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 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. 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.

4. Final report and public poster presentation: Select a journal article from list 3 “therapeutic RNA”. When you select an article, email your selection 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. 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, and more than two absences will result in a lower grade, barring extreme circumstances and discussion with the instructor. Students are required to contribute at least one question or comment per class during class oral presentations and discussions.

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 Accomodations 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.
Tentative Lecture and Discussion Schedule

January 18: Welcome to the Wonderful RNA World!

January 20: RNA synthesis
lecture: From rags to riches in the RNA World: the story of Stephen Scaringe and Dharmacon, Inc.
Jennifer Allen-Ayres, OU Career Services


January 25: lecture: RNA World Hypothesis Read Chapter 1 RNA World

January 27: tRNA lecture: 1\textdegree, 2\textdegree, 3\textdegree, 4\textdegree structure of tRNA

homework #1 RNA Synthesis due

January 30: class activity: build a model of tRNA

January 31: Add/drop deadline

February 1: continue class activity: build a tRNA model
February 3: lecture: the PDB and Pymol and looking at 3D tRNA structure 1EHZ
February 8: lecture: tRNA function in peptide synthesis: Read NSMB 2004 v11 p1101

February 10: ribosomal RNA Read Nature 2009 v461 p1234
homework #2 tRNA due

February 13: ribosomal RNA and Crystallography
Read Science 2000 v 289 p 905

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 and McPherson’s Chapter 1

February 17: lecture: continue rRNA and crystallography
second writing assignment (newspaper article) due

February 20: lecture: The story of 13-deoxytedanolide, from natural products drug discovery to structure-based drug design for ribosomal antibiotics

February 22: RNA enzymes Read Tom Cech’s Nobel prize acceptance speech

February 24: lecture: group I intron structure and function Read TIBS 2006 v 31 p41
homework #3 rRNA and crystallography due

February 27: lecture: telomerase structure and function
Read Phil. Trans. R. Soc. Lond. B 2004 v 359 p109, TIBS 2004 v29 p183
Deadline to select article for third writing assignment


March 2: RNA Dynamics and NMR Spectroscopy

March 5: lecture RNA NMR versus HIV-AIDS Read PNAS 2009 v106 p11931
March 7: mRNA and Splicing Read Cell 2009 v 136 p688
March 9: mRNA and splicing (cont.)

homework #4 RNA Enzymes due

March 12: visit to NMR facility, Dr. Susan Nimmo, director of NMR facilities

March 14: Interesting Noncoding RNAs Read Sharp 2009 Cell v136 p577

March 16: MFAT
homework #5 RNA Dynamics and NMR due

March 17-25: Spring break

March 26: third writing assignment (class powerpoint presentations and report) due

 Novel Noncoding RNAs: ribozymes, riboswitches, IRES, 5'UTRs, and other interesting RNAs
Class oral presentations

April 13: Class oral presentations completed and Summary and discussion on non-coding RNA
homework #6 Noncoding RNA due

April 16: Small RNAs and mRNA Expression
Deadline to select article for fourth writing assignment

April 18: lecture: RNAi therapeutic approaches Read Nature 2009 v457 p426

April 20: RNA Structure Prediction
April 23: lecture: From Sequence to Structure  
Read NBT 2004 v 22 p1457  
Read JVir 2009 v83 p6326

April 25: visit to Stephenson Research and Technology Center, Genome Sequencing facility  
Dr. Fares Najar, Research Scientist

April 27: lecture: From Sequence to Structure (cont)

April 30: visit to Oklahoma Center for Supercomputing and Education Resources (OSCER)  
Dr. Henry Neeman, Director OSCER

May 4: Foot and Mouth Virus IRES 1\(^{\circ}-2\^{\circ}-3\^{\circ} \) Read NAR 2011 v 39 p 8572

May 4: MC-SYM predict RNA 3\(^{\circ} \) Read Nature 2008 v 452 p 51

homework #8 RNA Structure Prediction due

May 8: fourth writing assignment (report and poster) due Therapeutics and RNA

May 10: poster session at Norman Public Library

May 11-12: 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
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

IRES, Riboswitches
Viral IRES: Science 2006 v314 p1450
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

Other Interesting RNAs
RNA logic gates to control gene expression: Science 2008 v322 p456
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

Aptamers
Macugen, a therapeutic aptamer for macular degeneration: PNAS 2005 v102 p18902
Theophylline (a bronchodilator) aptamer: Science 1994 v263 p1425
Thrombin aptamer: RNA 2008 v14 p2504
Osteopontin aptamer: Mol.Ther. 2009 v17 p153
RNA aptamers against HIV Gag JVIR 2011 v 85 p 305

Antibiotics bound to rRNA
Antibiotics bound to T. thermophilus 30S: Nature 2000v 407 p340
Pleuromutilin antibiotics bound to 50S ribosome: PNAS 2007 v 104 p4291
D. radiodurans 50S structure bound to antibiotics: Nature 2001 v413 p814
Restrictocin and rRNA: NSMB 2001 v 8 p968
Aminoglycosides bound to A-site: Science 1996 v274 p1367

Triplet repeats
Triple repeat RNA in muscular dystrophy: Science 2009 v325 p336
Targeting CUG repeats in muscular dystrophy: JACS 2009 v131 p9767

Viral RNA
PAN ENE RNA in Kaposi’s sarcoma associated herpesvirus: PNAS 2007 v 104 p 10412
Moloney Murine Leukemia Virus Dimerization Signal: J. Virol. 2010 v 84 p 898
HIV escape from RNAi: NAR 2005 v 33 p796
HIV RNA 20: Nature 2008 v 452 p51
Rhinovirus sequence variation and secondary structure: Science 2009 v 324 p 55

miRNA/RNAi/Antisense RNA
RNAi therapeutics for metastatic Ewing sarcoma in mice: Cancer Res. 2005 v 65 p 8984.
let-7 microRNA 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 p1931
microRNA-10b regulation in breast cancer: Nature 2007 v 449 p 682
RNAi against Ebola Virus: Lancet 2010 v 375 p 1896
siRNA on carbon nanotubes to treat stroke: PNAS 2011 v 108 p10952
Inhibitors of microRNAs for Hepatitis Virus C: JACS 2010 v132 p7976
Antisense against cytomegalovirus (first FDA approved RNA therapeutic): AAC 1993 v 37 p1945
Antisense against influenza: JVIR 2011 v 85 p1554

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

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.