Course Outline BGEN3020 Introduction to Human Genetics

Course Coordinator:
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Office hours: Appointments should be arranged in advance. Instructors will provide contact info. Course coordinator can be reached at merzd@ms.umanitoba.ca

Location of Class: Ft. Garry Campus. Parker 539 is the new room for this year.

Times/Dates: This is a 6 credit course, spanning Fall and Winter Semesters. Tuesday and Thursday 11:30-12:45.

Course 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.

Course Materials: A copy of the textbook Human Genetics 4th Edition by Strachan and Reid is on 2-hour Reserve in the Sciences Library. Lecture notes will be posted on JUMP/D2L prior to each lecture.

Grading: The course is divided into four terms, each of approximately 12 lectures. At the end of each term there will be an exam worth 20% or the final grade. In addition, there will be assignments given throughout the year. Assignment marks will also make up 20% of the final grade. Exams may involve any format of questions, including multiple choice, True or false, short answer, etc.

A+ 90-100%
A 80-89%
B+ 75-79%
B 70-74%
C+ 65-69%
C 60-64%
D 50-59%
F <50%

Academic Integrity: Please refer to UofM policies:
## Schedule for Fall Semester 2015-16

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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 Brief History of Human Genetics - (Merz)

Molecular Biology – (Gietz)
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 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

Overview of Cell Cycle - (Wigle)
• 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

Epigenetics - (Rastegar)
• Epigenetics and Chromatin Structure
• Epigenetic Mechanisms: Histone Post-translational Modifications
• DNA Methylation and Related Proteins
• Regulatory RNA
• Epigenetics and Early Development
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?
**Term 2. Pedigrees and Complex Traits**  
Goals: introduce “classical” human genetics

**Cytogenetics – (Dawson)**
- 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.

**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

**Immunogenetics – (Zelinski)**
- 

**Term 3. Genes and Development**  
Goals: The relationship between genotype and phenotype as it relates to clinical conditions.

**Complex Traits - (Liu)**
- 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

**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

Genetics of Ageing – (Merz)
• Definition of Ageing and Mechanisms (tie with chromosomes/telomeres)
• Heritability of Ageing (tie with Complex Traits)
• Model Organism Studies of Ageing
• Genes Associated with Longevity
• Discuss the Possibilities and Ethics of Extending Lifespan

Sexual Differentiation - (Nachtigal)
• 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

Ethics and Prenatal Diagnosis - (Burnett)
• 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

**Animal Models - (Ding)**
- 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. Populations and Clinical Genetics**
Goals: Human Genetics as it applies to the world around us: populations, diagnoses and treatments.

**Population Genetics - (Pemberton)**
- 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

**Unique Populations of Manitoba - (Triggs-Raine)**
- define unique populations as it refers to genetics.
- list the three major unique populations in Manitoba.
- describe the key characteristics of each of Manitoba’s unique populations.
- explain the advantages and disadvantages of unique populations with reference to gene identification.
- understand how personalized medicine can be applied in unique populations.

**NGS Methods and Analysis (Pemberton)**
- Exome sequencing
- RNA-Seq

**Next Generation Sequencing in the Clinic (Frosk)**
- Discuss the use of NGS in a clinical setting

**Metabolic Disorders - (Mhanni)**
- Diagnosis and Treatment of metabolic disorders
Bench to Bedside - (Simard)

• 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.
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