Northwestern University Medical Scientist Training Program

TOPICS IN MOLECULAR AND TRANSLATIONAL MEDICINE
2008-2009

Syllabus for NU Graduate Course Number MSTP 401

Med1 course: Adrian Gross, M.D.
Med2 course: Thomas McGarry, M.D., Ph.D. and Sarah Rice, Ph.D.
Sandra Lee, Ph.D.
Course Co-Directors

Course Description. This 2-year course prepares students to read original research articles in molecular and translational medicine, i.e., advances in the molecular biology of disease processes and in relevant translational science. Because the research interests of MSTP students span a broad range from basic science (cell and molecular biology, genetics, microbiology-immunology) to multi-disciplinary (neurobiology, pharmacology, cancer biology, pathology, drug discovery) and newer inter-disciplinary fields (neuroengineering, tissue engineering) and translational research (animal and cell culture models of the disease), the course is organized around these theme areas. This course draws from research faculty throughout the university: physician scientists engaged in basic and translational research (infectious diseases, molecular endocrinology, pharmacology, neurology, molecular cardiology, and cancer biology) and life scientists engaged in basic research in traditional disciplines (cell and molecular biology, microbiology, immunology, and genetics) and in newer multi- and inter-disciplinary research (drug discovery, and chemical biology, bioinformatics, biotechnology, biomedical engineering, chemical and biological engineering, tissue engineering, computational biology). To promote in students the development of critical scientific thought important to their future careers as physician-scientists, discussions focus on hypothesis-driven research, experimental designs, methods to test hypotheses, and interpretation of data. Each year students practice the basics of grant writing with faculty as mentors, by writing and presenting an original hypothesis-based research proposal. In the first year, the students write and present a brief original research proposal on a topic discussed in the first year course and the course faculty serves as mentors. In the second year, the students write and present another brief original proposal but this time the topic is their future thesis research topic and each student's thesis adviser serves as the mentor. First year MSTP students meet on Wednesdays and second year students meet on Thursdays, from 4:00-5:15 PM during fall, winter, and spring quarters.

Goals and Objectives. The course is designed to:

1. cover the basic sciences with the rigor necessary for careers in biomedical investigation.
2. promote the development of critical scientific thought.
3. help students develop the ability to formulate hypothesis-based research proposals.

Upon completion of this course, MSTP students will have participated in two years of weekly paper discussion and will have written and defended two brief research proposals. The students should be well prepared for graduate study and be able to:

1. identify the most important questions facing biomedical and translational researchers today

2. understand current techniques employed in biomedical and translational research
3. critically read scientific papers and assess their strengths and weaknesses
4. develop cogent, hypothesis-based research proposals
5. give clear, compelling oral presentations of the proposals and defend them

"What you get out depends on what you put in." Engaging the material and participating in the in-class discussions are critical for learning how to do research. As with any other skill, it takes practice to design good experiments to extend the work in question. To a large extent, the best practice you will get in this class from comes from wrestling with the questions you ask as you read each paper, not from listening to the discussions of the papers. These question include "Did the authors really show what they say they showed?", "Were those really the best experiments to test that hypothesis in the research?", "What questions or aspects did the authors not address?" and "What are the next steps and how would I take them?" The more you think about these questions in advance, the more interesting and deeper the discussions of the papers will be.

Location and Time. Ward 12th floor conference room (12-365), 4:00-5:15 PM on Wednesdays (M1 MSTP students) and Thursdays (M2 MSTP students). See pages 3 and 4 for detailed schedules.

Attendance. All first and second year MSTP students are required to attend all sessions unless excused in advance (contact Dr. Sandra Lee, s-lee@northwestern.edu). Absences in excess of 1 per quarter will require remediation.

Class Format.

The class sessions will follow a paper-discussion format, with a critical review of research papers centered on a particular theme in contemporary biology. The faculty members will choose the papers that will be distributed via the course web site at http://www.mstp.northwestern.edu/mstp_courses.htm.

