BIOL 4802/8802

Special Topics: Regulatory RNAs

Course Objectives:

- Appreciate the ubiquity of regulatory small RNAs (sRNAs) in diverse organisms.
- Compare/contrast molecular mechanisms of sRNA control in eukaryotes and prokaryotes.
- Understand how to validate sRNA/mRNA target interactions.
- Learn about processes under sRNA control in eukaryotes and prokaryotes.
- Discover the potential of engineering sRNAs for manipulating living systems.

Prerequisites:

For graduate level courses, Graduate Standing or Permission of Instructor is assumed

For undergraduates interested in enrolling, a grade of at least a C in Genetics (BIOL 2344/2354), Eukaryotic Molecular Genetics (BIOL 4668), or Prokaryotic Molecular Genetics (BIOL4608/6608) is required.

Reading Material:

Selected research articles

Supplemental Reading:

There are numerous review articles on regulatory RNAs in bacteria and eukaryotes, several are listed below:

JC Carrington & V Ambros (2003) Role of MicroRNAs in plant and animal development. *Science* **301**:336-338.

S Gottesman (2004) The small RNA regulators of Escherichia coli: roles and mechanisms. *Annu Rev Microbiol* **58**:303-28.

JM Liu & A Camilli (2008) A broadening world of bacterial small RNAs. *Curr Opin Microbiol* **13**:1-6.

LS Waters & G Storz (2009) Regulatory RNAs in Bacteria. *Cell* **136**:615-28.

Castanotto & Rossi (2009) The promises and pitfalls of RNA-interference-based therapeutics. *Nature* **457**:426-33.

A Nag & T Jack (2010) Sculpting the flower; the role of microRNAs in flower development. *Curr Top Dev Biol* **91**:349-78.

RJ Taft, KC Pang, TR Mercer, M Dinger & JS Mattick (2010) Non-coding RNAs: regulators of disease. *J Pathol* **220**:126-39.

Course format:

This 2-credit course meets once a week, on Mondays from 1 to 3 pm. This course will be primarily based on student presentations and ensuing discussions of primary research articles that are present in the syllabus. Students will be assigned as presenters and as reviewers during the first week of class. The first half of the course focuses on eukaryotic sRNAs, while the second half of the course emphasizes prokaryotic systems. The end of the course will focus on engineering and application of sRNA control.

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Attendance Policy:
Each student will be allowed one excused absence from class. Written verification will be required for additional absences. Students are expected to adhere to the Student Honor Code (http:www.honor.gatech.edu).

Grading:
Each student will be required to read the two research articles assigned for each week. All students in the class are expected to participate in discussions. In addition, 2 or 3 students will be specifically assigned to review each presentation and be required to lead the in-class discussion by asking questions of each presenter. Throughout the semester each student will prepare and present 2 or 3 of the articles as an in-class Powerpoint presentation. Both the material in the article and appropriate background material should be included in the presentation. Each presentation will be video-taped and each presenter will write view their own recording and write a self-evaluation of their presentation.

Student presentations	60%
Self-evaluations	10%
Review	30%

Grading will be assigned according to the following scale:
A = 90-100; B = 80-89; C = 70-79; D = 65-69; F = 64 or below.

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	Date	Topic	Papers	Student presenter	Student reviewer
1	Jan 10	Introduction central dogma; regulatory sRNAs		Hammer	
*	Jan 17	HOLIDAY			
2	Jan 24	Eukaryote pioneers of sRNAs	RC Lee, L Feinbaum & V Ambros (1993) The *C. elegans* heterochronic gene *lin-4* encodes small RNAs with antisense complementarity to lin-14 *Cell*. **75**:843-854.	student	student1 student2 student3
			A. Fire, et al. (1998) Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*. *Nature* **391**:806-11.	student	student1 student2 student3
3	Jan 31	Nuts and bolts: Slicer and Dicer	E Bernstein, AA Caudy, SM Hammond & GJ Hannon* (2001) Role for a bidentate ribonuclease in the initiation step of RNA interference. *Nature* **409**:363-6.	student	student1 student2 student3
			J Liu et al. (2004) Argonaute2 Is the Catalytic Engine of Mammalian RNAi. *Science* **305**:1437-41.	student	student1 student2 student3
4	Feb 7	sRNAs in plants	C Llave, Z Xie, KD Kasschau, & JC Carrington (2002) Cleavage of scarecrow-like mRNA targets directed by a class of *Arabidopsis* miRNA. *Science* **297**:2053-6.	student	student1 student2 student3
			A Molnar, et al. (2010) Small silencing RNAs in plants are mobile and direct epigenetic modification in recipient cells. *Science* **328**:872-5.	student	student1 student2 student3
5	Feb 14	sRNAs in chromatin remodeling	D Zilberman, X Cao & SE Jacobsen (2003) Modulation of heterochromatin protein 1 dynamics in primary mammalian cells. *Science* **299**:716-9.	student	student1 student2 student3
			T A Volpe, et al. (2002) Regulation of heterochromatic silencing and histone H3 lysine-9 methylation by RNAi. *Science* **297**:1833-7.	student	student1 student2 student3
6	Feb 21	sRNAs in human disease & diagnosis	J Lu, et al. (2005) MicroRNA expression profiles classify human cancers. *Nature* **435**:834-8.	student	student1 student2 student3
			J Kota et al. (2009) Therapeutic microRNA delivery suppresses tumorigenesis in a murine liver cancer model. *Cell* **137**:1005-17.	student	student1 student2 student3

