University of Trieste
MSc in Neuroscience (A.Y. 2024-25)
Molecular Neurophysiology – Signal transduction in Neurobiology

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After studying the pre-lecture material and attending/listening to the lectures on "Signal transduction, Calcium signaling, EC coupling mechanisms and cAMP signaling" you should be able to answer the following review questions:

REVIEW QUESTIONS

Signal transduction:

1. What is the mechanism by which lipophilic first messengers produce their biological effects on target cells?
2. What is a hormone response element (HRE)? Where can it be found in the cell, and what is its function?
3. What important first messengers utilise a tyrosine kinase as a receptor? What happens to the receptor after activation?
4. What are SH2 and PTB domains? How do they function in receptor tyrosine kinase signalling?
5. Outline the mechanism and function of the agrin-LRP4-MuSK signalling system.
6. Nicotinic acetylcholine receptors (nAChRs) are distributed differently in skeletal muscle fibres before and after innervation. Explain. Are they the same receptor before and after? Explain.
7. G-protein-coupled receptors (GPCRs) have a characteristic transmembrane topology. Sketch the basic structure of a GPCR and give some examples. Describe/sketch their basic signalling function in the cell membrane.
8. Give some examples of some typical 2nd messengers coupled to G-protein activation.
9. Activation of GPCRs can lead to changes in target cell ionic conductance. Outline the mechanism.
10. What is EPAC and what is its function? Do GPCRs desensitize? What are the mechanisms?

Calcium signaling:

1. *"Calcium-a life and death signal"*. Explain.
2. Give some examples of some intracellular proteins that can bind with intracellular Ca^{2+}.
3. What are CaM kinases and what are their function?
4. There are various ways in which Ca^{2} can enter cells and several mechanisms that control its intracellular concentration thereafter. Outline these mechanisms in a sketch.
5. What are IP_3 receptors? What is their function? What is NAADP and what is its function?
6. What happens to intracellular Ca^{2+} stores during prolonged agonist stimulation?
7. Mitochondria can also take up intracellular Ca^{2+}. Explain what happens when mitochondrial Ca^{2+} levels become abnormally high.

8. Summarise the major ON and OFF mechanisms responsible for regulating the concentration of intracellular Ca^{2+}. Sketch.
9. Does handling of intracellular Ca^{2+} alter with cell ageing? Explain.
10. What are fluorescent Ca^{2+}dyes and how can they be used experimentally? What are "Ca^{2+} sparks", "Ca^{2+} waves" and " Ca^{2+} oscillations" and what is their function?$^{+}$ How is CaM kinase II involved in the Ca^{2+} oscillations?
11. Ca^{2+} transients can be recorded in differentiating neurons and skeletal muscle cells *in vitro*, using fluorescent dyes. What is their function?

EC coupling mechanisms:

1. Outline the basic mechanisms involved in EC coupling in skeletal muscle. Sketch.
2. What is a *triad* in skeletal muscle and what is its function?
3. What is the relationship between dihydropyridine (DHP) receptors and ryanodine receptors in skeletal muscle?
4. Does normal skeletal muscle EC coupling require entry of extracellular Ca^{2+}? Explain.
5. Explain the cardiac muscle EC coupling mechanism.
6. In failing heart cells, there is a defect in EC coupling. Explain.
7. Name some pharmacological agents that can be used to modulate Ca^{2+} release from ryanodine receptors experimentally?

cAMP signalling:

1. What is the difference between $G\alpha_s$ and $G\alpha_i$ in G protein-coupled receptors?
2. It is clear that the specificity of cAMP signalling is achieved by special control of its main effector PKA. How is this brought about?
3. What are FRET? How is this phenomenon used in cell biology?
4. What is cyclic nucleotide phosphodiesterase (PDE)?
5. What is the mechanism by which cAMP signalling can be produced in cells?Are
6. Are intracellular cAMP transients spatially organized? If so, what are the hypothesized responsible mechanism?

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