Current Topics in Biochemistry/Capstone Course: What a Wonderful RNA World!
CHM 4933 Spring 2013

Time: MWF 12:30-1:20 pm
Place: PHSc 121
Instructor: Dr. Susan J. Schroeder
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Office: SLSRC 1160 or GLCH 28
Office Hours: by appointment
Question and Answer session: Friday 1:30-2:30 pm GLCH 28

Welcome to the Wonderful RNA World

Do you know how many small RNAs regulate cancer gene expression? No one knows yet the full count but this is one of the most exciting areas of cancer research. Did you realize that RNA can be a therapeutic molecule or a drug target? Have you ever taken a Z-Pack? The antibiotic in a Z-pack binds to bacterial ribosomal RNA and thus prevents bacterial protein expression and growth. Can you imagine a drug that could cure viral RNA infections, such as HIV-AIDS, hepatitis, or H1N1? This semester we will be exploring the wonderful world of RNA as a capstone for your chemistry and biochemistry studies at OU. You will use what you have learned in your previous chemistry and biochemistry classes to begin answering some of these questions. You will also learn how to communicate clearly what you have learned to other scientists and to the general public. There is no required text for the course, instead we will read about exciting new RNA research in scientific journals. Most course material will be available on the Desire2Learn (D2L) course website. So you only need to bring your enthusiasm, questions, and imagination to the first day of class.

Course Website (Desire2Learn): http://learn.ou.edu

Course Objectives:
1. Understand the many roles of RNA in gene expression
2. Gain awareness of RNA therapeutics and RNA drug targets
3. Synthesize chemistry and biochemistry knowledge in order to explore interdisciplinary RNA research
4. Analyze primary scientific literature
5. Develop skills for communicating scientific information at both advanced and general public levels

Prerequisites:
This course is intended to be the final course of an undergraduate degree in chemistry or biochemistry. Completion or concurrent enrollment in all courses required for an undergraduate degree in chemistry or biochemistry is expected.

Textbooks:
No specific textbook is required for this course. Scientific literature for the course will be available on the course website or OU libraries. Additional reference texts are suggested below.


Grading:

Written assignments and presentations
1. Resume and cover letter (10%)
2. Press Release/Newspaper article (15%)
3. Report and class oral presentation (25%)
4. Final report and public poster presentation (30%)
Class participation (20%)
Passing marks on homework sets

Written Assignments and Presentations
1. Resume and cover letter: Assume you are applying for a job at Dharmacon, Inc. Write a resume and cover letter for the job position. Follow OU Career Services, ACS, or AAAS guidelines for resume preparation. Grading will be based on the quality of writing, clarity, organization, and presentation. Grading will not be based on an individual’s accomplishments. Students are not required to include in the assignment a GPA or any personal information they would feel uncomfortable sharing.

2. Press Release/Newspaper article: Select a journal article from list 1 “further reading”. Other journal articles are acceptable with permission of the instructor. Write a newspaper article reporting on this scientific discovery. Identify the most important points of the journal article and summarize this information for a general public audience. Explain the impact of this research on the scientific field and on society.

3. Report and class oral presentation: Select a journal article from list 2 “noncoding RNA”. When you select an article, email your selection and two alternative choices to the instructor and, with the instructor’s approval, that choice will be removed from the list. Other journal articles are acceptable with permission of the instructor. Write an approximately 5 page report summarizing the new knowledge resulting from this research. Cite at least two additional sources of information on this topic. Clearly identify the scientific question addressed in this research and explain why this is an important question. Discuss the strengths and weaknesses of this journal article. Focus on a critical interpretation and analysis of the journal article. Prepare a 10 minute presentation that orally and visually communicates the main content of the written report. Approximately five minutes of questions from the class will follow the oral presentation. Submit both the report and an electronic copy of the presentation to the course website on the due date.

4. Final report and public poster presentation: Select a journal article from list 3 “therapeutic RNA”. When you select an article, email your selection and two alternative choices to the instructor and, with the instructor’s approval, that choice will be removed from the list. Other journal articles are acceptable with permission of the instructor. Write an approximately 5 page report summarizing the new knowledge resulting from this research. Cite at least two additional sources of information on this topic. Clearly identify the scientific question addressed in this research and explain why this is an important question. Discuss the strengths and weaknesses of this journal article. Focus on a critical interpretation and analysis of the journal article at an advanced level. Prepare a poster that visually communicates the main content of the report on a general audience level. Submit both the report and an electronic copy of the poster to the course website. The poster presentation will be at Norman’s Science Café at the public library in May.

