9.09J/7.29J - Cellular Neurobiology, Spring 2005
Massachusetts Institute of Technology
Department of Brain and Cognitive Sciences, Department of Biology
Instructors: Professors William Quinn and Troy Littleton
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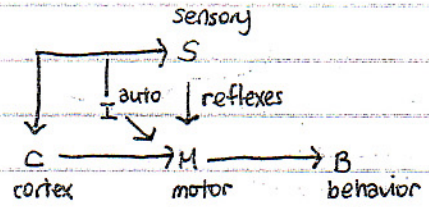
3/31/04

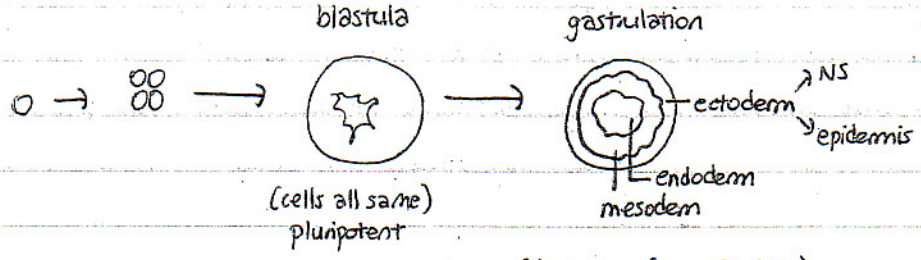
parietal lobe - contains major somatosensory region

temporal lobe - important in hearing, language



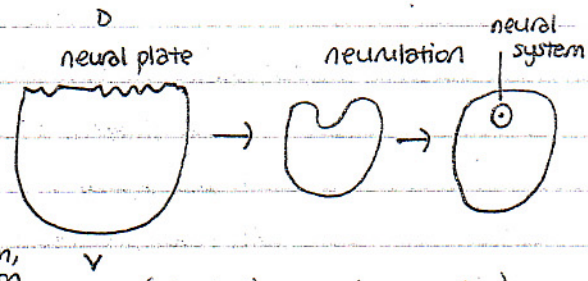
neural tube → forebrain, midbrain, hindbrain, spinal cord → medulla, pons, cerebellum, cerebral hemispheres

25 days 40 days 100 days



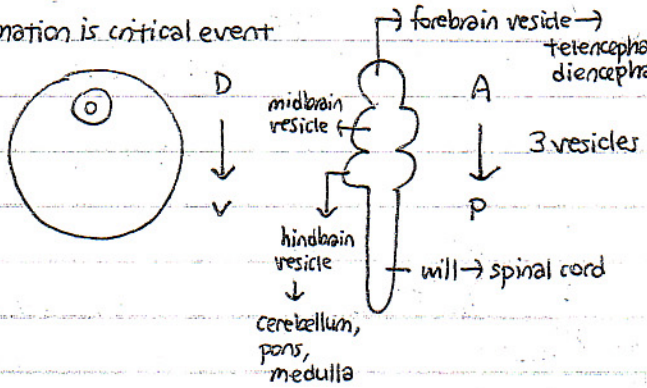
ectoderm: flattens on dorsal side, round still on ventral

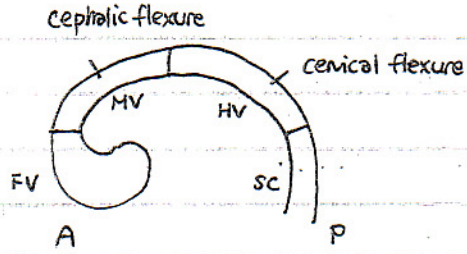
↳ forms grooved neural plate



- axis formation is critical event

(very in timecourse by organism)





