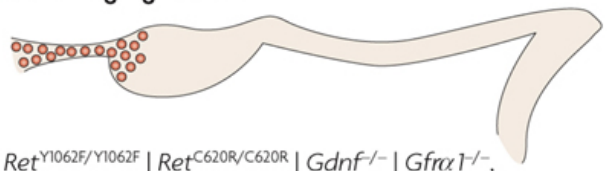
Ret$^{C620R/+}$ | *Gdnf*$^{+/-}$ | Hlx1$^{-/-}$

Colonic aganglionosis



Ret$^{51/51}$ | *Ret*$^{S697A/S697A}$ | *Ednrb*$^{s-l/s-l}$ | *Edn3*$^{ls/ls}$ | *Ece1*$^{-/-}$ | *Sox10*$^{Dom/+}$ | *Sox10*$^{LacZ/+}$ | *Ret*$^{+/-}$; *Ednrb*$^{s/s}$ | *Ret*$^{51/+}$; *Edn3*$^{ls/ls}$ *| *Sall4*$^{-/-}$ | β1-integrin$^{-/-}$ †

Total intestinal aganglionosis

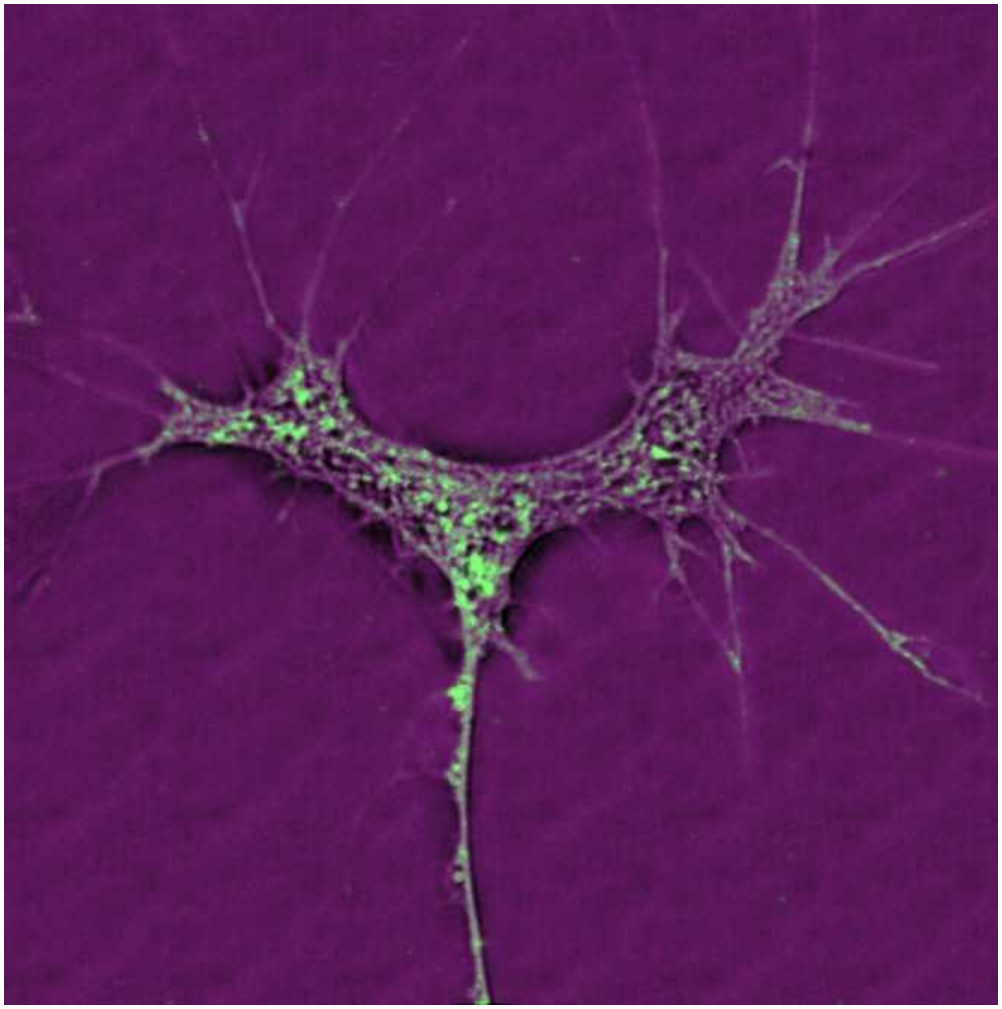


Ret$^{-/-}$ | *Ret*$^{Y1062F/Y1062F}$ | *Ret*$^{C620R/C620R}$ | *Gdnf*$^{-/-}$ | *Gfrα1*$^{-/-}$, *Sox10*$^{Dom/Dom}$ | *Sox10*$^{LacZ/LacZ}$ | *Ret*$^{51/51}$; *Edn3*$^{ls/ls}$ | *Sox10*$^{Dom/+}$; *Edn3*$^{ls/ls}$ ‡ | *Sox10*$^{Dom/+}$; *Ednrb*$^{s-l/s-l}$ ‡ | *Phox2b*$^{-/-}$ | *Pax3*$^{-/-}$