A draft of written assignments may be handed in one week before the due date in order to receive suggestions and comments prior to submitting a final version for a formal grade. Students are encouraged to discuss ideas and questions about the journal article with the professor. All written assignments will be submitted through the drop box on the course website, which utilizes the originality reports from turnitin.com

Participation in class is required. Attendance is required. More than two absences will result in a lower grade, barring extreme circumstances and discussion with the instructor. Excused absences follow university guidelines for requests prior to the date of the absence. Students are required to contribute at least one question or comment per class during class oral presentations and class discussions. The quality of the students’ questions and comments during discussions determines the students’ grades for class participation.
When reading scientific journal articles, keep the following questions in mind:

What questions were the researchers asking? Why is this an important question?
What techniques did the researchers use and why was this a good choice?
What was the most important result?
What control experiments were done?
What was good about the paper? What was not good about the paper?
What impact will these results have on other researchers and other experiments?
What would be the best experiment to do next?
What impact will these results have on society?
How would you describe the importance of these results to your fellow citizens?
How do these experiments relate to topics discussed in class?

If there is something that you don’t understand in the journal articles, then look for more information about this topic or ask one of the instructors for more information.

Homework sets are required and will be evaluated on a high pass, pass, or fail basis. Passing marks on homework is required. A second attempt to achieve a passing mark will be allowed within one week. Students may work together to solve homework problems, but the submitted work must demonstrate individual comprehension of the problem and target concepts.

University Codes and Policies of Behavior:

Refer to “University policies regarding instruction” which can be downloaded from the Provost’s website http://www.ou.edu/provost/pronew/content/memorand.html. Each student should acquaint themselves with the University’s codes, policies, and procedures involving academic misconduct, grievances, sexual and ethnic harassment, and discrimination based on a physical handicap.

University Attendance Policy:

Any student who is unable to submit written reports or presentations on their assigned day will receive a zero unless an excused absence is granted prior to the submission deadline.

Excused absences as defined by the Dean of the College of Arts and Sciences and outlined in the Faculty Handbook are as follows:

i. Personal illness. Please note that you will not be allowed to make up work unless you can provide a doctor’s note or encounter form verifying an illness serious enough to keep you from the exam.
ii. Death in the immediate family.
iii. Jury duty, military service or university educational functions. You must provide the Professor of Record with forewarning and documentation as well as a plan for making up required work.
iv. “Unavoidable circumstances”. This is considered on a case per case basis and is subject to documentation.

It is the policy of the University to excuse absences of students that results from religious observances and to provide without penalty for the rescheduling of examinations and additional required class work that may fall on religious holidays. Please notify the instructors as soon as possible to make arrangements for the observance of religious holidays.

When petitioning for an excused absence, documentation must be presented to the professor no later than the next class period. A copy of the documentation will be made, the professor will decide if the absence is excused and the student will be informed of the decision. All original documentation will be returned to the student.

University Academic Misconduct Policy:

Academic misconduct is an extremely serious offense and immediate action will be taken if this occurs. Academic misconduct is defined as any act that improperly affects the evaluation of a student’s academic performance or achievement. The following terms illustrate but do not delimit or define academic misconduct:
1) Cheating: the use of unauthorized materials, methods, or information in any academic exercise, including improper collaboration.

2) Plagiarism: the representation of the words, images, or ideas of another as one’s own.

3) Fabrication: the falsification or invention of any information or citation in an academic exercise.

4) Fraud: the falsification, forgery or misrepresentation of academic work, including the resubmission of work performed for one class for credit in another class without the informed permission of the second instructor, or the falsification, forgery or misrepresentation of other academic records or documents, including admissions material and transcripts; or the communication of false or misleading statements to obtain academic advantage or to avoid academic penalty.

5) Destruction, misappropriation, or unauthorized possession of University property or the property of another.

6) Bribery or intimidation.

7) Assisting others in any act proscribed by this Code.

8) Attempting to engage in such acts.

For complete information on the OU Academic Misconduct Code see:
http://www.ou.edu/studentcode
http://www.ou.edu/provost/integrity/
http://www.ou.edu/provost/pronew/content/memorand.html

**Academic misconduct (cont.):**

Any form of academic misconduct, as specified in the Student Code at OU and in the Chemistry Department’s Student Handbook, will be reported to the Department and the Dean for appropriate action.