- forebrain vesicle splits → cerebral hemispheres, diencephalon

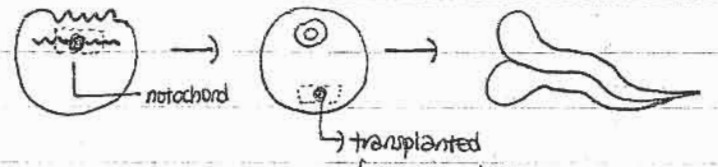
pons → rhombomeres → cranial nerves

cerebral cortex → prosomeres

1920's: ~~Spemann~~ Spemann & Mangold : transplanted regions to other regions

- looked in newts

- taking mesoderm w/ notochord, transplanting, → 2 NS



mesoderm forms notochord (runs down A→P axis)

→ transplanted from mesoderm (Spemann's organizer)

transplanted right after gastrulation

(notochord later forms from this mesoderm)

- if take earlier, so induces ~~becomes~~ forebrain structures

if take later, induces more caudal structures

- pathways by which cells can communicate : 6 pathways (fundamental)

- all have same principles (need signal from one cell, receptor on other)

(pathway from receptor → nucleus → changes in gene expression)

* 1. TGFβ

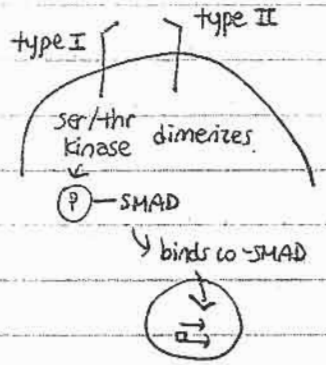
- BMPs, activin, DPP all components of this

↳ in invertebrates

- 2 classes of Rs (Type I, Type II)

- many different R isoforms, many ligands

- critical role in breast cancer, wound repair



3 amino acids: side chains can be phos.

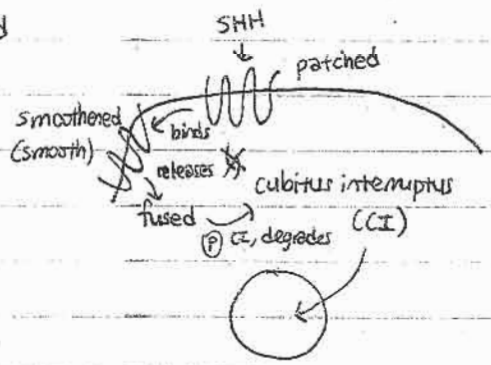
—OH ser

—CH_2-OH thr

tyr

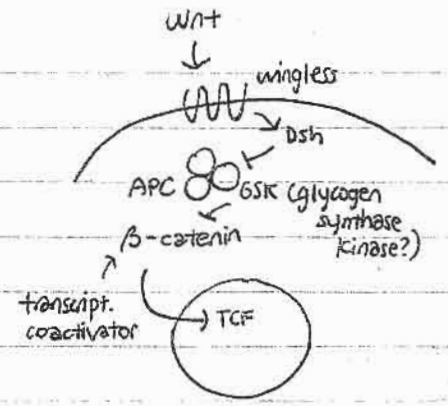
(formation of neural epithelium, also dorsal cell fates in spinal cord)

* 2. Hedgehog - Patched



- critical in basal cell carcinoma, early brain diseases

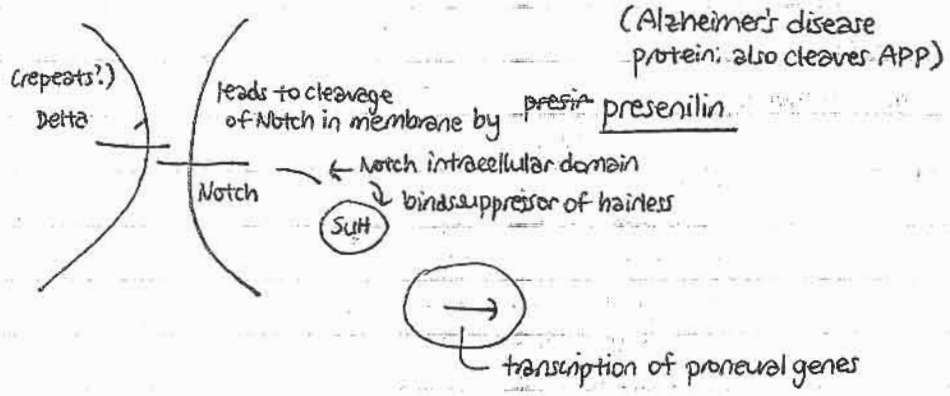
3. Wingless



all so far can work short or long range (diffusible)