Other

Nrtn$^{-/-}$ — Reduced neuron size and density of AChE projections
Gfrα2$^{-/-}$ — Reduced density of AChE projections
DCC$^{-/-}$ — Absence of submucosal ganglia
Ihh$^{-/-}$ — Partial intestinal aganglionosis and megacolon
Shh$^{-/-}$ — Ectopic ganglia formation
NT3$^{-/-}$ — Reduced number of myenteric and submucosal ganglia
TrkC$^{-/-}$ — Reduced number of myenteric and submucosal ganglia
Spry2$^{-/-}$ — Increased number of neurons throughout gut

The neuronal growth cone:

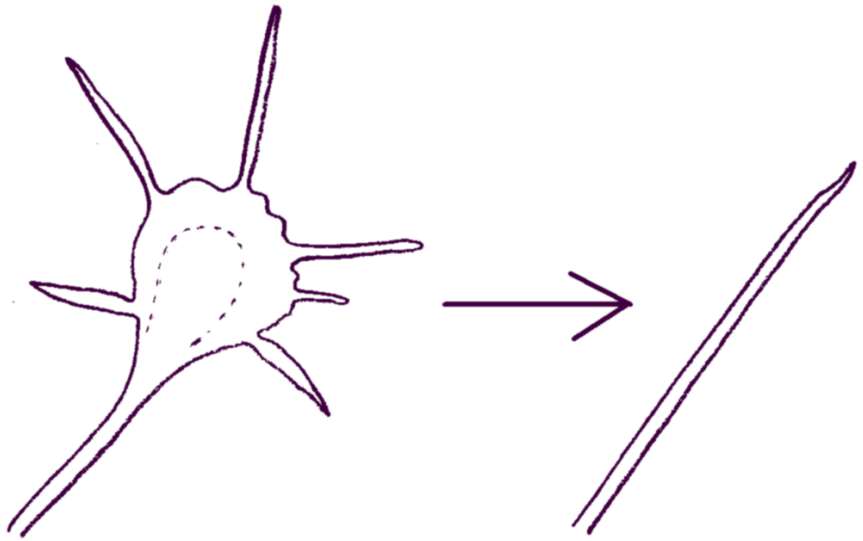


http://www.pdn.cam.ac.uk/staff/holt/delsgc.jpg

Grown cone navigation from eye (retina) to brain (optic tectum):