All written assignments will be submitted through the drop box in D2L with turnitin.com features enabled.

**University Policy of Reasonable Accommodations for Students with Disabilities:**

Any student in the course who has a disability that may prevent them from fully demonstrating their abilities should contact the professor of record as soon as possible to schedule a private appointment to discuss the accommodations necessary for the student to fully participate and facilitate the student’s educational opportunities.

**Note:**

The instructor reserves the right to change by addition and/or subtraction any and/or all materials contained in this syllabus. This includes, but is not limited to, course content, assignments, due dates, and portion(s) of the grades assigned to individual items within this course.
CHEM 4933 Tentative Lecture and Discussion Schedule

January 14: Welcome to the Wonderful RNA World!

January 16: **RNA synthesis**

lecture: From rags to riches in the RNA World: the story of Stephen Scaringe and Dharmacon, Inc.

January 18: **RNA Structure and tRNA** lecture: 1°, 2°, 3°, 4° structure in RNA, structure of tRNA

first writing assignment (resume and cover letter) due

January 21: Martin Luther King, Jr. holiday-no class

January 23: class activity: build a model of tRNA


January 25: continue class activity: build a tRNA model

**homework #1 RNA Synthesis due**

Last day to change credit and audit status

January 28: continue class activity: build a tRNA model

Last day to drop a class with no fees

January 30: guest lecture and class discussion with Prof. Michael Deem

February 1: Class discussion on *in vitro* synthesis of poliovirus RNA in *Read EMBO* 2006 v7 p S3

Write a magic bag question

**homework #2 tRNA structure due**

February 4: lecture: **RNA World Hypothesis** *Read Chapter 1 RNA World*


February 8: lecture: tRNA function in peptide synthesis: *Read NSMB* 2004 v11 p1101

second writing assignment (newspaper article) due

February 11: **ribosomal RNA and Crystallography** *Read Nature* 2009 v461 p1234

February 13: lecture: continue rRNA and crystallography *Read McPherson's Chapter 1*

February 15: visit to macromolecular crystallization and x-ray crystallography facilities

Dr. Leonard Thomas, director of crystallization and x-ray crystallography facilities

Read *FEBS* 2008 v 275 p 1

**homework #3 tRNA function due**

February 18: lecture: The story of 13-deoxytedanolide, from natural products drug discovery to structure-based drug design for ribosomal antibiotics

February 20: **RNA enzymes** *Read Tom Cech's Nobel prize acceptance speech*

February 22: lecture: group I intron structure and function *Read TIBS* 2006 v 31 p41

**homework #4 rRNA and crystallography due**

February 25: lecture: telomerase structure and function


March 1:  **mRNA and Splicing: The Life of an mRNA**  *Read Cell 2009 v 136 p688*

*Deadline to select article for third writing assignment*

March 4:  **mRNA and splicing: RNA Catalysis in the Spliceosome**  *Read Cell 2002 v 109 p149*

March 6:  **RNA Dynamics and NMR Spectroscopy**

March 8:  lecture RNA NMR versus HIV-AIDS  *Read PNAS 2009 v106 p11931*

*homework #5 RNA Enzymes due*

March 11:  lecture RNA NMR continues

March 13:  **Interesting Noncoding RNAs**  *Read Sharp 2009 Cell v136 p577*

March 15:  Class discussion  *Read PAN RNA and polyA tails: Science 2010 v 330 p 1244*

*Write a magic bag question*

*homework #6 RNA Dynamics and NMR due*

March 18-24:  Spring break

**Novel Noncoding RNAs: ribozymes, riboswitches, 5’UTRs, and other interesting RNAs**

March 25:  **third writing assignment (class powerpoint presentations and report) due**

Class oral presentations March 25-April 12

April 12:  Class oral presentations complete and Summary and discussion on non-coding RNA

April 15:  **Small RNAs and mRNA Expression**  *Read Cell 2009 v 136 p 642*

*homework #7 Noncoding RNA due*

April 17:  lecture: RNAi therapeutic approaches  *Read Nature 2009 v457 p426*

*Additional recent reviews: J. Biotech. 2011 v6 p1130, TIBS 2010 v28 p570*

*Deadline to select article for fourth writing assignment*

April 19:  Class Literature Discussion:  *Read NSMB 2004 v11 p599 Write a magic bag question*

