

Chem 6740 Cellular Communication by Small Molecules and Proteins

Spring 2008

Section, 001 CRN# 22429

Time M 3:30-5:00 or 5:30** and W 12:30-2

Location-WID 333

Professor Joanie M. Hevel

Office: Widtsoe 235 Lab Widtsoe 202

Phone: 797-1622

Office Hours : TBA, and by appointment

jhevel@cc.usu.edu

Text: *Principles of Biochemistry* 2005 (ISBN 0-7167-4339-6) by Lehninger as a reference

Other: You will need a 2 inch D-ring binder, computer access, and you will need to download the free software program Pymol

Prerequisites: Chem 5700 or equivalent

Grading:

2 One hour exams (100 pts each)	200pts
Projects	<u>250pts</u>
	450pts

Exams: Make-up exams are possible only for excused absences as specified in the 2006-2007 General Catalog.

Projects:

- #1 Bioinformatics and pymol-based: How structure governs function-30pts due Jan 22
- #2 Post-translational control of protein activity & disease-20pts due Feb 29
- #3 Analysis of Microarray data-100pts
- #4 Formulation of an experimental plan to follow-up on the microarray analysis-100pts

Course Objectives/ Goals:

Protein and Nucleic acid domains/structures

1. Ability to explain the concept of modular proteins as it relates to signaling
2. Evaluate how different protein domains bind their recognition elements and how specificity is achieved.
3. Apply knowledge of #1 and #2 to describe and/or design synthetic proteins that incorporate these features;
4. Ability to describe the use of nucleic acid structures in cellular signaling
5. Ability to apply the methodologies used to study both nucleic acid and proteins structures as they relate to cellular signaling
6. Ability to apply any techniques we discuss in class to evaluate data or devise an experiment to answer a question

Post-translational modifications

1. Successfully use a bioinformatics approach to translate a given DNA sequence; identify any potential sites for post-translational modifications; identify a potential subcellular localization for the protein based on the presence of any signal sequences; and be able to display and manipulate the 3-dimensional structure if one is available
2. Develop a comprehensive view of the ability of post-translational modifications to alter cellular signaling
3. Classify types of post-translational modifications
4. Ability to apply the methodologies used to study post-translational modifications as they relate to cellular signaling
5. Utilize information in #2 #3 and #4 to explain research data indicative of signaling due to post-translational modifications

Altering Gene Transcription/RNA Processing

1. Develop a comprehensive view of how gene transcription and RNA processing can be regulated
2. Apply these concepts to develop hypotheses about what is happening in a particular stimulus-response model when presented with a DNA microarray data set
3. Become familiar with techniques involving microarrays, in vitro transcription, SELEX/aptamers.

Small molecule regulators

1. Develop a comprehensive view of the variety of small molecules that are used to convey a cellular signal and their mechanisms of action.
2. Ability to hypothesize how the production of a given signaling molecule may impact the activity or structure of another macromolecule
3. Develop an understanding of how the synthesis of small signaling molecules can be regulated at various levels (protein structure, external stimuli, protein interactions, etc.)

Biosensors, Pathogen manipulation of signaling, Proteases

1. Ability to incorporate knowledge regarding protein modules, post-translational modifications, and small molecules to explain how various bio-sensors work and how bacteria and viruses interfere with normal cellular communication.
2. Develop an understanding as to how proteolysis is used to convey a cellular message.