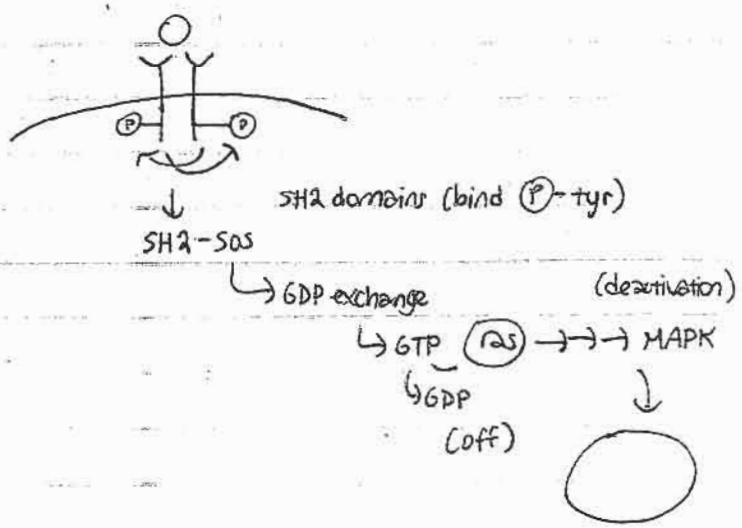
4. Notch / Delta

- local pathway, requires cells next to each other

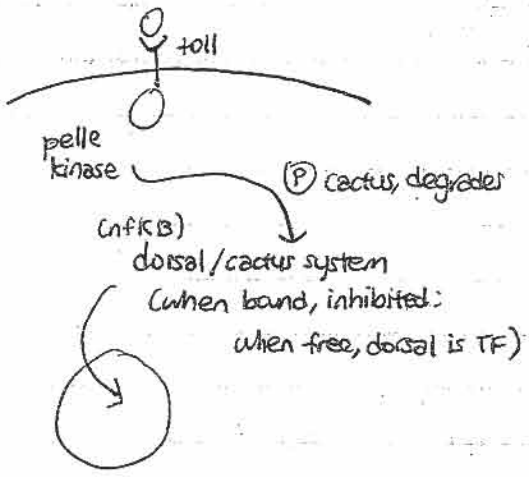


5. Receptor Tyrosine Kinase

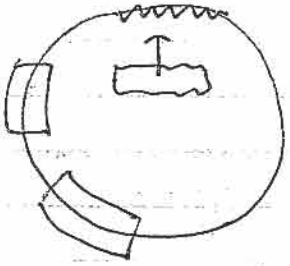
- common in cancer
- uses small ~~secreted molecules~~ G proteins, eg Ras
- kill vascular flow in tumors?



6. Toll/NFKB



Spemann's organizer (mesodermal region)



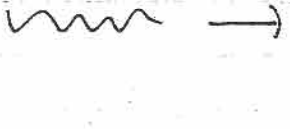
if take cells from anywhere, become neurons in culture (need to give another signal to get epidermis)

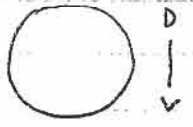
↳ BMP4 (high everywhere except neural ectoderm)

if add BMP4, → epidermal cells

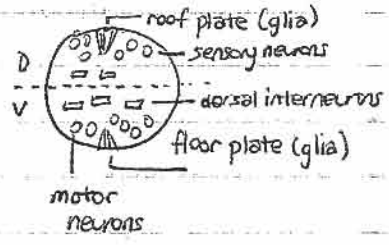
SO keeps BMPs from working (to get neural cells): secretes follistatin, chordin, noggin } bind & deactivate BMPs

neural plate → neural tube

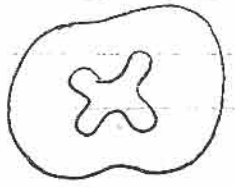


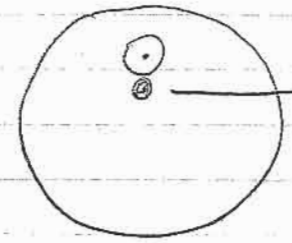


need to establish D-V, A-P axes



in spinal cord,





(mesodermal)
notochord: induces floor plate, motor neuron formation
(SHH pathway)