April 22:  **RNA Structure Prediction**


April 24:  lecture: From Sequence to Structure  *Read NBT 2004 v 22 p145, JVir 2009 v83 p6326*

April 26:  lecture: From Sequence to Structure (cont)

*homework #8 Small RNAs and mRNA Expression due*

April 29:  **visit to Stephenson Research and Technology Center, Genome Sequencing facility**

Dr. Fares Najar, Research Scientist

May 1:  **visit to Oklahoma Center for Supercomputing and Education Resources (OSCER)**

Dr. Henry Neeman, Director OSCER

May 3:  Class Literature Discussion Foot and Mouth Virus IRES 1°-2°-3°  *Read NAR 2011 v 39 p 8572*

*Write a magic bag question*

*homework #9 RNA Structure Prediction due*

May 7:  **fourth writing assignment (report and poster) due Therapeutics and RNA**

May 9:  Science Café poster session at Norman Public Library 6:30 pm

May 10-11:  Commencement
List 1: Further Reading

RNA Synthesis
Prebiotic RNA synthesis: Nature 2009 v 459 p239
Synthesis of Purine Precursors: JACS 2010 v 132 p16677 (for those who love organic chemistry)
Inorganic catalysis of RNA oligomerization (or Could there be RNA on Mars?): JACS 2009 v131 p13369
2’ACE chemistry: Methods Enz. 2000 v317 p3
Mismatches stall template-directed synthesis: JACS 2010 v 132 p 5880
Non polar isosteres in RNA helices: PNAS v100 p4469
Direct RNA sequencing: Nature 2009 v 461 p 814
In vitro poliovirus synthesis: Science 2002 v 297 p 1016
Polymerase crystallography: Science 2010 v327 p206

tRNA
tRNA biogenesis: Nature 2009 v 461 p1144
tRNA proofreading: NSMB 2009 v16 p348, 353, 359
tRNA selection: Cell 2002 v111 p721
modified nucleotides in tRNA: NSMB 2004 v11 p1186
CCA Adding enzymes and tRNA: Nature 2004 v 430 p640
Encoding non-natural tRNAs and amino acids: Angew. Chem. 2009 v 48 p4052

rRNA
Ribosomes unwinding mRNA structure: Cell 2005 v 120 p 49
Induced fit in ribosome PTC: Nature 2005 v438 p 520
H. marismortui 50S structure: Science 2000 v289 p905-930
T. thermophilus 30S structure: Nature 2000 v 411 p498
T. thermophilus 30S structure: Cell 2000 v102 p615
EF-TU and ribosome crystal structure: Science 2009 v 326 p688
EF-G and ribosome crystal structure: Science 2009 v 326 p649
E. coli 70S ribosome: Science 2005 v310 p 827
T. tetrahymena 60S structure: Science 2011
S. cerevisiae 80 S structure: Science 2011
List 2: Noncoding RNAs

Ribozymes
Group II introns: Science 2008 v320 p77
RNAse P: PNAS 2005 v102 p13392
   Nature 2005 v437 p584
   Cell 1993 v35 p849
RNAse P and OLE RNA: PNAS 2007 v104 p7815
Hepatitis Delta Virus crystal structure: Nature 1998 v395 p567
Hepatitis Delta Virus mechanism: JACS 2008 v130 p14504
Hairpin ribozyme: Nat. Chem. Biol. v5 p351
U6 and U2 RNA ribozyme: PNAS 2009 v 106 p11901
Diels-Alders ribozyme: NSMB 2005 v12 p218
RNA polymerase ribozyme: Science 2009 v 326 p1271
Ribozymes for peptidyl transfer: Nature 1996 v381 p442
Hammerhead ribozyme variation: Science 2009 v323 p 1308
Hammerhead motifs in mammalian cells: Nature 2008 v454 p899
Hammerhead crystal structure and mechanism: Cell 2006 v126 p309
Leadzyme: Chem. Biol. 2007 v14 p23
glmS ribozyme kinetics: JACS 2012 v134 p19043

Riboswitches
Riboswitches: Nature 2004 v 428 p281
Guanine riboswitch: Nature 2004 v432 p411
S-adenosymethionine riboswitch: Nature 2006 v441 p1172
Cyclic diGMP riboswitch: NSMB 2009 v16 p1218
B12 riboswitch: Nature 2012 v492 p133
Iron response element (IRE) RNA: PNAS 2012 v109 p8417

