Human Genetic Disease Colloquium Spring 2019
CMM/GENE/BIOC/MCB/PSIO 695D (3 units) **SYLLABUS ~~(Preliminary)~~v.1**
Tuesdays & Thursdays, 10:30 am – 12 noon
Life Sciences North 452

Instructor: **Linda L. Restifo, M.D., Ph.D.**
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Office hours: "Electronic Open-Door" policy. Contact Dr. Restifo by email to set up a meeting; she will respond promptly.

Prerequisites: permission of instructor. Contact Dr. Restifo to discuss your academic background, and whether it is adequate for this course. She may recommend that you take additional coursework first.

Overview of course rationale

- "disease-of-the-month-club" design:
  - **clinical + pathology –> genetics & biochemistry –> pathogenesis –> therapeutics**
- consideration of parallel approaches to **differential diagnosis**
  - given a particular patient with a constellation of symptoms and signs (S&S)
  - given a particular symptom or sign
  - given a particular disease/disorder
- emphasis on historical perspectives on biomedical and translational research
- explicit discussion of how assumptions about disease classification or etiology influence our scientific thinking
- focus on analysis of primary literature, but use of secondary sources (e.g., review articles) to introduce major topics

Topics/modules: 4 per semester [which change from year to year; see page 4]

- Each set of four covers a range of genetic mechanisms, phenotypic complexity, and degree of understanding of disease pathogenesis
- The modules typically progress from simple Mendelian genetics to disorders with complex, interacting multigenic and environmental risk factors. Options include:
  Module 1: cystic fibrosis, Duchenne muscular dystrophy, fragile X syndrome
  Module 2: hereditary cardiomyopathies, amyotrophic lateral sclerosis, Alzheimer's disease, hereditary peripheral neuropathies, epilepsies
  Module 3: types 1 or 2 diabetes mellitus, asthma, multiple sclerosis
  Module 4: schizophrenia, autism, systemic lupus erythematosus
- In some years, we will use one module to focus on a particular genetic mechanism, e.g., triplet-repeat expansion (e.g., Huntington's disease, fragile X syndrome) or somatic mutations (e.g., most cancers, ¿neurodegenerative diseases?)

Required text/reference book:

- Nussbaum, McInnes & Willard (2016). *Thompson & Thompson* ***Genetics in Medicine.*** 8th edition. Elsevier. Available for purchase ~$40 at amazon.com
- e-book available through UAHS Library (i.e., you don't have to purchase): http://sabio.library.arizona.edu/record=b7408786~S7

Format – unique, challenging, rewarding

- introductory lectures
- instructor-assisted, student-led presentations and discussions
- assigned readings (required for everyone)
- scheduled "formal" presentations
  - two per student (within and beyond the student's 'comfort zone')
  - selection of assigned readings and discussion questions with instructor
  - presenter will need to do additional reading beyond assigned papers
- peer review (required; see template on page 6)
  - format: address comments to third party, not to your fellow student
- in-person feedback sessions with instructor: students will receive a summary of peer feedback, including anonymized comments from fellow students.

Tentative Schedule Overview for Spring 2019 [there is no final exam]

Jan10	**Course & people introduction, vote on topics**
Jan 15,17,22,24	**Classification of disease; categories of mutation; genetic disorders & modern molecular medicine**
Jan 29,31; Feb 5,7,12,14	**Module I**
Feb 19,21,26,28; Mar 12,14	**Module II** [note: no class Mar 5 and 7 - Spring Break]
Mar 19,21,26,28; Apr **2,4**	**Module III**
Apr 9,11,16,18,23,25	**Module IV**
Apr 30	**Course wrap-up**

Assessment/evaluation of students [see detailed holistic grading rubric, page 5]

- Regular letter grades will be assigned (A, B, C, D, E)
- **Attendance and participation (50% of grade)**
  In order to participate effectively in class discussion, you need to be able to refer to the assigned papers. Therefore, bring them to each class. If you have read them as electronic files, you may bring your laptop instead. But, **each student is responsible for having access to all the assigned papers during class**.
- **Presentations (50% of grade)**
  - identification of key issues and unresolved questions addressed by the papers
  - **clear, critical assessment of experimental design, data analysis, conclusions**
    - classify the authors' interpretations and conclusions:
      - strongly supported by the available data; no major competing model; OR
      - consistent with available data; other models supported as well; OR

- highly speculative, with little data to support OR refute the model.
- **future research directions**
  - what are the most important questions to answer next?

Guidelines for effective presentations

- care in paper selection
  - what kind of papers are "good" for this course?
- use and misuse of PowerPoint®
  - avoid excessive text on slides! – the slides are not your script
  - DO NOT USE Microsoft template do-dads and non-meaningful movement
- caution(!): getting information from the internet
  - maintain a list of all URLs that you use
  - you MUST show sources of all figures, including adaptations
- avoid embarrassing questions: know your terminology!
- be critical: don't believe everything you read – ask: *do data support conclusions?*
- be selective: don't present every figure; rearrange to tell the story your way
- balancing time for your "script" and discussion, 50/50 split.

