

BGEN 3020 6 Cr. Introduction to Human Genetics

Course Outline

Term

Fall and Winter

Day, Time, Place

Tues, Thurs: 11:30-12:45

Place : Armes 115

Course Coordinator

David Merz

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Office Hours: by appointment

Brief Description

The course is intended to provide the student with an overview of the field of human genetics from the research laboratory to the clinic. The content will include molecular genetics, epigenetics, cytogenetics, complex traits, animal models to study genetic disorders, prenatal diagnosis and ethics. Eligible students include Genetics Honors and Major students in their third or fourth year of study.

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Course Learning Outcomes

Assignment Descriptions & Expectations for Student Participation

Assignment/Task	Quantity	% Weight	Total %	Due Date
Assignments	About 10		20%	
Term Test 1			20%	Oct 27
Term Test 2			20%	Dec 8
Term Test 3			20%	TBD
Term Test 4			20%	TBD

Assignments.

Assignments will be given by instructors. Due dates will be given at that time.

Mid-Term Examinations

Each section of the course will be graded with a Term Test. There is no cumulative Final Exam.

Calculation of Course Grade

A minimum grade of 50% is required to pass this course.

Numeric Grade	Letter Grade
90% to 100%	A+
80% to 89%	A
75% to 79%	B+
70% to 74%	B
65% to 69%	C+
60% to 64%	C
50% to 60%	D
0% to 49%	

Course Material

The *Course Materials Database (CMD)* has been created within UMLearn. It contains general information and information and materials specific to this course. Check it frequently. Please check the Class-by-Class Syllabus for the reading list.

Schedule – Fall Term

BGEN3020 Fall Term 2016

Sept 8 Th	Course Intro (D Merz)
Sept 13 Tu	Cell Cycle Overview (J Wigle)
Sept 15 Th	Molecular Genetics (D Gietz)
Sept 20 Tu	Molecular Genetics (D Gietz)
Sept 22 Th	Molecular Genetics (D Gietz)
Sept 27 Tu	Cytogenetics (A Dawson)
Sept 29 Th	Cytogenetics (A Dawson)
Oct 4 Tu	Cytogenetics (A Dawson)
Oct 6 Th	Fall Term Break
Oct 11 Tu	Pedigrees (S Clarke)
Oct 13 Th	Pedigrees (S Clarke)
Oct 18 Tu	Pedigrees (S Clarke)
Oct 20 Th	Pedigrees (S Clarke)
Oct 25 Tu	Cytogenetics Tutorial (A Dawson)
Oct 27 Th	<u>First term exam</u>
Nov 1 Tu	Cancer Genetics (K McManus)
Nov 3 Th	Cancer Genetics (K McManus)
Nov 8 Tu	Population Genetics (T Pemberton)
Nov 10 Th	Population Genetics (T Pemberton)
Nov 15 Tu	Population Genetics (T Pemberton)
Nov 17 Th	Immunogenetics (T Zelinski)
Nov 21 Tu	Immunogenetics (T Zelinski)
Nov 24 Th	Metabolics (A Mhanni)
Nov 29 Tu	Metabolics (A Mhanni)
Dec 1 Th	Bayes Tutorial (S. Clarke)
Dec 6 Tu	
Dec 8 Th	<u>Second Term Exam</u>

Class-by-Class Syllabus – Fall Term

Module 1. Genes, chromosomes and cells

Goals of Module 1: To give an overview of human genetics from the level of DNA and cells.

Intro to course and Overview of Human Genome -

Overview of Cell Cycle

- Describe the stages of the cell cycle
- Describe how chromatin is packaged within the nucleus
- Compare and contrast the steps involved in mitosis versus meiosis
- Explain the process of chromosomal recombination and how it can lead to chromosomal abnormalities
- Contrast reciprocal and Robertsonian translocations

Molecular Biology

Gene Structure and Function

- To understand the structure of DNA and how it is replicated.
- To understand the structure of a gene.
- To understand the Central Dogma of Molecular Genetics
- To understand the how the genetic code is used.
- To understand how proteins are produced & modified.

