Biology of MicroRNAs and other small RNAs 2013
Mondays 1-3 pm
Second floor library (next to room 284), SPH/PI building, 1601 W. Taylor Street
Neil Smalheiser, instructor neils@uic.edu, 3-4581

This course will discuss recent research findings and open questions regarding microRNAs and other small RNAs. The emphasis is on mammalian systems and medical applications, but model organisms such as C. elegans, yeast and plants are all within scope. Following a few introductory lectures, we will follow a seminar/journal club format. Grading is based on attendance and participation -- each person is expected to attend nearly all classes (with brain engaged), and will choose one topic to present in detail.

Course schedule:
1/14 - Introductory overview lecture on microRNAs.
1/21 – no class (MLK Day)
1/28 – guest lecture on methods of measuring microRNAs (Giovanni Lugli)
2/04 – guest lecture on miRNAs in cancer (Larisa Nonn)
2/11 – guest lecture on miRNAs in system biology and psychiatric disease (Chunyu Liu)
2/18 – guest lecture on RNAi (Zain Paroo)
2/25 – seminar/journal club presentation
3/04 – seminar/journal club presentation
3/11 – seminar/journal club presentation
3/18 – seminar/journal club presentation
3/25 – no class (spring break)
4/01 – seminar/journal club presentation
4/08 – seminar/journal club presentation
4/15 – seminar/journal club presentation
4/22 – seminar/journal club presentation
4/29 – seminar/journal club presentation (final class of the semester)

Students may choose to present on a wide range of topics. For example:
1. miRNA biogenesis (transcription, drosha and cofactors, dicer and cofactors, RISC loading, mirtrons and other alternative pathways).
2. miRNA effector pathways (translation inhibition, mRNA degradation, nuclear targets including ncRNAs, promoters and splicing)
3. miRNA-target interactions (computational models of target prediction, experimental methods of target validation, network analysis).
4. miRNA in cellular functions (relation to transcription factors, signaling pathways, cellular stress responses, cell fate determination)
5. role of miRNAs in specific contexts (development, cancer and other diseases, virus infection, immune function, synaptic plasticity).
6. miRNA biotechnology (knockouts, transgenics, transfection and knockdown, in vivo therapies).
7. Relation of miRNAs to other small RNAs (endogenous siRNAs, genomic repeats, transposable elements, piRNAs, ncRNA-derived small RNAs).
8. miRNAs and evolution (how miRNAs arise, role in directing evolution, role in human evolution in particular).
9. Additional topics are possible; please discuss with the instructor.
Grading Rubric

A: Attendance score = 0 to 100% of classes attended
(Absences should be requested and approved in advance)

P: Participation weighting = 0.8 to 1.2
   = 0.8 if present in body only (texting, sleeping, etc.)
   = 1.0 if normally attentive, ask some questions
   = 1.2 if contributes actively

Pres: Presentation score: 0 to 100%
20% organization and quality of presentation
20% amount and quality of content
20% accuracy of understanding
20% detailed consideration of mechanisms
20% new and original ideas, thoughts, proposals

Final grade is calculated as \[(A \times P) + \text{Pres}\]/2,
i.e. the average of the attendance score (weighted by participation) and the presentation score.

A = 90-100%
B = 80-89%
C = 70-79%
D = 60-69%
F = <60% (may also include cases of misconduct, cheating, or plagiarism)
How to Read Independently and Prepare a Presentation

Start with a few general review articles. Usually, articles by thought leaders which are published in high impact journals are the best to read, but avoid those which are too laden with jargon, poorly written, or that summarize current experiments without pointing to the future.

Anne O’Tate (http://arrowsmith.psych.uic.edu) can be used to help find articles.

Next, identify a few of the key early experimental studies and read them carefully. Knowing the historical context is very valuable to help understand how and why they were discovered, and how and why they were studied in a particular way. There is a predictable “flow” of information from the earliest studies moving slowly across the rest of science, that is important to be aware of.

Another reason to read early studies is that they usually discuss many possible mechanisms and functions that are not initially studied but are taken up again years later. E.g. the first paper describing drosha described 2 separate drosha complexes, but only one of them (Microprocessor) was initially followed up. Very often, a single experimental paper will be taken to establish a “rule” or expectation which inhibits further exploration and establishes dogma prematurely. E.g. the 5’-seed rule for matching miRNAs to their targets. E.g. miRNAs were supposed to inhibit translation of miRNAs but not affect their stability. E.g. miRNAs were supposed to have post-transcriptional effects but not affect transcription in the nucleus. People who come into the field in the middle may have a hard time learning what is truly known and what is worth exploring further.

Next, choose a topic of personal interest to you. This can be based on a particular disease or biological pathway; a model organism that you are studying for your thesis; or a more general interest in genomics, evolution, or biotechnology tool development. Deliberately read in a “scattered” fashion, to see the type of topics that people are working on, the current state of knowledge, the current research frontiers and what is fascinating yet NOT being worked on. Reading should go beyond the miRNA literature to include related or overlapping subjects. Depending on the topic, it would be relevant to read about noncoding/antisense/linc RNAs, epigenetics, gene therapy, personalized medicine, human genetics (CNVs, SNPs, GWAS), and so on.

Use this personal reading to formulate a hypothesis that will be proposed and discussed in your presentation:

What is the background to the hypothesis?
What prior studies have been carried out?
What is the hypothesis? (Ideally, it is novel and original, thought up by you)
What is the rationale – why do you think it might be true? If true, why would it be important to prove?
How can the hypothesis be tested? Outline a series of experiments that could provide compelling support or refutation of the hypothesis.
Novel, original, important hypotheses are not hard to find, even for undergraduates! They are laying around abundantly for the taking.

**Example:** An extremely brief example of a presentation from a nutrition grad student in a previous class:

Background - microRNAs were recently discovered to be abundant in exosomes expressed in colostrum and breast milk.

Hypothesis - These might serve a function in the newborn, either to assist development of the gut, or help establish immunity.

How would this be tested? - First, need to show whether exosomes in breast milk can be taken up by the gut of a newborn infant. Next, what happens to the miRNAs after that – are they degraded, or do they exert functional effects within gut cells? Are they repackaged and secreted into the blood? Do they get taken up by other cell types, e.g. liver, dendritic cells, macrophages?

Is this an important, possibly fundamental discovery worth exploring, or not? Is it likely to be true? Is it feasible to test with current tools?