

Course Materials for Week 8: Protein Kinases

Susan Taylor (University of California, San Diego; HHMI)

Assignment Questions

Part 1

1. Phosphates are involved in many biological processes such as (select all that apply):
 - a. energy metabolism
 - b. nucleoside structure
 - c. cell signaling
 - d. activating kinases
 - e. none of the above
2. Phosphates play an important role in glucose storage and release. _____(enzyme) breaks down glycogen into glucose. When it is _____it is turned on/active.
3. When there is low glucose in our bloodstream we want to turn glycogen into glucose. This process involves a signaling cascade that starts with glucagon, which turns on the production of the second messenger that regulates PKA. What is this second messenger?
 - a. Heterotrimeric G Protein
 - b. cAMP
 - c. Adenylate Cyclase
 - d. ATP
 - e. Glucose
4. PKA is activated by which of the following: (select all that apply)
 - a. binding of the regulatory subunits to the catalytic subunits
 - b. phosphorylation of glycogen phosphorylase
 - c. phosphorylation of glycogen phosphorylase kinase
 - d. the release of the catalytic subunits from inhibition by cAMP
5. The three residues that are phosphorylated by kinases are:

6. The SH2 domain serves as an adaptor by binding to _____.
7. Src kinase is regulated by which of the following (select all that apply):
- a. phosphorylation in the kinase domain
 - b. phosphate that keeps it in a closed conformation
 - c. phosphorylation in the SH2 domain
 - d. dephosphorylation which opens up the kinase
 - e. dephosphorylation that causes an inhibitory complex

Part 2

8. Kinases can be divided into two main subdomains. The N-lobe is mostly associated with binding _____ the C-lobe is mostly associated with binding _____.
9. Which subdomain feature is the entire PKA kinase organized around (select all that apply)?
- a. glycine-rich loop
 - b. F-helix
 - c. catalytic loop
 - d. H-helix
 - e. none of the above
10. Which subdomain links the N and C lobes together (select all that apply)?
- a. Subdomain V
 - b. Subdomain VII
 - c. Subdomain II
 - d. Subdomain IX
 - e. none of the above
11. PKA kinase switches between an open and closed conformation. Which form is it in during catalysis? _____
12. Chronic myelogenous leukemia is caused by a constitutively active Abl tyrosine kinase. How did Gleevec inhibit the kinase? (what structural part of the kinase does Gleevec bind to?) _____

13. A threonine to methionine mutation in the Abl kinase results in resistance to Gleevec. How does this mutation make the kinase into an oncogene again (select all that apply)?

- a. threonine acts as a gatekeeper in the ATP site, removing this makes the kinase constitutively active
- b. methionine binds more strongly to ATP, making the kinase constitutively active
- c. methionine helps stabilize the regulatory spine to make the kinase constitutively active
- d. methionine prevents Gleevec from binding and inhibiting the constitutively active kinase
- e. none of the above

Assignment Answers:

- 1. a, c, and d
- 2. glycogen phosphorylase, phosphorylated
- 3. b
- 4. d
- 5. serine, threonine, tyrosine
- 6. phosphor-tyrosine
- 7. a, b, c, and d
- 8. ATP, peptides
- 9. b
- 10. a
- 11. closed
- 12. breaks regulatory spine
- 13. c and d

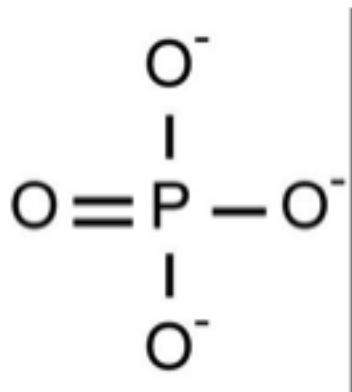
In-Class Quiz Questions

- 1. Draw a phosphate molecule.
- 2. Chronic myelogenous leukemia is caused by a constitutively active Abl tyrosine kinase. How did Gleevec inhibit the kinase? (what structural part of the kinase does Gleevec bind to?)
- 3. Scientists have discovered a new drug that inhibits an overactive kinase implicated in cancer.

- a. If this drug binds to the kinase, name three possible ways it could inhibit kinase activity?
- b. If this drug does not bind to the kinase, how else might it block kinase overactivity?

In-Class Quiz Answers

1.



2. Breaks regulatory spine

3. The answer should have at least three ways a kinase could be blocked that are different from one another. Otherwise this should be graded as more of a participation question.