Mutation and instability of Human DNA

- To understand the types of changes in DNA that can occur in DNA.
- To understand the difference between transition and transversion mutation.
- Understand how mutations can be classified.
- Understand why mutations occur more frequently in males.
- Understand the mechanism that can cause certain types of mutation

Nucleic acid hybridization Assays

- Understand how nucleic acid probes are produced.
- Understand the principles of nucleic acid hybridization.
- Understand how cloned DNA can be used to screen uncloned DNA.
- Understand RFLP analysis of uncloned DNA.
- How probes can be used for in situ hybridization
- How microarrays can be used.
- Next Generation Sequencing - principles

Cytogenetics

- Morphology of human chromosomes
- Discuss genetic disorders caused by chromosomal rearrangements; numerical and structural abnormalities; chromosome balance and imbalance.
- Discuss uniparental disomy and imprinting disorders.

Epigenetics - (Rastegar)

- Epigenetics and Chromatin Structure
- Epigenetic Mechanisms: Histone Post-translational Modifications
- DNA Methylation and Related Proteins
- Regulatory RNA
- Epigenetics and Early Development
- MeCP2; the link between Genetics, Epigenetics & Human Disease

Cancer genetics - (McManus)

Intro to Cancer Genetics I

- Describe what is meant by, “cancer results from the loss of cell cycle regulation”.
- Explain how tumors arise through the hyperplasia to carcinoma pathway
- Detail why low grade tumors have a better prognosis than high grade tumors
- List and describe 6 factors that contribute to tumor development (provide examples)
- Explain & detail how defects in mis-match repair (MMR) contribute to Lynch Syndrome
- List the 3 major types of genes implicated in tumorigenesis

Intro to Cancer Genetics II

- Describe 3 specific genetic alterations/mechanisms that can convert a proto-oncogene into an oncogene
- Compare and contrast characteristics of Oncogenes & Tumor Suppressor Genes & provide examples
- Explain why sporadic retinoblastoma (RB) never occurs in both eyes, but does & occurs earlier with the heritable form
- Describe why defects in DNA repair genes are associated with cancer
- List and compare the 2 mechanisms of DNA double strand break repair & describe which is “error-free”
- Define chromosome instability & list common approaches used to assess it & list any caveats/limitations
- Provide an example & describe a therapeutic approach that specifically targets either an oncogene or tumor suppressor gene/DNA repair gene
- Describe what is meant by the statement, “The development of a tumor is a multi-genic, multi-factorial and multi-step process”

Stem Cells – (Rastegar)

- Stem Cells and Their Unique Properties
- Different Types of Stem Cells and Their Origins
- Ethics or politics of embryonic stem cells.
- Possibilities for treatment of genetic disorders

Cancer Stem Cells - (Ogilvie)

- What are cancer stem cells?
- How are cancer stem cells different from normal stem cells?
- What are the problems associated with cancer stem cell theory?
- What are the problems associated with malignant brain tumours?

Pedigree Analysis - (Burnett)

- Describe the basic rules of Mendelian inheritance
- Describe the exceptions to these rules
- Describe Non-Mendelian patterns of inheritance
- Describe imprinting
- Describe the 2-hit theory for cancer
- Calculate genetic risks based on a pedigree (includes Bayes)
- Draw and interpret an appropriate family tree

Term 2. Population Genetics and Complex Traits

Goals: introduce “classical” human genetics

Cancer genetics

Intro to Cancer Genetics I

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Population Genetics

- Hardy-Weinberg principle of allele and genotype frequencies
- Statistics based on Hardy-Weinberg principles:
 - Expected heterozygosity
 - Inbreeding coefficient
 - Fixation index
- Population genetic perspective on disease genetic studies

Immunogenetics –

Metabolic Disorders -

- Diagnosis and Treatment of metabolic disorders

Class-by-Class Syllabus – Winter Term

Term 3. Genes and Development

Goals: The relationship between genotype and phenotype as it relates to clinical conditions.

