

2012 --- Problem Set #3

1. Define the relevance of the following terms to the course:

Broca's Aphasia:

SMAD:

Rita Levi-Montalcini:

Lissencephaly:

Radial Glia:

Lateral Inhibition:

Spemann's Organizer:

Neuralation:

Prosomeres:

Neurologin:

2. Answer the following multiple-choice questions. Circle all that apply (a, a and b, b and d, etc).

2-1. Cranial nerves involved in eye movement include:

- a. CN II
- b. CN IV
- c. CN V
- d. CN VI

2-2. The following are components of the basal ganglia:

- a. Thalamus
- b. Putamen
- c. Amygdala
- d. Globus Pallidus

2-3. Which of the following receptor-ligand pairs is correct:

- a. Slit-DCC
- b. Agrin-Musk
- c. Wiggless-Patched
- d. Neurexin-Neurologin
- e. Ephrin-TGF β

2-4. Floor plate cultures from mutant mice lacking slit would be expected to:

- a. Attract commissural axons
- b. Repel commissural axons
- c. Have no effect on commissural axons

2-5. Which of the following are molecules involved in the pathway for clustering

acetylcholine receptors at the mammalian neuromuscular junction?

- a. gephyrin
- b. BDNF
- c. neuroligin
- d. MuSK
- e. agrin

- 2-6. Potential strategies to repair CNS damage include:
- f. Insertions of astrocytes into the sites of CNS damage
 - g. Antibodies to block Schwann cell myelin proteins
 - h. Steroids to prevent inflammation
 - i. Inducing downregulation of GAP-43

Answer the following questions (For the problem set, answer them all; for the exam you'll have some choices, i.e. answer 3 of 4).

3. The development of the spinal cord is a commonly used model for neuronal development and axonal pathfinding. Describe the mechanism by which the dorsal and ventral structures of the spinal cord are patterned early in development. Be sure to include specific details about the signaling pathways involved?

4. You have been lucky enough to get a UROP position for the summer in a hot neuro lab on campus doing mutagenesis in mice to identify loci important in neuronal function. You excitedly hop on the bandwagon and start generating mutants and looking for cool mutant mice. You find one line that when homozygosed gives a terrible little mouse with little to no movement that dies shortly after birth. With great anticipation of getting a Nobel prize for your beautiful phenotype you molecularly identify the lesion and find that it is due to a mutation in the SHH locus, resulting in a loss of function phenotype.

- a. Describe a class of morphological phenotypes you might expect when you look at neural development of the spinal cord in mutant animals
- b. Given your inclination towards medicine and general good will towards man and animal alike, you decide you can no longer live with yourself knowing you've created such a terrible little strain of mice. Therefore, you decide to spend the rest of your summer trying to cure the little beasts. Given the homozygotes you've already generated are dead, you decide to pursue 2 strategies to prevent future homozygotes from developing such a cruel fate. First you've gotten the brilliant idea that you'll perform a second mutagenesis to look for suppressors of the phenotype you found in point a above. What loci would you expect to hit to get either loss-of-function or gain-of-function phenotypes that might allow your little mutant mice to be a bit healthier as homozygotes. Describe how the pathway in question would be affected by your new mutation.
- c. After much attempts, and many months, you decide 2 things – one, next summer you'll work with *Drosophila* or *C.elegans* because of their rapid life cycle and ease of genetic approaches, and two, that you must switch over to a more direct

put-back approach. What type of genes (dominant gain-of-function, dominant-negative, etc.) might you generate in the test tube and put back in mutant animals to overcome the loss of SHH. What cell-type specific promoters would you be looking for to do your putbacks. Describe how the pathway (s) in question would be affected by your new put-backs.

5. After your failure to cure your Shh mice from last summer, you decide to move in a different direction to pursue your Nobel Prize as an undergraduate UROPer. You decide that the ability to reconstruct a synapse from a presynaptic neuron growing in culture onto non-neuronal COS cells would be quite an accomplishment and set off to make it happen.

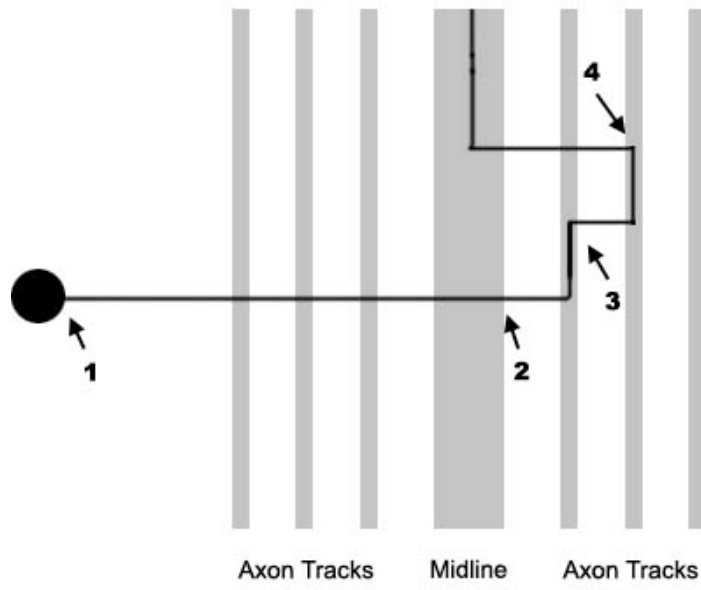
- a. What are the important parameters you would need to think about in terms of pre and post-synaptic specializations that define a synapse?
- b. Assuming you are using cultured motor neurons, what types of proteins would you want to start transfecting into your epithelial cells to make a NMJ synapse and why?
- c. Having accomplished your task, you now want to go for the homerun and use central glutamatergic neurons to construct a CNS synapse. What are some important differences between the CNS synapse and NMJ? What genes would you begin transfecting in to the COS cell to form a postsynaptic CNS synapse?

6. Describe in detail one case of a local cue used in axonal pathfinding and one case of a long-range cue in pathfinding. Describe the pathways, pointing out what properties of each cue are important in their function.

7. You're a conceptual artist, inspired by biology, who wants to make a piece titled "Axon Etch-A-Sketch". Luckily, you know people in a Drosophila lab studying axon guidance, and they tell you they have a hitherto-unheard of way of turning robo and DCC expression on and off at will in a single labeled axon in a commissureless mutant strain. The genes you can control are:

1. robo1
2. robo2 (lower affinity for slit than robo1)
3. DCC

To etch-a-sketch the axon as shown in the diagram below, which genes will need to be turned on or off at points 1-4?



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