MIDTERM 2
MCB 160, SPRING 2007
100 points
7 questions
7 pages

BE SURE TO PUT YOUR NAME AT THE TOP OF EVERY PAGE!!!!!!!!!!
CHECK THAT YOU HAVE SEVEN QUESTIONS!!!
WRITE IN INK!!!

Name _____

SID # _____

GOOD LUCK!!!

Do not write below this line (for grading purposes only).

1.	/22
2.	/22
3.	/20
4.	/14
5.	/8
6.	/6
7	/8
Total	

Name: _____

1. G protein-coupled receptors allow cells to detect and respond to extracellular ligands. The signaling pathways for GPCRs diverge, allowing cells to have a variety of responses (22 pts).

A) Rodbell won the Nobel prize for discovering that GTP and ATP were necessary for cells to become activated by epinephrine. Why is ATP necessary (2 pts)? Why is GTP necessary (2 pts)?

ATP---Adenylate cyclase breaks down ATP to cAMP; necessary for producing second messengers

GTP--- G proteins in inactive form bind GDP, in active form, bind GTP; necessary for G protein activation

B) Name the signaling molecules that are activated in response to odors in vertebrate olfactory neurons (6 pts).

Olfactory receptor, Golf, adenylate cyclase, cyclic nucleotide-gated channel

C) Name the signaling molecules that are activated in response to pheromones in mouse vomeronasal neurons (6 pts).

V1R or V2R, Gq, phospholipaseC, TRP2

D) A mouse pheromone receptor put into mouse olfactory neurons does not activate the olfactory signal transduction cascade. How could you engineer a G protein to couple to the pheromone receptor and activate the olfactory transduction cascade? (6 pts)

Take Golf, remove the last three amino acids, and replace them with the last three amino acids of Gq. Now the G protein should bind the V1R or V2R receptor and activate adenylate cyclase.

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2) The visual system creates a topographic map of projections from the retina to the optic tectum. The molecular mechanisms underlying axon guidance in this system are becoming understood (22 pts).

A) What is a topographic map (6 pts)?

Axons from neurons at neighboring positions in the periphery synapse at neighboring positions in the brain. A neuron's relative position in the periphery is maintained in its axonal projections in the brain.

B. In the frog, axons from the left eye invade both the left and the right optic tectum. Early in development, projections are contralateral. Later in development, ispsilateral connections form. How does this occur (6 pts)?

Ephrin ligand becomes expressed at the optic chiasm later in development. This repels axons away from the midline.

C. Projections from the retina to the tectum in the green witch toad use unusual axon guidance molecules. A receptor tyrosine kinase called WIT is found on retinal axons, and its expression is graded from high to low along the anterior to posterior retina. Its ligand is a repulsive cue called WITL. WITL is found in the tectum, in a gradient from low to high along the anterior to posterior tectum. Where do anterior retinal axons synapse in the tectum (2 pts)? Posterior retinal axons (2 pts)?

Anterior axons project to anterior tectum (High receptor stops at low ligand)
Posterior axons project to posterior tectum (Low receptor stops at high ligand)

D. If a dominant negative WIT (dnWIT) was expressed in the anterior half of the retina only and its expression was graded from low to high in the anterior retina, what would be different about the retinal-tectal map compared to C? Assume that WIT and WITL expression is the same as in C. Assume that low levels of dnWIT are the same as low levels of WIT, and high levels of dnWIT equal high levels of WIT. Explain your answer (6 pts).

Most anterior axons (high WIT, low dnWIT)---project more posteriorly because have less effective WIT

Mid anterior axons (lower WIT, high dNWIT)--- project anywhere because they will not have any functioning receptor and will not recognize ligand (equally appropriate answer---axons will not stop)

Posterior axons project to posterior tectum (Low receptor stops at high ligand)

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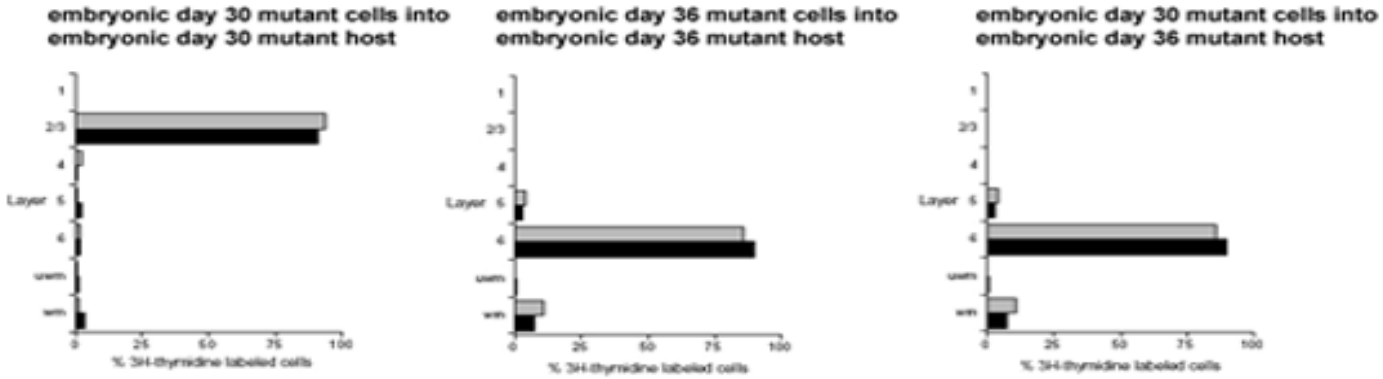
3. Different cell layers of the cortex are generated during development (20pts).