The recommended class structure is as follows:

Class Format

The class sessions will follow a paper-discussion format, with a critical review of research papers centered on a particular theme in contemporary biology. The faculty members will choose the papers. The recommended class structure is as follows:

1. Preceptor should provide a 10 – 20 min introduction placing the paper to be discussed into its general context within the field. Insofar as first year courses in the medical school rarely provide a background for the subject matter of the journal club, first year students may also need to be exposed to relevant basic concepts in the field. These concepts might include, for example, specific cell lineage/differentiation schemes or an enumeration of neuron types and connections within a circuit.

2. The rest of the session will be devoted to the student presentation. The paper will be posted in advance by the preceptor. The student presenter/discussion leader will also be chosen in advance. The discussion leaders' responsibility is to detail the specific question addressed, provide background and significance specific to the paper, describe the experimental strategy or approach, and discuss and critique the figures in conjunction with the class. The student leader should also prepare the figures for class viewing (e.g. PowerPoint

presentation or overheads). Student leaders are highly encouraged to meet with the preceptor for 1 hour to discuss the presentation prior to class. If a face-to-face meeting is not possible, correspondence should occur beforehand by e-mail.

3. The leader should call on the other students to contribute to the discussion of the figures and their interpretation, and the other students should be prepared to respond having read and considered the paper.

4. The discussion leader and students will provide a final assessment of the paper and suggest or predict future lines of experimentation.

5. The preceptor should serve as a resource during the presentation for questions about technique or interpretation of results. The preceptor should also be prepared with several key questions to facilitate discussion during and after the presentation.

Student Journal Club Presentations.

Be succinct.

1. Abstract: Provide 2-3 introductory sentences and then STATE THE MAIN QUESTION. The examples below are from the first session's paper.

> For example: "Color vision requires that the signals in adjacent foveal cones be compared. Surprisingly, EM studies of the primate fovea show that cones are indiscriminately connected by gap junctions. This paper addresses the question: To what extent do signals spread between blue and green cones in the cone dominant retina of the ground squirrel?"

[Important: Does the paper formulate an identifiable, well-defined question?]

2. Background and significance: The preceptor should give the global context for the paper. As background, the student presenter should briefly detail the findings of the 2-3 most recent and important antecedents.

> For example: a) Lamb & Simon (1976) showed that coupling between cones of the same spectral type "averages-out" uncorrelated membrane voltage fluctuations, improving the ability to detect light signals that are correlated in adjacent cones by optical blur; b) Roorda & Williams (1999) showed that red-, green-, and blue-sensitive cones are intermixed in the primate fovea; c) Tsukamoto and Sterling (1992) provided EM evidence that primate foveal cones are indiscriminately connected by gap junctions. Lamb & Simon (above) show that coupling can be beneficial when cones are of the same spectral type, but coupling between spectral types should degrade color vision, particularly for blue cones which are surrounded by longer wavelength cones. The question is, "Does the EM appearance of gap junctional plaques equate with functionally significant electrical coupling, especially between blue and longer wavelength cones?"

[Important: Don't get bogged down here. Show a slide with 3-4 parts, each illustrating the one important finding from 3-4 previous papers]

3. Experiments and results: First, identify and state the overall strategy taken in the paper.

> For example: The first aim of the experiments is to see whether blue cones, which are 10% of all cones, can be selectively targeted for study. The second aim is to study coupling with a variety of redundant approaches.

Second, describe the figures individually. What is the experiment? What is the conclusion? Do they match? Are the controls (positive and negative) and "n's" appropriate? Are there additional results in the text?

Third, provide the logical link or connection between figures. Is the flow logical or random?

4. Discussion: Do the overall results support the conclusion as stated in both the discussion of the paper and abstract? What future lines of experimentation follow from the paper?