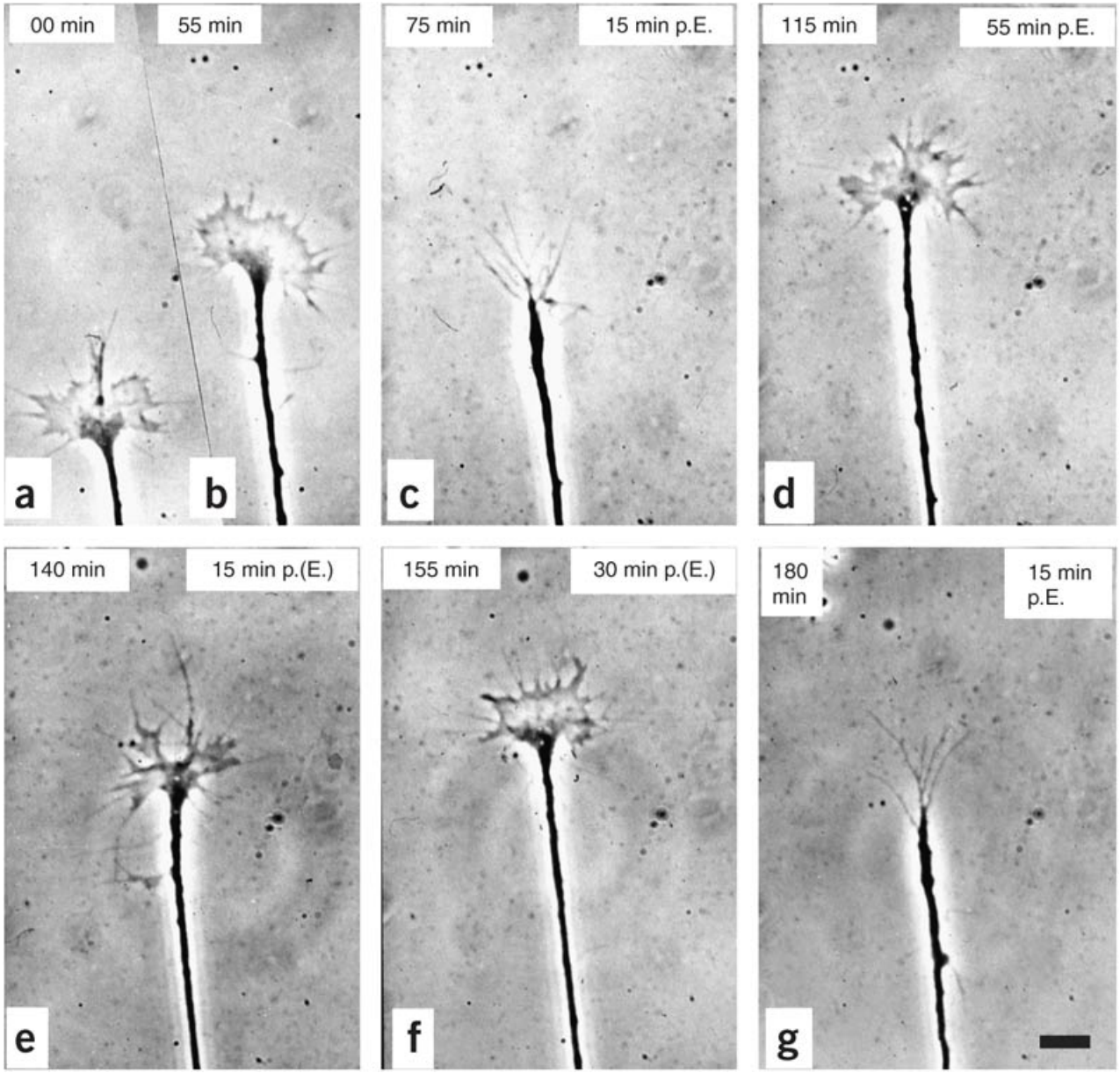
http://www.pdn.cam.ac.uk/staff/holt/index.html

Repulsive substrates cause growth cones to collapse:

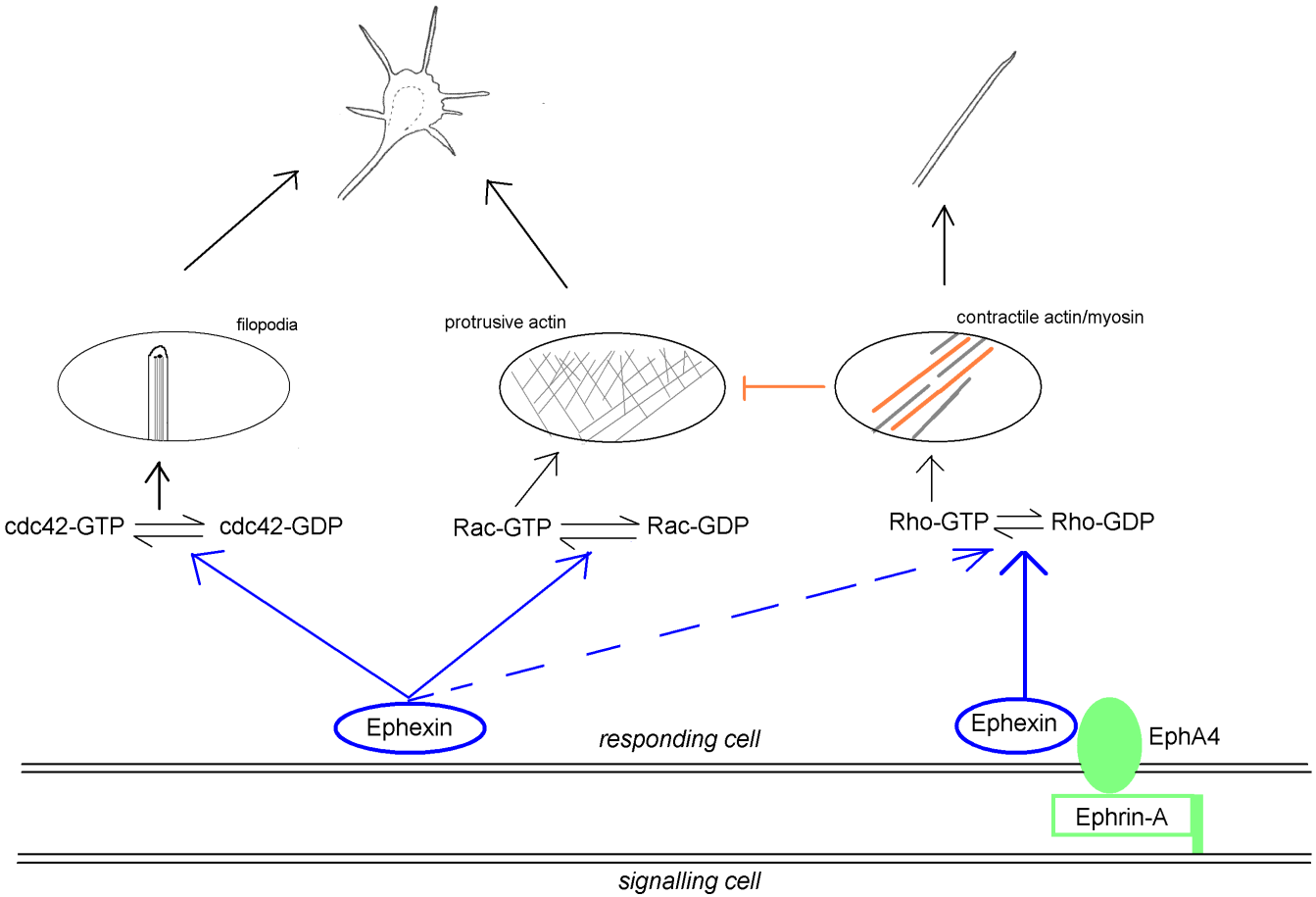


normal collapsed

Real pictures: (2 applications of collapse-inducing ephrin)