A. Explain the model for how the layers of the cortex form (6 pts).

Progenitor cells divide to become neurons that occupy the cortical layers.
The cortical layers develop inside-out.
Progeny of progenitor cells migrate away from the marginal zone and invade the cortical layers. First-born neurons occupy layers 6 and 5. Last born neurons occupy layers 2/3/
The cortex develops in a process called progressive restriction. At early times, progenitors are competent to take on early or late cell fates. At later times, they are competent to take on the late cell fate.

B A mouse mutant called "Tipsy" was identified because it has very poor motor coordination. A series of cortical transplantation experiments were done to determine whether there are defects in cortical development in this mouse. Progenitor cells were taken out of the mutant, labeled then put back into the mutant host to determine which layers the cells invade. These experiments were done in the embryonic day 30 animal and the embryonic day 36 animal. In addition, progenitors from embryonic day 30 were transplanted into embryonic day 36. Each experiment was done twice (the grey bar is one experiment, the black bar is the second experiment.) The results are shown below.



What is the defect in "Tipsy" mouse cortical development (6 pts)?

Cortical layers develop outside-in. Early born neurons take occupy layers 2/3. Late born neurons occupy layer 6. Progressive restriction still occurs as early born neurons transplanted into a late host take on the late fate (in this case, occupy layer 6).

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C. Design two experiments to test whether the defect is in the "Tipsy" cortical cells or the "Tispy" cortical environment (8 pts). Briefly describe the experiments and how you would interpret the results.

1) Transplant "Tipsy" embryonic day 30 cells in not a normal day 30 cortex.

A. If "Tipsy" cells are normal, then they will occupy the same layers as the host cells would (layers 5/6).

B. If "Tipsy" cells are defective, then they will occupy the same layers as in the Tipsy mutant (layer 2/3).

2) Transplant normal embryonic day 30 cells into the "Tipsy" embryonic day 30 cortex.

A. If "Tipsy" environment is normal, then normal cells will occupy the same layers that they would in a normal mouse (layers 5/6)

B. If the "Tipsy" environment is defective, then normal cells will occupy the same layers as "Tipsy" cells. (layers 2/3)

It is possible that both the cells and the environment will be defective in the 'Tipsy" mutant. (The outcome would be B in both experiments.

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4. A. How does the ear transform sound into a change in neural activity? Describe the steps from a sound arriving at the outer ear to activation of hair cells. Be explicit; describe how sound vibrations are processed in the outer, middle and inner ear and how hair cell transduction occurs (8 pts).

Outer ear--- Sound vibrations set up vibration in the tympanic membrane
Middle ear---Vibrations in the tympanic membrane cause three small bones to move, setting up a vibration in the oval window.
Inner ear---Vibrations in the oval window set up fluid movement in the cochlea through the scala vestibuli and out the scala tympani
Hair cells---Vibrations in the fluid set up a movement in the basilar membranes. This causes a deflection in hair cells. Hair movement causes ion channels to open and the cells to depolarize. Movement is thought to cause tension in the tip link between hairs and this tension is thought to directly gate ion channels.

B. How does calcium entry cause adaptation in hair cells (6 pts)?

Calcium activates motor proteins which move ion channels to a new position. This relieves the tension on tip links and causes a fraction of ion channels to close.

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5. Why are more men red-green colorblind than women (8 pts)?

Red and green opsins are very near each other on the X chromosome and share a great amount of sequence similarity. This makes them prone to copying errors and recombination errors, resulting in frequent deletions and frameshifts. Men inherit only one X chromosome. If this chromosome has mutations in the red-green pigments, they will be colorblind. Because women have 2 X chromosomes, they will need to inherit two mutated chromosomes in order to be color blind.

6. Why don't cats taste sugars (6 pts)?

No T1R2

7. What is the signaling cascade leading to programmed cell death? How do neurotrophins affect this cascade? (8 pts)

Eg1 inhibits ced9 inhibits ced4 activates ced 3
(OR BH3 inhibits Bcl2 inhibits Apaf1 activates caspase)

Neurotrophins increase the amount of ced 9