

QUESTIONS ABOUT AXON GROWTH AND NEURON SURVIVAL

Q: Concerning the study question, “What are trk receptors? (What binds to them, and what is the result?)”: i’ve looked for the trk receptors in the slides, and maybe i’m just missing it but i’ve gone through slides from class 9 on.

This topic was covered more extensively in past years. With the greater emphasis on evolution and on basic connection patterns, some development topics had to be truncated this year. Apparently, the trk receptors were not mentioned.

The trk receptors are tyrosine kinase receptors to which neurotrophins (like NGF, or BDNF) bind. The ligand would induce dimerization of the trk receptors, with protein conformation changes so that each of the pair can phosphorylate a specific tyrosine site of the other in the pair. Phosphorylation then triggers some intracellular signaling pathway (e.g., the famous one involving MAP kinases), leading to expression of transcription factors, then neurite growth and other effects.

Concerning the question, “Describe or name two effects of hormones on brain development”: i’m not really sure what about hormones...Are the eph and ephrins hormones? or are they like growth factors?

Ephrins are membrane-bound proteins, found, e.g., in cells of the developing midbrain tectum. Receptors that bind to these molecules are the Eph receptors, found in the membranes of retinal ganglion cells and their axons. The interaction of these receptors and their ligands (Ephrins) affects growth (e.g., causes repulsion), so the actions are like those of growth factors.

Some hormones, like thyroxine, can induce apoptosis (e.g., apoptosis of Mauthner cells in the frog). Furthermore, hormones are believed to be at least in part responsible for sexual differentiation of certain brain structures. E.g., testosterone, converted to estrogen intracellularly in males, can increase number of neurons in the sexually dimorphic nucleus of the preoptic area. This region is ~5 times larger in the male brain than in female (at least in mice). Other CNS regions are affected also, and some of this will be mentioned in a later class.

Concerning questions about bcl 2: i haven't seen bcl 2 anywhere in the slides so i'm not really sure how to answer the questions.

This molecule was mentioned very briefly when we talked about CNS regeneration, but the topic was not covered in much detail. The same was true for apoptosis. In such cases, you can find answers by a little reading, e.g., after a web search.

Bcl-2 is a molecule that prevents apoptosis. (It was discovered in a cell line from a human B-cell lymphoma – a proto-oncogene -- hence the name.) Specifically, it prevents activation of caspases, which can cleave DNA within the cell nucleus. In transgenic mice with bcl-2 overexpression, axotomy (e.g., of retinal ganglion cells or of facial nerve)

would not result in cell degeneration, or at least there would be much less degeneration than in normal animals.

In class, bcl-2 was relevant to two topics. First, apoptosis, because it prevents apoptosis during early stages of development. Second, bcl-2 was discovered to promote the initiation of axon growth in retinal ganglion cells (a discovery here at MIT). This effect appears to be separate from the effect on preventing cell suicide.