Schedule of First Year MSTP Topics in Molecular and Translational Medicine (TMTM) 2008-2009, ("MSTP Journal Club"), Wed. 4:00-5:15 PM, Ward 12-365

Theme		Faculty Preceptor, Department	Student Leader	Comments
Theme 1 - Infectious Diseases				
1-1	September 10, 2008	Introduction by Dr. Adrian Gross, Molecular Pharm. and Biol. Chem.		
1-2	September 17, 2008	Dr. David Engman, Pathology		
1-3	September 24, 2008	Dr. Richard Longnecker, Microbiology-Immunology		
1-4	October 1, 2008	Dr. Alan Hauser, Microbiology-Immunology		
1-5	October 15, 2008	Dr. Liming Li, Molecular Pharmacology and Biological Chemistry		
1-6	October 22, 2008	Dr. Hank Seifert, Microbiology-Immunology		
Theme 2 – Protein Structure and Function & Signal Transduction				
2-1	October 29, 2008	Dr. Sarah Rice, Cell and Molecular Biology		
2-2	November 5, 2008	Dr. Kathy Green, Pathology		
2-3	November 19, 2008	Dr. Ishwar Radhakrishnan, BMBCB		
2-4	December 3, 2008	Dr. Murali Prakriya, Molecular Pharmacology and Biological Chemistry		
2-5	December 10, 2008	Dr. Adrian Gross, Molecular Pharmacology and Biological Chemistry		
2-6	January 7, 2009	Dr. Hossein Ardehali, Medicine-Cardiology		
2-7	January 14, 2009	Dr. Cara Gottardi, Medicine-Pulmonary		
Theme 3 - Developmental Biology				
	January 21, 22, and 23, 2009	Students attend all M2 research presentations		
3-1	January 28 2009	Dr. Eugene Xu, OB-GYN		
3-2	February 4, 2009	Dr. Greg Beitel, Biochemistry, Molecular Biology, and Cell Biology		
3-3	February 18, 2009	Dr. Hans-Georg Simon, Pediatrics		
3-4	February 25, 2009	Dr. Thomas McGarry, Medicine-Cardiology		
4) Theme 4 - Neurobiology				
4-1	March 4, 2009	Dr. Warren Tourtellotte, Pathology		
4-2	March 11, 2009	Dr. Dane Chetkovich, Neurology		
4-3	March 18 2009	Dr. Steve DeVries Ophthalmology		
4-4	April 8, 2009	**OPEN**		Re-schedule Dr. Jaime Garcia-Anoveros, Anesthesiology can do Apr 15 or Mar 188
4-5	April 15, 2009	Dr. Xiaolin He, Molecular Pharmacology and Biological Chemistry		
4-6	April 22, 2009	Dr. Gordon Shepherd, Physiology		
4-7	April 29, 2009	Dr. Christine DiDonato, Pediatrics		
4-8	May 6, 2009	Dr. Robert Vassar, Cell and Molecular Biology		
	TBA	Deadline to Submit Proposals		
	TBA	Attend M1 "Mock" NIH Study Section Meeting with Dr. Adrian Gross		

Schedule of Second Year MSTP Topics in Molecular and Translational Medicine (TMTM), 2008-2009 ("MSTP Journal Club"), Thu. 4:00-5:15 PM, Ward 12-365

