Signaling Pathways - Written Exam - 25.06.21 (1)-2

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Signaling Pathways -...

Physiology

1. **Calcium and phosphate homeostasis; parathyroid glands; parathyroid hormone; vitamin D; calcitonin; steroid hormones (effects on Ca and Pi metabolism); bone physiology; hypocalcemia; hypercalcemia.**

2. **Describe: Osmosis; Tonicity; Regulation of cell volume; The Gibbs-Donnan Effect**
   Volume and composition of body fluid compartments; Ionic composition of extracellular and intracellular fluids

Cell Signaling

Give a brief explanation of the reason(s) why each of the three options you discarded in the quiz above be not the appropriate statement for the given stem text.

1. **The insulin signaling pathway includes which of the following steps?**
   - a) ligand-induced dimerization of the receptor
   - ● phosphorylation of IRS proteins
   - c) phosphorylation of SH2 domains
   - d) IRS dimerization

2. **Cytochromes P450 (CYP proteins) are:**
   - ● a superfamily of enzymes that typically act as monooxygenases
   - b) hemoproteins approximately 450 nm in greatest dimension
   - c) mitochondrial enzymes that require 02 and ATP as cofactors for hydroxylation processes
   - d) lipophilic molecules subjected to phosphorylation by NADPH

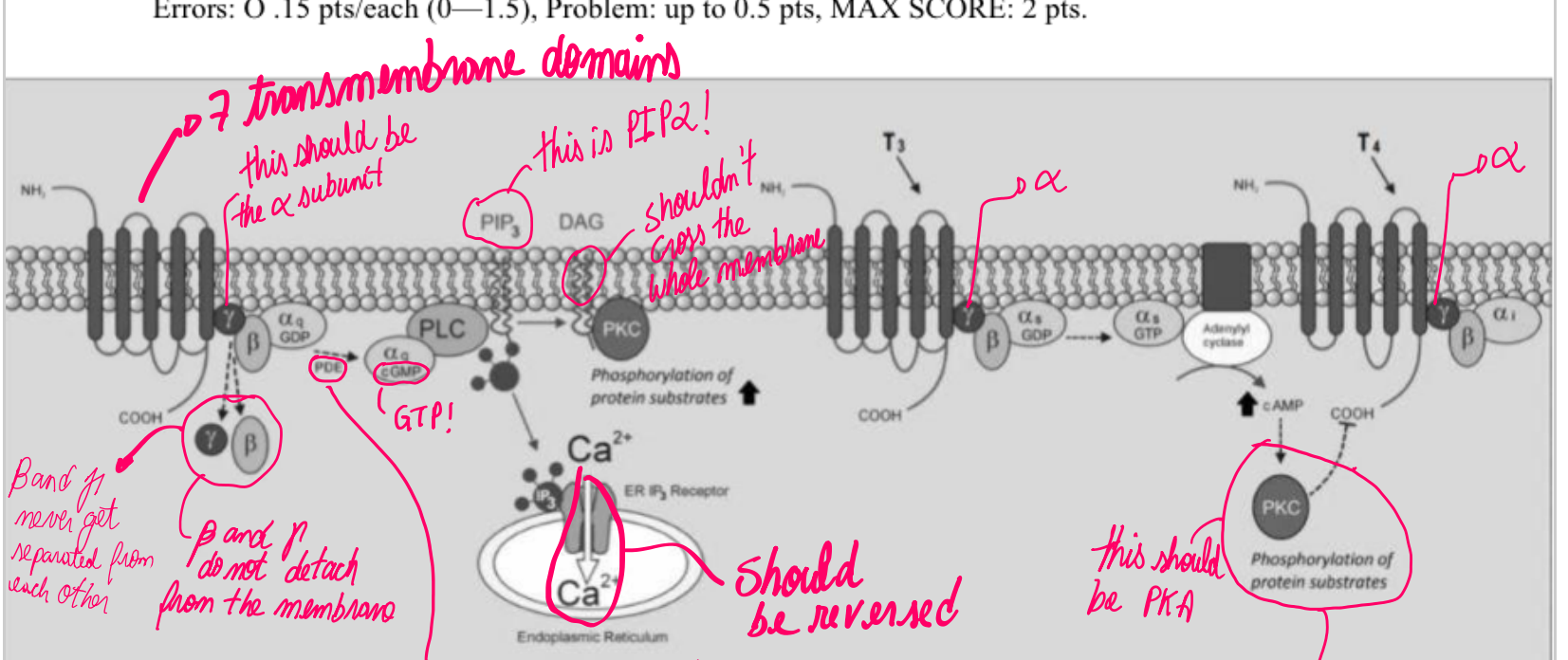
3. **Which of the following statements is true of the cAMP molecule?** Gq → activates phospholipase C
   - a) when active, it is bound to cGMP
   - b) is activated by Gq proteins Gs | Gα
   - c) is inhibited through phosphorylation by PKB
   - ● is included in pathways with (beta)-adrenergic receptors