Additional Reference Materials

- essential: **medical dictionary**
- **OMIM**: https://www.ncbi.nlm.nih.gov/omim/ or http://omim.org/
- **ClinicalTrials.gov**: https://clinicaltrials.gov/ [*not* clinicaltrials.org]

Attendance Policy

Regular attendance is essential for understanding of the material and, obviously, for participation in class discussion. Absences pre-approved by the UA Dean of Students (or Dean designee) will be honored. All holidays observed by organized religions will be honored for those students who show affiliation with that particular religion.

Accessibility and Accommodations:

If you anticipate barriers related to the format or requirements of this course, please meet with Dr. Restifo so that we can discuss ways to ensure your full participation in the course. If you determine that disability-related accommodations are necessary, please register with Disability Resources (621-3268; http://drc.arizona.edu/students) and notify Dr. Restifo of your eligibility for reasonable accommodations. We can then plan how best to coordinate your accommodations.

Classroom Policies Regarding Effective Learning:

Individuals in groups can learn best when all are considerate of each other. Therefore, it is expected that you will endeavor to make the environment in the classroom conducive to effective learning. This includes:

- turning off your cell phone
- only using your laptop for class-related activities
- refraining from conversation that is not geared toward the topics of the day

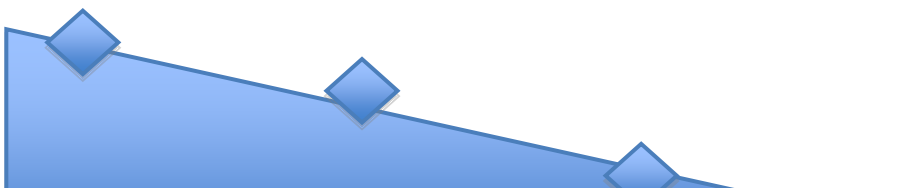
Read the full Student Code of Conduct at:
https://public.azregents.edu/Policy%20Manual/5-308-Student%20Code%20of%20Conduct.pdf

Academic Integrity
Students are encouraged to share intellectual views and discuss freely the concepts and controversies presented in or emerging from course materials. However, graded work must be the product of independent effort unless otherwise instructed. Students are expected to adhere to the Code of Academic Integrity. The policies related to such issues as cheating and plagiarism will be strictly enforced. See:
http://deanofstudents.arizona.edu/policies-and-codes/code-academic-integrity

Syllabus Changes:
Information contained in the course syllabus, other than the grade and attendance policies, may be subject to change with reasonable advance notice, as deemed appropriate by the instructor.

Examples of Topics/Modules from previous years:

Disease:	I. Muscular Dystrophy	II. Epilepsies	III. Multiple Sclerosis	IV. Schizophrenia
Genetics	Monogenic, X-linked recessive; some carriers affected.	Diverse, some familial Mendelian; sporadic may have *de novo* dominant mutations; genetic heterogeneity-- many genes involved	Most cases non-Mendelian; (+) genetic susceptibility; lots of genetic heterogeneity.	Most non-Mendelian; (+) genetic susceptibility; lots of genetic heterogeneity.
Pathogenesis	Well understood at molecular & cellular levels.	Well understood, but superficial; ion channel or synaptic dysfunction; why is Sz activity bad for brain development? some environmental; GXE?	Well-understood cellular mechanism: autoimmune, with myelin destruction; environmental factors, triggers	Poorly understood; starts long before Dx criteria reached; developmental! environment plays a role.
Phenotype	3 organs: skeletal muscle, heart, brain; Becker vs. Duchenne	Sudden synchronous hyperexcitability, focal or generalized; motor movements common, but manifestations vary.	Episodic CNS deficits in different places at different times; progressive.	Complex neurobehavioral & cognitive; criteria changing (DSM).
Diagnosis	Delayed 2-3 yrs; newborn screening in Ohio.	Easy (usually); EEG with video for confirmation.	May be easy, but often delayed; CSF and MRI helpful.	Difficult, esp. at onset; becomes apparent over time.
Treatment (drug or biological)	Clinical trials for drugs based on genetics & cell biology.	Many drugs, used in diverse combinations; some cases intractable; surgical excision of Sz focus.	Yes, several immunomodulators can delay second episode.	Yes (for psychosis), but inadequate & with severe side effects.
Alternatives	Cystic Fibrosis (+newborn screening); Fragile X syndrome (FXS)	Muscular dystrophies, Alzheimer's Dz, Parkinson's Dz, Cardiomyopathies, Amyotrophic Lateral Sclerosis, Peripheral neuropathies	Asthma Type 1 Diabetes mellitus Type 2 Diabetes mellitus	Autism Spectrum Disorders (ASD) Systemic Lupus Erythematosus (SLE)