Other Interesting RNAs
RNA logic gates to control gene expression: Science 2008 v322 p456
Cooperative RNA replicators: Nature 2012 v491 p72
Prohead RNA: Science 1987 v236 p690
Quorum sensing RNAs: PNAS 2007 v104 p11145
H/ACA snoRNA: PNAS 2007 v104 p6655
GOLLD and HEARO RNA: Nature 2009 v 462 p 656
Misfolded tRNAs and ALU elements: PNAS 2011 v108, p 10974
List 3: RNATherapeutics & Targets

**miRNA/RNAi/Antisense RNA**

- **RNAi therapeutics for metastatic Ewing sarcoma in mice:** Cancer Res. 2005 v 65 p 8984.
- **miRNAs in p53 tumor suppression network:** Nature 2007 v 447 p 1130
- **let-7 miRNA in oncogenic transformation:** Science 2007 v 315 p1576
- **RNAi screen for gene expression changes to paclitaxel in lung cancer cells:** Nature 2007 v 446 p 815
- **miRNA profiling for detection and diagnosis in ovarian cancer cells:** PNAS 2007 v 104 p 11400
- **miRNA expression profiles in human cancer cells:** Nature 2005 v 435 p 834
- **ARES and microRNAs in tumor necrosis factor gene expression:** Science 2007 v 318 p 1931
- **Antisense RNA against tumor suppressor p15:** Nature 2008 v 451 p 202
- **microRNA-10b regulation in breast cancer:** Nature 2007 v 449 p 682
- **Breast cancer miRNA profile:** PNAS 2012 v 109 p 3024
- **miRNA155 in lymphoma:** PNAS 2012 v 109 p E1695
- **microRNAs regulate insulin sensitivity:** Nature 2011 v 474 p 649
- **siRNA on carbon nanotubes to treat stroke:** PNAS 2011 v 108 p 10952
- **Click chemistry for siRNA delivery:** JACS 2012 dx.doi.org/10.1021/ja303251fl
- **Polyporphosphonium polymers for siRNA delivery:** JACS 2012 dx.doi.org/10.1021/ja207366k
- **U1 RNA role in UVB irradiation, sunburns, and skin cancer:** Nature Medicine doi:10.1038/nm.2861
- **Inhibitors of microRNAs for Hepatitis Virus C:** JACS 2010 v 132 p 7976
- **RNAi against Ebola Virus:** Lancet 2010 v 375 p 1896
- **Antisense against cytomegalovirus (first FDA approved RNA therapeutic):** AAC 1993 v 37 p 1945
- **Antisense against influenza:** JVIR 2011 v 85 p 2639
- **siRNA inhibition of hepatitis in mice:** Nature Biotech. 2003 v 21 p 639
- **siRNA nanocpasules against HIV:** JACS 2012 doi:10.1021/ja304649a
- **shRNA sequence analysis of HIV, Hepatitis C, and influenza:** PNAS 2012 v 109 p 869

**Aptamers**

- **Macugen, a therapeutic aptamer for macular degeneration:** PNAS 2005 v 102 p 18902
- **Theophylline (a bronchodilator) aptamer:** Science 1994 v 263 p 1425
- **Thrombin aptamer:** RNA 2008 v 14 p 2504
- **Osteopontin aptamer:** Mol.Ther. 2009 v 17 p 153
- **RNA aptamers against HIV Gag:** JVIR 2011 v 85 p 305

**Antibiotics bound to rRNA**

- **Antibiotics bound to T. thermophilus 30S:** Nature 2000 v 407 p 340
- **Pleuromutilin antibiotics bound to 50S ribosome:** PNAS 2007 v 104 p 4291
- **D. radiodurans 50S structure bound to antibiotics:** Nature 2001 v 413 p 814
- **Restrictocin and rRNA:** NSMB 2001 v 8 p 968

**Triplet repeats**

- **Triple repeat RNA in muscular dystrophy:** Science 2009 v 325 p 336
- **Targeting CUG repeats in muscular dystrophy:** JACS 2009 v 131 p 9767

Journal abbreviations

- **JACS:** Journal of the American Chemical Society
- **PNAS:** Proceedings of the National Academy of Science, USA
- **NSMB:** Nature Structure and Molecular Biology
- **NAR:** Nucleic Acids Research
- **JVIR:** Journal of Virology

All other journal abbreviations are standard citation abbreviations. Each paper topic is described with a short phrase; note that this is not the full title of the paper.