Date (pdf)	Content (Papers & web sites)
	Protein and Nucleic acid domains/structures
1/11 (1-3); 1/14** (4-5) & learn how to use Pymol; 1/16 (6-7); 1/23 (8); 1/28** (9-11); 1/30 (12-13); 2/4 (14-15); 2/6 (16-18 and review)	Protein Modules (1-7) PROJECT #1 due Jan 22 Riboswitches(8-9) MicroRNAs and RNAi (10-13) In class discussion of pdf #14 Aptamers (15-18)
Feb 11**, tentative	EXAM Mon 3:30-5:30
2/13	Post-translational modifications (19)
2/13 (20-22); 2/19 (23-26); 2/25** (27-30); 2/27 (31-34)	Phosphorylation- Kinases/Phosphatases (20-22) Methylation-Methyltransferase/Demethylase (23-28) Deamidation & Glycosylation (29-30) Hydroxylation-Hydroxylases (31-32) Oxidation-Reduction (33-34) PROJECT#2 Due2/29
Mar 3 **, tentative	EXAM Mon 3:30-5:30
	Altering Gene Transcription/RNA Processing
3/5(TBA)	Review of the basics Specific examples Monitoring changes in gene transcription
3/17 intro to IPA ; 3/19 IPA	Introduction to Analyzing DNA Microarrays-Initiate PROJECTS 3 & 4
3/24** in class work with IPA 3/26 in class work with IPA	
IF WE HAVE TIME....	Small molecule regulators (36-42)
	Cyclic nucleotides etc. Nitric oxide Peroxide Carbon monoxide Ozone? Transcription activation domains
	IN CLASS presentations of current microarray analysis
IF WE HAVE TIME....	Biosensors, Pathogen manipulation of signaling, Proteases (Reading TBA)
	PROJECTs 3 & 4 DUE-counts as final exam

List of Reading Material (all pdfs are available on BBVista)

Protein and Nucleic acid domains/structures

1. proteindomains Science.pdf
2. Vogel et al. multidomain protein review.pdf
3. PDZ STKE.pdf

First assignment introduced (PROJECT #1) http://smart.embl-heidelberg.de/smart/set_mode.cgi?NORMAL=1 and Pymol

4. Pro recognition.pdf
5. SH2&PTB STKE.pdf
6. Dueber, JE, signaling switch.pdf (IN CLASS DISCUSSION)
7. Briesewitz burrowing surfaces.pdf

PROJECT #1 DUE

Riboswitches

- 8 riboswitch review.pdf
9. SAM riboswitch Nature Struc Bio.pdf (IN CLASS DISCUSSION)

MicroRNAs and RNAi

10. http://www.nature.com/focus/rnai/animations/rnai_revised_500x280.wmv
11. <http://www.nature.com/nature/journal/v448/n7156/full/448855a.html>
12. small double RNA activate.pdf (IN CLASS DISCUSSION)
13. miRNA&hemato.pdf

14. Murayama et al., multidomain protein inhibition.pdf (IN CLASS DISCUSSION)

Aptamers

15. 2006 aptamer review.pdf
16. aptamer vs nfkb works in vivo.pdf
17. Merino & Weeks (2003) JACS 125:12370-12371
18. prion aptamer.pdf

EXAM

Post-translational modifications

19. PTMWalsh1.pdf

Phosphorylation

20. PTMWalsh2.pdf
21. Src&Abl.pdf
22. NetworKIN.pdf

Methylation

23. PTMWalsh5.pdf
24. PRMT review
25. JMJD6 demethylase.pdf
26. Wei, Y., et al., (2003) Biochemistry 42:7044-7049
27. Lin, Q. et al., (2001) JACS 123:11608-11613 (IN CLASS DISCUSSION)
28. PIMT.pdf

Deamidation

29. BclxL.pdf

Glycosylation

30. PTMWalsh10.pdf

Hydroxylation

31. PTMWalsh12.pdf
32. HIF.pdf

Oxidation-Reduction

- 33 PTMWalsh4.pdf.
34. PTP1B&MS.pdf (IN CLASS DISCUSSION)

EXAM

Tentative

36. Marletta NO function.pdf
37. Marletta eNOS complicated.pdf
38. Snyder CO.pdf
39. HO vs NOS.pdf
40. Li JACS apatamer.pdf
41. Mapp JACS sm mol act dom.pdf
42. Schultz JACS sm mol PP inter.pdf (IN CLASS DISCUSSION)