Current Understanding of Genotype – Phenotype relationships

CMM 695D: Human Genetic Disease
Professor Linda L. Restifo

Components of Holistic Grading

Spring 2019

Component	Expectations for grade of: C	B	A	Comments
I. Participation				***Evaluated at each class session***
In-class discussion of assigned readings:	Assignments read superficially, with significant gaps in understanding. Questions & comments sparse and/or of limited relevance.	Assignments read in full. Questions & comments address basic, relevant information. If quiet/shy, receptive to being drawn into discussion by instructor.	Assignments read deeply, with effort made to understand difficult material. Questions & comments reveal understanding of methods, assessment of data, insight about relative significance and limitations of findings. Able to connect information across levels of analysis and across disease topics.	***This is the most important aspect of participation, but obviously attendance must come first.***
Attendance and Professionalism	<<<<<----------	<<<<<----------	No unexcused absences. Respectful of peers and instructor, especially when opinions on scientific merit or research significance or value of different approaches are mixed.	*Chronic lateness detracts from this category. We may not reach consensus (neither does the Supreme Court); the goal is to present 'arguments' based on evidence, with respect.*
Peer review	Late submissions or incomplete forms or minimal/trivial comments.	Timely submission of completed form, with limited comments or suggestions that may not explain scores given.	Timely submission of completed form, with thoughtful, substantive comments that explain the scores and provide constructive criticism.	*Peer review is a fundamental part of professional life, especially in biomedical sciences.*
II. Presentations				***Each student will do two***
Analysis	Some difficulty explaining the concepts, methods, data, or interpretations of the assigned papers.	Basic understanding of techniques used. Student's interpretations reflect those of authors of assigned papers.	Integrates information from papers & background to provide not only 'facts' but an assessment thereof, including strengths & limitations of methodology and authors' conclusions. Able to connect information across levels of analysis and between diseases.	***This is the most important aspect of presentation content.***
Preparation	Minimal background material used; assigned papers presented with limited context.	Takes initiative in seeking relevant background information and additional papers.	Active role in paper selection (with instructor). Understanding of selected papers, including methods, enhanced by background reading of relevant material. Online supplements of assigned papers incorporated in presentation.	*Starting early is an investment that pays off very well at the time of your presentation.*
Slide design and content	Limited effectiveness in adding to the understanding of the papers. Limited or confusing explanations of figures. Problematic text (too much, too little, error-prone).	Figures from assigned papers explained clearly and correctly. Rare errors on slides.	Images/graphs/diagrams enhance audience understanding. All images from authoritative sources. Figures annotated or highlighted for clarity. Text enhances spoken content & images, but does not 'take over' the presentation.	*Use simple slide design and avoid PowerPoint 'tricks'. All sources must be declared. Beware: reliable sources for general public are often not authoritative for scientific purposes.*
Delivery	Varying degrees of difficulty due to lack of understanding or organization.	Generally logical and coherent. Terms pronounced and used correctly.	Engaging style that promotes interest and discussion. Well-organized, creative approach to scientific storytelling. Terminology defined, methods explained. Voice, tone, demeanor, and appearance are those of a professional.	*Practice, practice, practice. Do a full 'dress rehearsal,' not just talking to your computer screen. PowerPoint Presenter Tools can be helpful.*
Other	Resistance to guidance, or limited improvement.	Improvement between 1st & 2nd, with good use of feedback from peers & instructor	Excellent coachability, with ability to apply advice to new topics in 2nd presentation.	*Some students have made dramatic improvement in just a couple months.*

Please use highlighting to indicate your answers to questions #1-10. Thanks!

CMM/BIOC/GENE/MCB/PSIO 695D: ***Human Genetic Disease Colloquium***
Peer Evaluation Form

Date: _____
Presenter: _____ (1st or 2nd presentation)__
Topic: _____
Reading Assignments:

Content

1. The important scientific/medical **issues** were clearly articulated by the presenter.

Strongly Agree Agree Disagree Strongly Disagree Not applicable

2. The presenter explained the **experimental approach**(es) or **study design** and discussed their relative merits.

Strongly Agree Agree Disagree Strongly Disagree Not applicable

3. The presentation was **organized** in a logical and easy-to-follow manner.

Strongly Agree Agree Disagree Strongly Disagree Not applicable

4. The presenter **assessed the validity** (or lack thereof) of the authors' **conclusions**.

Strongly Agree Agree Disagree Strongly Disagree Not applicable

5. The speaker had a good understanding of the relevant **background literature**.

Strongly Agree Agree Disagree Strongly Disagree Not applicable

6. **Visual aids** (overheads, slides, blackboard) were used in an effective manner.

Strongly Agree Agree Disagree Strongly Disagree Not applicable

Presentation

7. **Voice**

Volume:	Excellent	Very Good	Good	Fair	Poor
Speed:	Excellent	Very Good	Good	Fair	Poor

8. **Poise**

Overall:	Excellent	Very Good	Good	Fair	Poor
Eye contact:	Excellent	Very Good	Good	Fair	Poor

9. **Response to questions:**

Excellent Very Good Good Fair Poor

Overall value of the presentation

10. The student's presentation **enhanced my understanding** of the assigned readings

Strongly Agree Agree Disagree Strongly Disagree Not applicable

Overall comments/suggestions:

Please use highlighting to indicate your answers to questions #1-10. Thanks!