Medical Genetics (MDGEN) 601
(Winter Term)
Tuesday 1-2:50 pm; Thursday 1:00-1:50 pm
Room 8-56 Medical Sciences Building

Instructors
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Please email instructors if there are questions or requirements to arrange an on-line appointment.

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

Basic concepts and topics in cutting-edge medical genetics research and clinical applications

Overview:

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 is composed of 4 sections with 11 topics:

- **Section I: Basic concepts, principles, and sub-disciplines in Medical Genetics**
    1. Mendelian Inheritance patterns, Non-traditional patterns of inheritance, and multifactorial diseases
    2. Biochemical Genetics, Developmental Genetics, and Immunogenetics
    3. Cancer Genetics
    4. Epigenetics
- **Section II: Genetic models and Imaging techniques**
    1. Model organisms and Human cell models
    2. Imaging techniques and the clinical applications
- **Section III: Genetic Testing and screening**
    1. Genetic/Genomic testing and their clinic applications
    2. Genetic screening for genetic diseases
    3. Gene expression studies and the clinical applications
- **Section IV: Management of Genetic disorders**
    1. Gene therapy, genomic therapy, cell therapy, and Enzyme replacement therapy for human diseases
    2. Precision Medicine

Format:
The Tuesday class will consist of a lecture by an instructor providing background on the topic for that week. On Thursdays there will be student-leading 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 participate 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%

Description of each topic:

Section I: Basic concepts, principles, and sub-disciplines in medical genetics

Lecture 1： Mendelian Inheritance patterns, Non-traditional patterns of inheritance, and multifactorial diseases (ZW)

(Basic concepts and associated diseases. Autosomal inheritance, sex-linked inheritance, mitochondrial inheritance, epigenetic inheritance, multifactorial diseases)

Lecture 2: Biochemical Genetics, Developmental Genetics, and Immunogenetics (ZW)

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 (ZW)

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 (ZW)

Basic Concepts of Epigenetics:Definition, Mechanisms, Functions: Genomic Imprinting

Clinical Application of Epigenetics: Biomarkers and Therapies

Epigenetic clock

Epigenetic Inheritance

Protein-Based Inheritance: Prion

Section II: Genetic models and Imaging techniques

Lecture 5: Model Organisms (ZW) and human cell models (PK)

(Yeast, drosophila, C. elegans, zebra fish, and mouse)

(fibroblasts, iPSCs, organoids, humanized animal models)

Lecture 6: Imaging techniques and the clinical applications (ZW)

(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 (PK)

(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 (PK)

(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 (ZW)

(RNA microarray, RNA sequencing, Single cell sequencing, single nucleus 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 (ZW)

(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)

Timetable

Week and date	Tuesday (Lecture)	Thursday (Journal Club)
Week 1 **January 6 and 8**	**Lecture 1 (ZW)** **Mendelian Inheritance patterns, Non-traditional patterns of inheritance, and multifactorial diseases**	**Course Introduction and Sample Paper Presentation by Instructor ZW**
Week 2 **January 13 and 15**	**Lecture 2 (ZW)** **Biochemical Genetics, Developmental Genetics, and Immunogenetics**	**Student presentation** **Paper 1:**
Week 3 **January 20 and 22**	**Lecture 3 (ZW)** **Cancer Genetics**	**Student presentation** **Paper 2**
Week 4 **January 27 and 29**	**Lecture 4 (ZW)** **Epigenetics**	**Student presentation** **Paper 3**
Week 5 **February 3 and 5**	**Lecture 5 (ZW&PK)** **Model Organisms (ZW) and human cell models (PK)**	**Student presentation** **Paper 4**
Week 6 **February 10 and 12**	**Lecture 6 (ZW)** **Imaging techniques and the clinical applications**	**Student presentation** **Paper 5**
Week 7 **February 17 and 19**	**Reading week** **work on proposal**	**Reading week** **work on proposal**

Week 8 **February 24 and 26**	**Lecture 7 (PK)** **Genetic/Genomic testing and clinic applications**	**Student presentation** **Paper 6**
Week 9 **March 3 and 5**	**Lecture 8 (PK)** **Genetic screening for genetic diseases**	**Student presentation** **Paper 7**
Week 10 **March 10 and 12**	**Lecture 9 (ZW)** **Gene expression studies and the clinical applications** **Graduate students submit their proposal**	**Student presentation** **Paper 8** **Graduate students are assigned the proposal for review**
Week 11 **March 17 and 19**	**Lecture 10 (PK)** **Gene therapy, cell therapy, and Enzyme replacement therapy for human diseases**	**Student presentation** **Paper 9** **Undergraduate students are given the final assignment**
Week 12 **March 24 and 26**	**Peer Review of Proposal**	**Student presentation** **Paper 10**
Week 13 **March 31 and April 2**	**Lecture 11 (ZW)** **Precision Medicine**	**Student presentation** **Paper 11**
Week 14 **April 7 and 9**	**Oral presentations of Proposal** **Final assignment due for 401 students**	**No class**

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 not, 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 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 11 before class. We will then undergo peer review in addition to feedback from the instructors. The finalized version of the proposal is due April 8 before class.

Proposal Details

Format: Limit of 5 pages of text with 2 cm margins, 12-point font and single space. 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 a 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 25 and March 27.

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 Drs. Wang and Kannu via email.

Oral Presentation of proposal

Oral presentations on April 8 & 10.

Each student will prepare a 10–15-minute summary of their proposal with 2-5 minutes for questions. (the exact time will be determined based on the number of students)

PowerPoint or "chalk talk" may be used.

Academic Integrity

The University of Alberta is committed to the highest standards of academic integrity and honesty. Students are expected to be familiar with these standards regarding academic honesty and to uphold the policies of the University in this respect. Students are particularly urged to familiarize themselves with the provisions of the Student Academic Integrity Policy and the Student Conduct Policy (on the University of Alberta Policies and Procedures Online (UAPPOL) website) and avoid any behavior which could potentially result in suspicions of cheating, plagiarism, misrepresentation of facts and/or participation in an offence. Academic dishonesty is a serious offence and can result in suspension or expulsion from the University.

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 Behavior

If a student does plagiarize, he/she will receive a zero on that assignment and a failing grade in the course. Depending on the extent of plagiarism, this may also result in expulsion from the graduate program.