4. **Heat Shock Proteins (HSPs) may**
   - a) catalyze the degradation of hormone receptors by hydrolytic cleavage of the ligand binding domain (LBO)
   - ● hamper the DNA-binding function in steroid hormone receptors
   - c) mediate cell signaling by conveying pregnenolone in the bloodstream
   - d) mediate the binding of plasma membrane phospholipids to glucocorticoid receptors

5. **The bacterial pathogen B. pertussis impairs the functioning of signal transduction mechanisms in target cells through**
   - a) secretion of ADP toxins
   - b) endocytosis of JAK-STAT receptors
   - ● molecular deactivation of target G.i proteins
   - d) ADP-acetylation of target nuclear proteins → ADP ribosylation

GRAPHICAL PROBLEM (TYPE A2)
Directions
Spot the errors in the picture below AND complete the assigned problem.

Evaluation criteria
Errors: O .15 pts/each (0—1.5), Problem: up to 0.5 pts, MAX SCORE: 2 pts.



PDE is what inactivates cGMP / cAMP

PKC should always be on the inner surface of the membrane

List of errors:

1:
2:
3:
4:
5:
[add more lines up to error row 10]

Problem:

List the molecular mechanisms that can turn off the signaling pathways described in the figure.

1: - PDE on cAMP → breaks the phosphodiester bond
2: - PIP2 / IP3 → some bonds may be broken ... → study the mechanisms 'cause she likes them
3:
4:
5:

FILL IN THE BLANKS (TYPE AS)
Directions
Enter the missing words in the blanks by choosing from the corresponding drop—down

Evaluation criteria
Matching words: 0.1 pts-/each MAX SCORE: 2 pts.

Since its initial discovery as a proto-oncogene, the serine/threonine kinase Akt (also named ...PKB.........) has become a major focus of attention because of its critical role in regulating various cellular functions including metabolism, growth, proliferation, survival, transcription and protein synthesis. The Akt signaling cascade is activated by ...receptor tyrosine kinases....... receptors that induce the production of 3,4,5 phosphatidyl inositol triphosphate.... (PIP3) by phosphoinositide 3-kinase (.PI3K........). PIP3 is a phospholipid..... molecule that serves as a plasma membrane docking site. for proteins like Akt and its upstream activator, namely PDK1........, harboring pleckstrin-homology (PH) domain, At the membrane level, the activator can phosphorylate.. Akt at Thr308, thus leading to partial activation of Akt. In addition, phosphorylation of Akt at Ser473 by mTORC2 stimulates its full enzymatic activity. Conversely, Akt is dephosphorylated by protein PP2A, which is an enzyme of the ..PIKK (→ "kinase" in the exam)...... family. Working in opposition to P13K is the tumor suppressor named Phosphatase and TENsin homolog (PTEN), which inhibits the Akt-dependent signal by dephosphorylation. of PIP3 to obtain .PI(4,5)P2... (phosphatidylinositol 4,5 biphosphate...). Akt is a major mediator of cell survival through direct inhibition of pro-apoptotic proteins like Bad or inhibition of pro-apoptotic signals generated by transcription factors like FOXO. Akt is also critically involved in the regulation of cell metabolism through interaction with many downstream targets, including PFKFB2 (→ in the exam the option was "not in the list").. which stimulates biosynthesis. Akt also affects glucose metabolism by increasing translocation of transcription factors (?) (→ "not in the list" or "transcription factors") . Due to the critical role of Akt in regulating diverse cellular functions, its dysregulation is implicated in a number of human diseases including cancer, diabetes, cardiovascular disease and neurological diseases. In human tumors, PTEN is frequently lost through somatic mutations, thus preventing the Akt-signal .dephosphorylation In addition, known activating mutants of Akt cause increased phosphorylation at the T308/309 and S473/474, .threonine..... and serine residues........, which are essential for full activation of the Akt kinase/protein. . Molecular targeted therapy designed to modulate the pathway components has seen progress in the clinic. However, due to the important role of the Akt protein in glucose .metabolism (→ or lowering)...., undesired........ side effects (mimicking diabetes mellitus) are observed in some patients treated with certain inhibitors of the Akt signaling pathway.

* On the exam, the gaps are lists of options from which you'll have to choose the most appropriate one.