Dysmorphology and Limb Defects,

Dysmorphology

- Define “dysmorphology”
- Distinguish between major and minor malformations and give examples of each
- Define and give clinical examples of the following types of defects:
 - Malformations
 - Disruptions
 - Deformations
 - Dysplasias
- Define and give clinical examples of the following **patterns** of defects:
 - Associations
 - Field Defects
 - Sequences
 - Syndromes

Limb Defects

- Describe axis formation in the embryo.
- Describe and illustrate the steps of mammalian limb development.
- Differentiate between skeletal dysplasias and dysostoses
- Describe three different ways to characterize limb defects and why they are important
- Describe the three main regions important in limb development
- Discuss the implications of mutations in ZRS and ROR2
- Discuss three intriguing aspects of limb anomalies and give three clinical examples

Sexual Differentiation -

- Outline the general stages of sexual differentiation and relevant organs with respect to gonadal development
- Discuss the role of hormones in appropriate organ (e.g. internal duct) development
- Discuss the implications of disruption of two important developmental genes in sexual differentiation
- Define and explain how disruptions in hormone production relate to sexual differentiation
- Discuss how abnormal response to hormone production can affect sexual differentiation
- Discuss various causes for abnormal sexual differentiation in individuals with 46, XX and 46, XY karyotypes
- Discuss 4 different sex chromosome disorders

Stem Cells

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Cancer Stem Cells

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Animal Models

- Rationale for using the Mouse as a Model of Human Genetic Disease.
- Gain of function versus Loss of Function Transgenics
- Methods of Generating Transgenic Mice
- Homologous Recombination to Introduce Mutations

Term 4. Clinical Genetics

Goals: Human Genetics as it applies to the world around us: populations, diagnoses and treatments.

Complex Traits

- Describe the goal of each genetic analysis method
- Specify the differences between monogenic and complex traits/diseases, linkage and association analyses, and IBD and IBS
- Define linkage disequilibrium and population stratification, and their effects on case-control genetic studies
- Calculate recurrence risk ratio and odds ratio
- Interpret heritability
- Understand the literature on gene mapping

NGS Methods and Analysis

- Exome sequencing
- RNA-Seq

Next Generation Sequencing in the Clinic

- Discuss the use of NGS in a clinical setting

Ethics and Prenatal Diagnosis

- List the major indications for prenatal diagnosis of genetic disease in the fetus.
- Describe the various techniques used in prenatal testing, including their risks, complications and limitations.
- Discuss the psychosocial and ethical problems associated with prenatal diagnosis and screening.
- Describe the basic principles of medical ethics
- Describe the basic principles of genetic counseling

Bench to Bedside

- Describe SMA, its clinical spectrum and steps taken to identify the causal gene.
- Explain how the genomic structure of the SMA locus contributes to the dose-dependent effect on SMA disease severity and be able to distinguish between a causal and modifier gene.
- Guilt by Association: Elaborate on potential SMN gene functions.

- Describe the derivation of different SMA animal models and elaborate on how animal studies have been used to understand SMA disease pathology and test treatment strategies.

General Academic Policies

Plagiarism

Students familiarize themselves with the University of Manitoba's policy on ***Cheating, Plagiarism and Fraud*** available here:

http://umanitoba.ca/student/resource/student_advocacy/cheating_plagiarism_fraud.html

Students can download the booklet entitled ***Cheating, Plagiarism and Fraud***, which covers the material provided on the website. The university has purchased plagiarism detection software called "iThenticate" and this program is available to all students with a U of Manitoba ID. You must check your submitted documents (abstract, paper) and provide the results of this check at the time of submission.

Accommodations for Students with Disabilities

Students must contact ***Student Accessibility Services***, not the instructor, to request accommodations at:

<http://umanitoba.ca/student/saa/accessibility/> or 204.474.7423 or TTY: 204.474.9790 or student_accessibility@umanitoba.ca

Voluntary Withdrawal/Refunds

Any student contemplating withdrawing from a course is encouraged first to contact the program coordinator for advice and suggestions on how to continue with the course and/or program. A refund/withdrawal schedule can be found at:

http://umanitoba.ca/student/records/fees/irregular_refund_vw_deadlines.html

Respectful Work and Learning Environment

The University of Manitoba supports a climate of respect in the workplace and in the learning environment, where individuals or groups of individuals are free from harassment and discrimination. For the University of Manitoba's Respectful Work and Learning Policy, including information on human rights and sexual harassment, please go to: http://umanitoba.ca/human_rights/respectful_work.html.

For a complete list of Extended Education policies, please refer to:

http://umanitoba.ca/faculties/coned/gen_info/policies.html

<http://umanitoba.ca/admin/governance/571.html>