Medical Genetics (MDGEN) 601

Selected Topics in Winter Term 2027

Tuesday 1-2:50 pm; Thursday 1:00-2:00 pm
Room 8-56 Medical Sciences Building

Instructors: One Basic Scientist; One Clinician

Overview

This is a combined course with MDGEN 401, but with separate assignments and evaluation.

This course will cover the fundamental medical genetic concepts and modern techniques in both laboratory research and clinical application Specific examples of diseases seen in the genetic clinics will also be used to illustrate key genomic principles.

This course will introduce topics such as:

- Mendelian Inheritance patterns, Non-traditional patterns of inheritance, and multifactorial diseases
- Animal Models and their applications in genetics
- Human cell models Induced pluripotent stem cells (IPSCs) organoids, etc.
- Genetic/Genomic testing and their clinic applications
- Gene expression studies and the clinical applications
- Imaging techniques and the clinical applications
- Genetic screening including prenatal screening and other screening for genetic diseases
- Gene therapy, genomic therapy, cell therapy, and Enzyme replacement therapy for human diseases
- Precision Medicine

Instruction consists of lecture material, discussion and student-directed learning sessions. There will be a focus on reading and discussion of current research articles. Students are expected to read and critically evaluate research articles and participate in group discussions of topics. Students will be expected to present a critical review of papers that are assigned as well as prepare a grant proposal on a topic that was discussed in class.

Format

The Tuesday class will consist of a lecture by an instructor providing background on the topic for that week. There may also be a discussion of a paper relevant to the theme of that week. On Thursdays there will be student led presentation of an assigned research article relevant to the theme of the week. **It is expected that all students will have read papers assigned for each class and will participated in discussions**.

Attendance Policy

As class participation will be reflected in the student's grade, students are expected to attend all classes. Students are expected to read and critically evaluate research articles and participate in group discussions of topics. All students (not just those assigned to present) are expected to have read all papers assigned for each class and be ready to participate in evaluation and discussion.

Mark Breakdown

Participation/ Discussion.....25%
Presentation.....25%
Weekly assignments.....5%
Peer Review written/presentation.....15%
Proposal.....25%
Oral Presentation of Proposal 5%

The Course Contents

The course consists of 85% fixed contents with 15% by instructor's choice.

Section I: Basic concepts, Principles, and Sub-disciplines in Medical Genetics

- **Lecture 1: Mendelian Inheritance patterns, Non-traditional patterns of inheritance, and multifactorial diseases**
  - (Basic concepts and associated diseases. Autosomal inheritance, sex-linked inheritance, mitochondrial inheritance, epigenetic inheritance, Protein-Based Inheritance, multifactorial diseases).
- **Lecture 2: Biochemical genetics, developmental genetics, and immunogenetics**
  - **Biochemical Genetic**: Prevalence of Metabolic Disease, Inheritance of Metabolic Defects, Defects of Metabolic Processes including Carbohydrate Metabolism, Amino Acid Metabolism, Lipid Metabolism.
  - **Developmental Genetics**: Principles of Development, Developmental genetics of color pattern establishment in cats including Chetah; Genetics of developmental disorders.
  - **Immunogenetics**: Immunological Tolerance; Autoimmune Diseases; Immunodeficiency Diseases.
- **Lecture 3: Cancer genetics and others by instructor's choice**
  - **Introduction**: Basic concepts, cancer prevalence, cancer hallmarks, history of cancer genetics.
  - **Genetic mechanisms underlying cancer**: Oncogenes, tumor suppressors genes, DNA repair genes, driver genes, passenger genes, and the origin of cancer.
  - **Hereditary Cancer**: History, Lynch Syndrome, Two-hit model of carcinogenesis, Hereditary Breast and Ovarian Cancer syndrome (HBOC), Cancers caused by oncogenic virus.
- **Lecture 4 Epigenetics**
  - Basic Concepts of Epigenetics: Definition, Mechanisms, Functions: Genomic Imprinting.
  - Clinical Application of Epigenetics: Biomarkers and Therapies.
  - Epigenetic clock.
  - Epigenetic Inheritance.

Section II: Genetic Models and Imaging Techniques

- **Lecture 5: Model organisms and human cell models**
  - (Yeast, drosophila, C. elegans, zebra fish, and mouse).
  - (fibroblasts, iPSCs, organoids, humanized animal models).
- **Lecture 6: Imaging techniques and the clinical applications or by Instructor's choice**
  - **Microscopy**: Wide field, confocal, high resolution, EM etc.
  - **Application**: Cytogenetics, Chromosome Banding, karyotype, Spectral karyotyping, Fluorescence in Situ Hybridization (FISH), in vivo imaging.

Section III: Genetic Testing and Screening

- **Lecture 7: Genetic/genomic testing and clinic applications**
  - **(**Concepts/principles, major methods including linkage analysis (indirect testing)): allele-specific mutation detection by PCR, Gene-specific Sanger sequencing, Microarray-based genotyping, Whole-genome, and whole-exome sequencing using Next Generation Sequencing and Third-generation sequencing.
  - **Clinical application**: Diagnosis, Interpretation, and classification of genomic variants).
- **Lecture 8: Genetic screening including prenatal screening and other screening for genetic diseases**
  - (Genetic screening vs genetic testing, types and methods of the most common prenatal genetic screenings including Newborn Screening (Blood), Universal newborn hearing screening, Heterozygote Screening, inborn errors of metabolism).
- **Lecture 9: Gene expression studies and the clinical applications**
  - (RNA microarray, RNA sequencing, Single cell sequencing, spatial transcriptomics, clinical applications).