Metabolic Biochemistry

1. **Concerning pyruvate dehydrogenase**
   - a. it contains covalently bound NAD
   - b. it is located in the inner mitochondrial membrane
   - c. it is inhibited by CoASH
   - d. It is activated by phosphorylation
   - ● FAD reduced in E3 donates electrons to NAD+

2. **Concerning blood glucose regulation: (ONLY ONE ANSWER IS INCORRECT)**
   - a. Under conditions of high blood sugar, the ß cells secrete insulin
   - ● Stimulation of insulin receptor induces the expression of enzymes involved in gluconeogenesis
   - c. Diabetics have lower levels of plasma membrane localized GLUT-4 than nondiabetics
   - d. After a meal glycogen synthase is activated
   - e. Glucagon increases the expression of glucose-6-phosphatase

3. **Which of the following you expect if you observe an increase of fructose-2,6-bisphosphate?**
   - a. Increased activity of PKA
   - b. Increased glucose-6.phosphatase
   - ● Enhanced formation of ATP by glycolysis
   - d. Increase of gluconeogenesis
   - e. The tandem enzyme works as a phosphatase

4. **In uncontrolled Type I diabetes we observe**
   - a. Decrease of lipolysis
   - b. High levels of fructose-2,6-bisphosphate in hepatocytes
   - ● High levels of plasma ß-hydroxybutyrate
   - d. Increased activity of phosphoprotein phosphatase-1
   - e. Increased activity of glucose-6-phosphatase in muscle

5. **HMGCoA reductase (ONLY ONE ANSWER IS WRONG)**
   - ● in mitochondria is involved in ketone body synthesis
   - b. may be inhibited by phosphorylation
   - c. is involved in the synthesis of Coenzyme Q
   - d. catalyzes two consecutive reductions
   - e. is a cytosolic enzyme

6. **Concerning VLDL (ONLY ONE ANSWER IS WRONG)**
   - a. They are very rich in triacylglycerols
   - b. They are synthesized in the liver
   - c. Their lipids are hydrolyzed by lipoprotein lipase
   - ● Their deficit is the cause of familial hypercholesterolemia
   - e. They are larger than HDL

7. **Concerning heme metabolism**
   - a. The nitrogens of heme derive from aspartate
   - ● The initial reaction of heme biosynthesis takes place in mitochondria
   - c. A product of heme oxygenase is > C02
   - d. Glucuronated bilirubin is carried by albumin
   - e. In obstructive jaundice (icterus) bilirubin cannot be glucuronated

8. **Concerning amino acids**
   - ● All aminocids can be oxidized to acetyl COA
   - b. Histiidine is a ketogenic amino acid
   - c. Methionine enters the Krebs cycle at the level of oxaloacetate
   - d. Glutamate dehydrogenase is a cytosolic enzyme
   - e. Decarboxylation of serine yields glycine

9. **ONLY ONE STATEMENT CONCERNING ONE-CARBON METABOLISM IS FALSE**
   - a. The major donor of IC units is serine
   - b. Methylation of homocysteine requires B12 Coenzyme
   - ● Formyl FH4 is required for pyrimidine (purine) biosynthesis
   - d. The synthesis of T MP requires methylene FH4
   - e. The formyl group has the oxidation level of formic acid

10. **Complete the following reactions**
    - a. Alanine + α-ketoglutarate --> pyruvate + glutamate
    - b. Citrate + ATP..... + CoASH → Oxaloacetate + ADP + acetyl CoA
    - c. HMG-CoA --> Acetyl CoA + .acetoacetate
    - d. Malate + NADP⁺..... --> Pyruvate + C02 + NADPH + H+
    - e. DAG + CDP-choline --> Phosphatidyl choline + CMP
    - f. Glyceraldehyde-3-P + NAD⁺.... + Pi.... --> 1,3-BPG.. + NADH + H+ → subst. level ph.
    - g. Methyl Malonyl CoA + CO2 + ATP..... --> Methylmalonyl COA + ADP. + H2O....

11. **Write al coenzymes and prosthetic groups, if any, involved in the action of the following enzymes. If they derive from a vitamin, write which vitamin is.**
    - a. Isocitrate dehydrogenase
    - b. Pyruvate dehydrogenase complex
    - c. Acetyl COA carboxylase
    - d. Alanine transaminase
    - e. Serine decarboxylase
    - f. Serine hydroxymethyl transferase
    - g. Transaldolase
    - h. Transketolase

    good luck!

12. **Write the reactions for palmitate biosynthesis from alanine. How many alanine molecules are required? Write the ATP balance.**

    → see on Virtuale