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7	Feb 28	A bacterial immune system - CRIPSRs	R Jansen, JDA van Embden, W Gaastra & LM Schouls (2002) Identification of genes that are associated with DNA repeats in prokaryotes. *Mol Microbiol* **43**: 1565-75.	student	student1 student2 student3
			LA Marraffinin &EJ Sontheimer (2008) CRISPR interference limits horizontal gene transfer in *Staphylococci* by targeting DNA. *Science* **322**: 1843-5.	student	student1 student2 student3
8	Mar 7	sRNAs that regulate protein activity (Hfq-independent)	MJ Liu et al. (1997) The RNA molecule CsrB binds to the global regulatory protein CsrA and antagonizes its activity in *Escherichia coli. J Biol Chem* **272**: 17502-10.	student	student1 student2 student3
			JA Opdyke, J Kang & G Storz (2004) GadY, a Small-RNA Regulator of Acid Response Genes in *Escherichia coli. J Bacteriol **146:*** 6698-705.	student	student1 student2 student3
9	Mar 14	The bacterial RNA chaperone, Hfq	A Muffler, D Fischer & R Hengge-Aronis (1996) The RNA-binding protein HF-I, known as a host factor for phage Qb RNA replication, is essential-for *rpoS* translation in *Escherichia coli. Genes & Devel* **10**:1143-51.	student	student1 student2 student3
			A Sittka, et al. (2008) Deep sequencing analysis of small noncoding RNA and mRNA targets of the global post-transcriptional regulator, Hfq. *PLOS Genetics* **4**: 1-20.	student	student1 student2 student3
*	Mar 21	SPRING BREAK			student1 student2 student3
10	Mar 28	Hfq-dependent, negatively-acting sRNAS	K Maki, K Uno, T Morita & H Aiba. (2008) RNA, but not protein partners, is directly responsible for translational silencing by a bacterial Hfq-binding small RNA. *PNAS* **108**: 10332-7.	student	student1 student2 student3
			DH Lenz, et al. (2004) The small RNA chaperone Hfq and multiple small RNAs control quorum sensing in *Vibrio harveyi* and *Vibrio cholerae. Cell* **118**: 69-82.	student	student1 student2 student3
11	Apr 4	Hfq-dependent, positively-acting sRNAS	JH Urban & J Vogel (2008) Two seemingly homologous noncoding RNAs act hierarchically to activate glmS mRNA translation. *PLOS Biology* **6**:631-42.	student	student1 student2 student3
			N Majdalani, C Cunning, D Sledjeski, T Elliott & S Gottesman (1998) DsrA RNA regulates translation of RpoS message by an anti-antisense mechanism, independent of its action as an antisilencer of transcription. *PNAS* **95**:12462-7.	student	student1 student2 student3

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12	Apr 11	Engineered sRNAs and therapeutic potential	SM Elbashir, et al (2001) Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells. *Nature* 411:494-8.	student	student1 student2 student3
			J DeVincenzo (2010) A randomized, double-blind, placebo-controlled study of an RNAi-based therapy directed against respiratory syncytial virus PNAS 107:8800-5.	student	student1 student2 student3
13	Apr 18	sRNA/mRNA validation	J. Brennecke, A. Stark, RB Russell, SM Cohen (2005) Principles of microRNA-target recognition. PLOS Biology 3:404-18.	student	student1 student2 student3
			X Zhao &JP Bardill (in review) Sequence determinants for sRNA regulation of virulence by the quorum sensing system in *Vibrio cholerae*	Hammer lab member	
14	Apr 25	Conclusion		Hammer	