Theme		Faculty Preceptor, Department	Student Leader	Comments
Theme 1 – Molecular Cell Biology and Disease				
1-1	September 11, 2008	Dr. Kathy Farrow, Pediatrics	Ali	
	September 18, 2008	**M2 Class Meeting with Drs. Engman and Hauser**		
1-2	September 25, 2008	Dr. Paul Schumacker, Pediatrics	Maryna	
1-3	October 2, 2008	Dr. Joe Bass, Biochemistry, Molecular Biology, and Cell Biology	Keith	
1-4	October 10, 2008	Dr. Jonathan Licht, Medicine-Hematology-Oncology	Andrew	
1-5	October 23, 2008	Dr. John Crispino, Medicine-Hematology-Oncology	Sara	
1-6	October 30, 2008	Dr. James Surmeier, Physiology	Andy	
1-7	November 13, 2008	Dr. Nalini Rajamannan, Medicine-Cardiology	Josh	
Theme 2 – Bioengineering and Biotechnology				
2-1	November 20, 2008	Dr. Jack Kessler, Neurology	Rob	
2-2	December 5, 2008 Friday??	**OPEN**	Anaar	Re-schedule Dr. Dixon Kaufman, Surgery, on Friday (Anaar)
2-3	December 11, 2008	Dr. W. Miller, Chemical and Biological Engineering	Eugenie	
2-4	January 8, 2009	Dr. Douglas Losordo, Medicine-Cardiology	Betty	
M2 Research Proposal Presentations Videoconference from Wieboldt 421 to Tech L363 and live video streaming on the internet, Wednesday, January 21, Thursday January 22,and Friday January 23 (2:00-6:00 PM). Click here for schedule of oral presentations.				
Theme 3 – Bioengineering and Biotechnology				
3-1	February 13, 2009	**OPEN**	Ye	Re-schedule Dr. Silverman, Chemistry and Drug Discovery Program on Friday
3-2	February 19, 2009	**OPEN**	Woon Teck	Re-schedule Dr. Thomas Meade, Chemistry, ??
3-3	February 26, 2009	Dr. Lonnie Shea, Chemical and Biological Engineering	Woon Teck	
3-4	March 12, 2009	Dr. Martin Watterson, Molecular Pharmacology and Biological Chemistry		Check later
Theme 4 – Microbiology-Immunology				
4-1	April 2, 2009	Dr. Paul Bryce, Medicine-Allergy	?	Check later
4-2	April 16, 2009	**OPEN**		Re-schedule Dr. Bob Schleimer, Medicine-Allergy
4-3	April 30, 2009	Dr. William Muller, Pathology		
4-4	May 7, 2009	Dr. Douglas Kuperman, Medicine - Allergy		

RESEARCH PROPOSALS

Please limit your written proposal to 10 single-spaced pages, not including references (10-12 point font, 1 inch margins)

Guidelines for Research Proposals by M1 and M2 Students

1. During summer quarter after the M1 year, M1 students will write mini research proposals consisting of one Specific Aim based upon a research article presented in the M1 class and the class will critique all proposals in a mock study section on Friday, August 1, 2008, facilitated by Dr. Adrian Gross, M1 Course Director. M1 students will develop a SINGLE research question/hypothesis based on a paper from the M1 course. This question/hypothesis will form the basis for one "Specific Aim" of the M1 proposal. M2 students, in consultation with their thesis advisors, will develop a SINGLE research question/hypothesis based on their future thesis research project. This question/hypothesis will form the basis for two "Specific Aims" of the M2 proposal that will be developed in such a way that a single graduate student can accomplish the research goals in a 3-year period. Thesis advisors are expected to attend their M2 student's 30-minute presentations on January 24 or 25, 2008.

2. Use about one-third to one half of the first page to write a paragraph summarizing the essential background for the proposal and clearly stating the hypothesis to be tested. Include enough information that the reader can appreciate what you want to do and why it is important, but don't include extraneous information not directly related to the question at hand. In new paragraphs list the Specific Aims of your proposal in the following format:

   Specific Aim 1. **To identify binding partners for protein XYZ. Describe the experimental approach you will take to address the aim.**

   Write 2-3 sentences describing your experimental approach to the problem.

3. In the following 2-3 pages, give pertinent Background information on the problem. What is known and what remains to be determined? Conclude with a paragraph describing the Significance of your proposed research.

4. In the next 2 pages, give key preliminary results that are important for your proposed research.

5. In the remaining pages, outline experiments designed to test your hypothesis. Give the rationale for the approach you have chosen. Describe the step-by-step process you will take to rule-in or rule-out the possibilities (hypothesis is correct or incorrect). Depending on the Aim, you might list 4-6 experiments (different approaches, methods) that you might use to get to the answer you seek. At the end of this section, discuss the possible outcomes and interpretations. Briefly discuss approaches you might use if yours doesn't work.