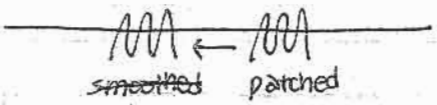
↓ glial

↳ notochord secretes high [SHH] → floorplate
diffuses lower [SHH] → motor neurons
very low [SHH] → ventral interneurons

(different Rs w/ different SHH affinity, turn on different TFs)

morphogen: different pathways induced by different conc.

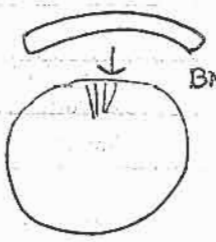
- if put notochord in dorsal region, get ventral cell fates
- if take away notochord, get all dorsal structures (from dorsal signals diffusing)



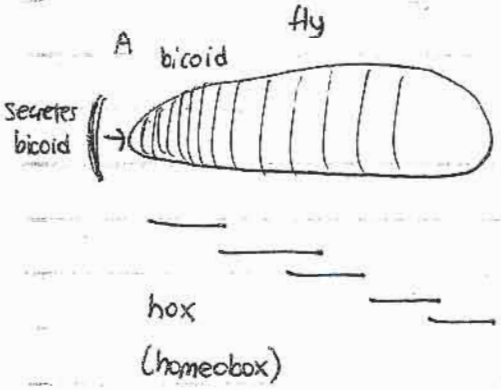
dominant
if make ~~dom-neg~~ smooth, turn cells into motor neurons

if mutate patched, get dorsal structures

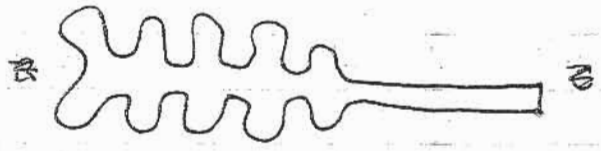
- still get dorsal structures (SHH not necessary here)
- but if take away dorsal epidermis above it, don't get dorsal structures



↓ glial
BMPs turn on roof plate → BMPs
sensory neurons
dorsal interneurons



bicoid turns on hox genes at different conc.
- different combinations of hox genes give segments
- in vertebrates, also conc. of morphogens (BMPs inhibited as go ~~face~~ forward)



inhibit
BHPs for forebrain

noggin
chordin
follistatin

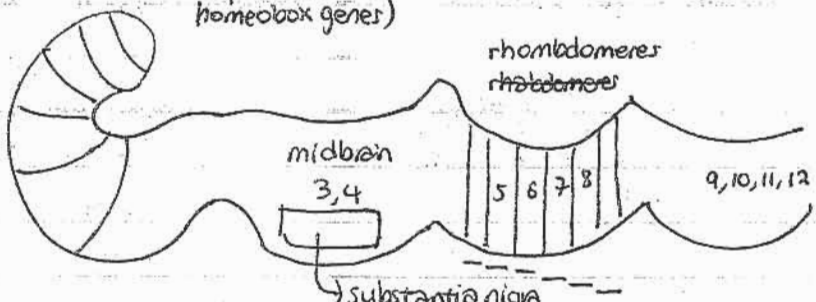
baseline fate

forms midbrain

FGF
retinoic acid
(signal formation of posterior structures)

morphogens secreted to do this

prosomeres (diffrent patterns of homeobox genes)



(if remove SHH, remove this)

if delete hox genes, can convert 1 rhombomere to other (turn 1 nerve into another)

different combinations of hox genes give different rhombomere identities

Know: 1. SHH pathway

2. know BMPs (dorsal fates) pathways