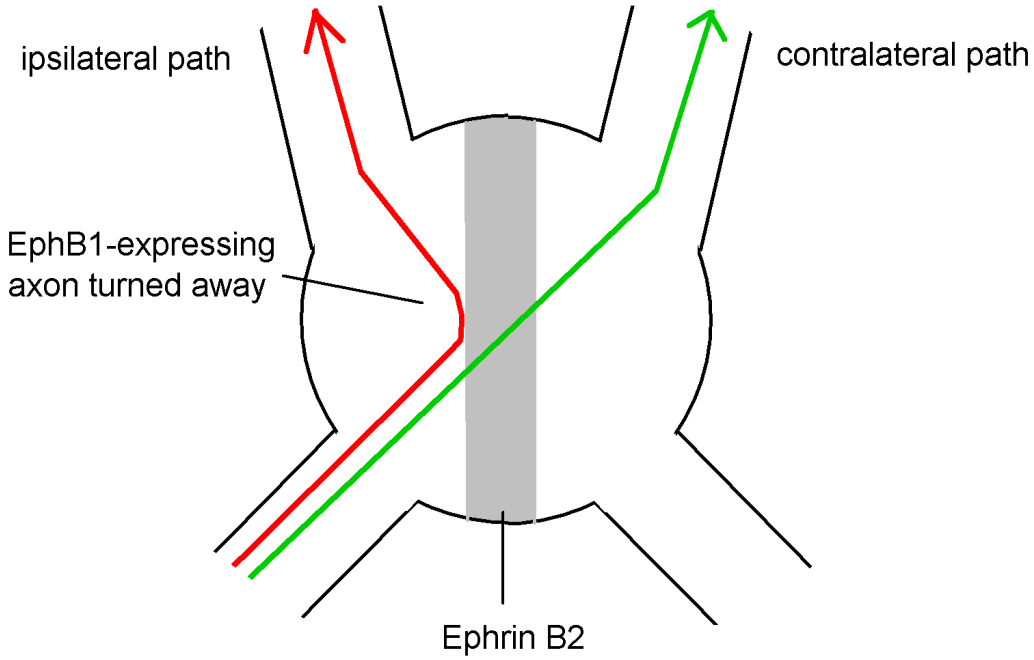
How ephrins repel



Pic: Davies, Mechanisms of Morphogenesis

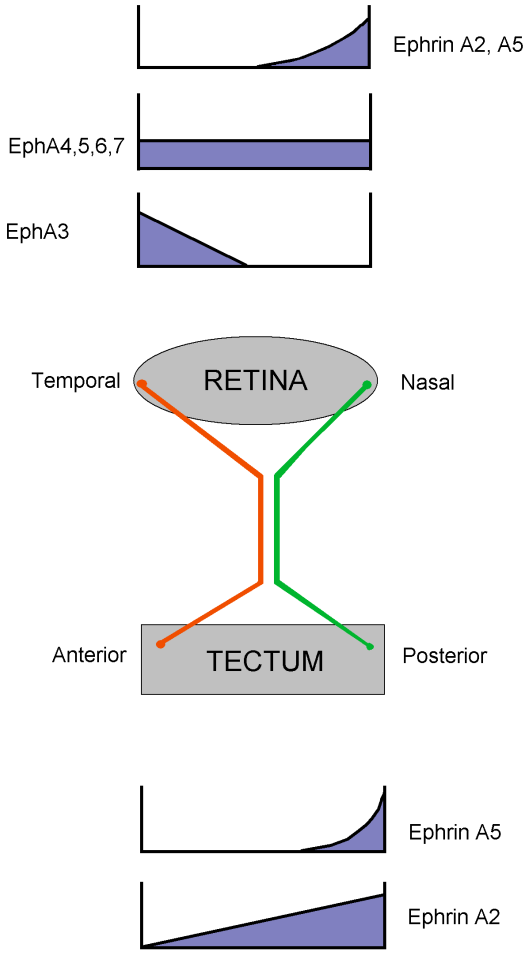
This is what it really looks like (in a dish)

Use of ephrins in sorting retinal axons concerned with binocular vision



Pic: Davies, Mechanisms of Morphogenesis

And letting us see at all…



Of course, even as adult we have some cells that move:

The movie shows a neutrophil hunting bacteria (by chemotaxis for bacterial products)

Again, see http://golgi.ana.ed.ac.uk/coursenotes/ for slides and movies