6. List pertinent references beginning on a separate page and cite these in the text. 5-10 references for this exercise should be sufficient. List the complete citation (including authors and title) in a standard format (there are many, just be consistent).

Helpful Hints

1. Be sure that your hypothesis is based in "reality." Don't dream up an unlikely hypothesis and then design experiments to test it. You should work with your faculty advisor to decide on a final hypothesis from two or three that you come up with.

2. Be specific in your hypothesis. Don't bite off more than you can chew. Taking the necessary time to think through the hypothesis, whether it's testable, how much is involved, etc., will save you lots of time when you come to write the experimental plan.

3. State your hypothesis clearly in your proposal, on the Specific Aims page and also in the Background.

4. Be sure that your experiments actually answer the question you are asking. A common problem some students have is that they describe clearly and eloquently experiments that don't answer the question being tested.

5. Leave out the experimental detail (buffer composition, cloning vectors). It is sufficient to state that the cDNA will be subcloned into bacterial expression vectors, the recombinant protein will be produced in E. coli and specific antiserum will be raised by standard methods.

6. Use Medline to look up references, methods, etc. Use Endnote or a similar program to make reference management easier. It's often nice to have three windows open on the computer at all times—the Word document, Medline and Endnote—it makes writing and referencing a snap!

7. Be neat and eliminate typographical errors. Use indenting and leave lines between sections and experiments. You would be surprised how irritating typos, disorganization and crowded text can be, especially if your proposal is the tenth in a stack of twelve grants a primary reviewer is reading late at night.

Guidelines for Oral Presentations by M2 Students

1. Make 1-3 slides outlining the background and rationale for your proposal. Instead of a lot of text, cartoons may be helpful. **Clearly state the hypothesis you are testing.**

2. Make 3-5 slides outlining the experiments you will perform; again use cartoons where possible. **Clearly indicate the rationale for these experiments, relating them back to the Specific Aim and hypothesis.**

3. Make a summary slide that shows schematically how all the experiments you have proposed will answer the question you are asking in your specific aim.

4. **Practice presenting these so that you can do them in 20 minutes total**, being sure to include the possible outcomes and interpretations. Your colleagues and faculty preceptors will "interrupt" with questions so that the total time per person is at most 30 minutes because the videoconference schedule will not permit "running late".

5. Please arrive 15 minutes before the first presentation to transfer your presentation from your removable storage device (flash drive or CD) onto the resident PC (no Macs for videoconferencing). If your presentation uses any downloads or unusual fonts, you should

bring these in the same folder on your removable storage device as your PPT slides. If you will prepare your presentation on a Mac, remember to insert your images as jpeg files instead of tif files because differences in tif file compression on a Mac often precludes these files opening on a PC. Also please bring your file to the MSTP Office no later than the morning of your presentation to ensure that it (especially images) will open on a PC.

Email Distribution Lists 2008-2009

M1 Class	l-campochiaro@northwestern.edu (Laura Campochiaro) clarence-chan@northwestern.edu (Clarence Chan) d-escobar@northwestern.edu (David Escobar) r-heuermann@md.northwestern.edu (Robert Heuermann) andy.hung@northwestern.edu (Hsiang-Hua Hung) j-klosowiak@northwestern.edu (Julian Klosowiak) hsin-pin-lin@northwestern.edu (Hsin-Pin Lin) a-mcewen@northwestern.edu (Abbye McEwen) laura-moore@northwestern.edu (Laura Moore) sanders.oh@md.northwestern.edu (Sanders Oh) dipal-patel@md.northwestern.edu (Dipal Patel) skpatel83@md.northwestern.edu (Silpa Patel) m-schieber@northwestern.edu (Michael Schieber) r-skory@northwestern.edu (Robin Skory) angelica-zhang@md.northwestern.edu (Angelica Zhang)
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