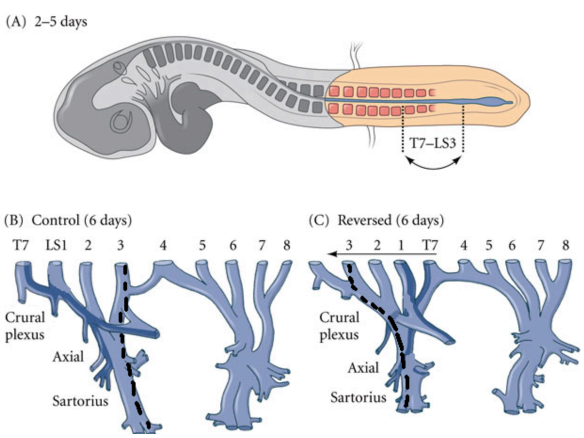
MCDB 4650 Problem Set 11

1. (1) Which reason/reasons given below explain why netrins can be repulsive to some axons and not to others?
a. There could be different numbers of netrin ligands in the axons of different neurons
b. There could be different numbers of netrin receptors in the axons of different neurons
c. Neurons could respond differently to binding of netrin because of downstream effects in different cells
d. Different neurons could have different DNA regulatory sequences

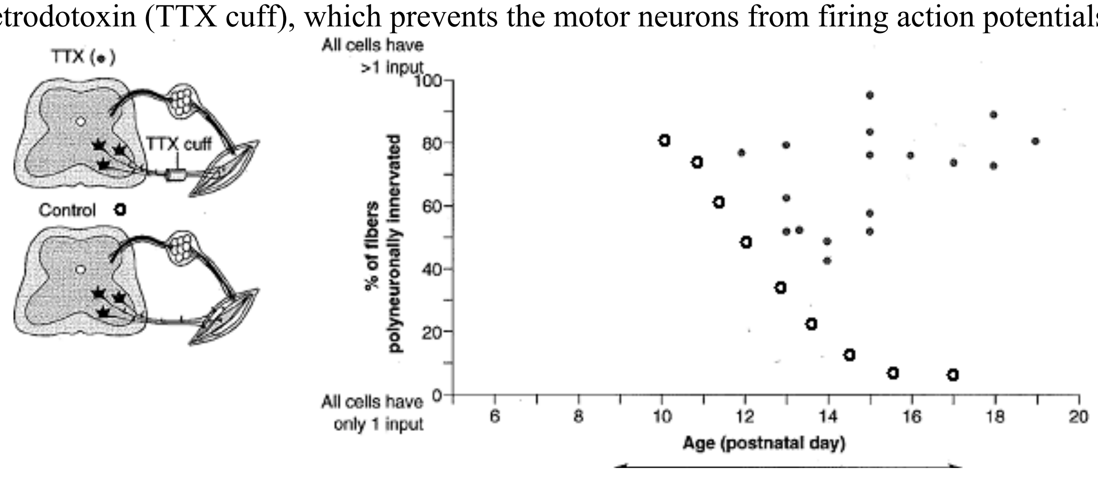
You are investigating several lines of *Cre-lox* targeted knock-out mice with nervous system defects. Determine the single most likely gene that has been removed in a tissue-specific and/or time-dependent fashion that could cause the defect(s) from the descriptions below. Assume that the mice survive long enough for you to measure the phenotypes described below. Select one gene for each from the following list that could have been knocked out to give the phenotype described. Explain your answer in one sentence.
List of possible genes: Shh, BMP, FGF, NGF, BDNF, Netrins, Ephrins, Semaphorin, Notch, Delta
2. (1) Mouse 1 can see when its eyes first open, but begins to lose its response to visual cues by 2 weeks after birth and is effectively blind by 3 months of age.
3. (1) Mouse 2 responds to visual cues but cannot respond to directionality; ie, cannot tell nasal from temporal or up from down.
4. (1) Mouse 3 can perceive sensory input (ascertained by recording from neurons in the spinal cord), but cannot execute motor responses to this information.

5. (1) In the figure shown below, a length of spinal cord (comprising the region T7-LS3) was reversed in a 2-day old embryo (a. shows the region of reversal). The normal pattern of axon projections (along the nerves shown, dotted line for nerve LS3, solid line for nerve T7) from these regions to innervate specific muscles is shown in panel b. From looking at panel c. (the results of the reversal), select the reasonable conclusion(s) you could make:



a. The neurons in the spinal cord are not yet committed to a particular fate by the time of this experiment.
b. When the neurons are moved to a different environment, the signaling in that region induces different fates, allowing the axons to innervate different targets.
c. The neurons in the spinal cord are committed to a particular fate by the time of this experiment.
d. There are likely different transcription factors expressed in different cells along the spinal cord that dictate the future target of the neuron.

6. (1) In the figure below, the number of fibers in the muscle that are innervated by more than one neuron is shown on the Y axis; age of the animal is shown on the X axis. The graph shows how the % of fibers that are innervated by more than one neuron changes over time (control, a normal soleus muscle, connected normally to the spinal cord, is shown as open circles). In the experiment, the animal's motor nerves are treated with tetrodotoxin (TTX cuff), which prevents the motor neurons from firing action potentials. The result is shown as filled dots. Describe briefly what you can conclude from this experiment.



7. (1) Imagine that you further manipulated this situation. You're still looking at the TTX inhibited motor neurons and their target muscle, but now you additionally inhibit nerve growth factor in the soleus muscle at postnatal day 14. What do you think would happen?

8. (1) Which of the following statements is/are true?

a) Many neurons die due to lateral inhibition from the neurons fated to survive
b) Neurotransmitter receptors accumulate in the post-synaptic cell membrane due in part to information from the pre-synaptic cell.
c) Once synapses are formed during development, that circuitry is always maintained through adulthood
d) Removal of a limb bud kills the neurons that would innervate the limb because their axons are cut
e) Neural activity contributes to determining patterns of synaptic connectivity
f) Growth factors like BDNF are important for initial synapse formation but not for maintenance of the synapse.

9. (2) The projection of axons from the frog retina to frog tectum differs from the projections of mammalian axons in one major way. Because the frog's eyes are on opposite sides of their heads, they do not have binocular vision. One eye projects information entirely to one side of the tectum, while the other eye projects information to the other side of the tectum (see panel A. below). Curious about what would happen if one were to try to force binocularity on a frog, scientists created a three-eyed frog by transplanting retinal projenitor cells between the two normally developing eyes. This did in fact lead to a frog with three eyes (this alone is kind of amazing—a whole eye develops AND makes connections to the cortex just like a normal eye!). When they did tracing experiments (following molecules transported from ganglion cells to cell of the cortex), they obtained the result shown in panel B of the figure (note, if they had injected tracer into any of the three eyes, they would see the same result). In addition, when they recorded from cells in the tectum, they found that some responded to light displayed to the central eye and one of the lateral eyes.
Is this experiment consistent with how we know the mammalian cortex is patterned? Explain briefly.