Section IV: Management of Genetic disorders

- **Lecture 10: Gene therapy, cell therapy, and Enzyme replacement therapy for human diseases (PK)**
  - (Basic Concepts of Gene therapy, Types of Gene therapy (Gene replacement therapies and Gene-block therapies), Genome editing using CRISPR technology (Basic concepts, Precise gene editor, base editor, primer editor, Delivery and application, Exon Skipping Therapies, Cell Therapies (Adult stem cells (ASCs), Embryonic stem cells (ESCs), and induced pluripotent stem cells (iPSCs)).
- **Lecture 11: Precision Medicine**
  - (Introducing general concepts and principles of Precision medicine. Focusing precision Oncology: Disease subtyping using biomarkers and various Omics including genomics, transcriptomics, epigenomics, proteomics, metablomics, etc., as well as deep phenotyping; Tailored treatment (Targeted therapies: antibodies and small molecules, Pharmaco-omics, and Functional Precision Medicine), Ethics, genetic counselling).
- **Lecture 12: Instructor's Choice**.

List of Discussion Papers

Presentation

Each student will present a critical evaluation of a paper assigned to them. The presentation will be no longer than 40 min to allow for round table discussion and should cover the details outlined below. It is up to the presenter to decide what figures need to be presented in light of critical assessment of the claims by the authors.

- Background, which includes a succinct summary of previous relevant literature and any key methodologies
- Knowledge gap and rationale
- Main figures the support or do not support the claims of the paper (please see note above – not all figures and/or panels need to be presented)
- Discussion of the paper (some areas to cover are below):
  - What are the main claims of this paper and how significant are they?
  - Are these claims novel? If not, please specify papers that weaken the claims to the originality of this one.
  - Are the claims properly placed in the context of the previous literature? Have the authors treated the previous literature fairly?
  - Do the experimental data support the claims? If not, in your opinion, what other evidence would be required?
- What did you like about the paper?
- Would any other experiments improve the paper?
- How much better would the paper be if these experiments were performed and how difficult do you think they would be to do?
- Does the paper offer enough details of its methodology that its experiments could be reproduced?
- Is this paper outstanding in its discipline?
- If yes, what makes it outstanding? If no, why not?
- Is the manuscript clearly enough written so that it is understandable to students/scientists outside the immediate field?
- If not, how could it be improved? (Please concentrate on matters of organization and content.)
- Have the authors provided adequate proof for their claims without overselling them?

The presentation will be in the format of a round table discussion. The student assigned to the paper will present using power-point slides to provide background information, figures and critique. Everyone is expected to participate in the roundtable discussion and questions.

Research Proposal

- The proposal is a research plan that encompasses approaches discussed in class. The proposal can be based on the student's own research, but must include novel approaches (see below for details)
- Summary Page: The one-page summary page is due on February 27 in class. The summary page is similar to an abstract providing succinct background and rational to the proposal hypothesis, and a short description of the experimental aim(s) to address the hypothesis. Feedback will be provided by email by the instructors.
- Note that references are not allowed in the summary. Formatting requirements: 2 cm margins, 12 pt font, single spaced.
- The first complete draft of the proposal is due **March 12** in class. We will then undergo peer review in addition to feedback from the instructors. The finalized version of the proposal is due April 9th by 4 pm.

Proposal Details

- **Format**: Limit of 5 pages of text with 2 cm margins, 12-point font and single spaced. Please indicate page numbers in the footer and title of the proposal in the header of each page. Please do not include your name in the proposal to enable anonymous peer review. Note that references are not included in the 5-page limit. Images and schematics are included in the 5-page limit. The summary page is not included in the 5-page limit.
- **Content**: Addressing the points below, describe the proposed research.
- This proposal is a research plan based on a topic relevant to the course material. The topic can be relevant to student's own research project, but has to explore novel methodologies and assays not currently used by them. You should assess what is known in the field at this time and critically analyze the approaches currently used and present approaches that could advance what is currently known.
- We are not looking for a grant proposal in terms of specific experimental minutiae (e.g., drug concentrations), but rather a logical hypothesis driven research plan that would include the types of experiments that could be used and a description of how one would validate the approaches you choose.
- The proposal should therefore include some relevant background, development of hypothesis, rationale of the hypothesis and research question with a general experimental plan and interpretation of expected results.

Peer Review

- Students will prepare a written review of research proposals submitted. Students will receive a copy of the proposal they are to review by **March 13**. The peer reviews will occur on March 26th and March 28th.
- Specific guidelines on how to formulate the review will be provided.
- Some points to be included: 1) Short summary of the grant, 2) Innovation/originality including description of rationale (Concept and rationale), 3) Feasibility and approaches to the research objectives (Strengths and weaknesses of the proposed approaches).
- Note: Submit all writing assignments to Instructors via email.

Oral Presentation of Proposal

- Each student will prepare a 10-minute summary of their proposal with 2 minutes for questions.
- PowerPoint or "chalk talk" may be used.

Plagiarism

30.3.2(1) No Student shall submit the words, ideas, images or data of another person as the student's own in any academic writing, essay, thesis, project, assignment, presentation or poster in a course or program of student (From: Code of Student Behaviour). If a student does plagiarize, they will receive a zero on that assignment and a failing grade in the course. Depending in the extent of plagiarism this may also result in expulsion from the graduate program.