Graduate School of Public Health
Department of Human Genetics
Cancer Genetic Counseling
HUGEN 2061
Wednesday and Friday 9 to 10:30 AM
Location: A216 Pitt Public Health
Credit Hours: 1.0
Spring 2020

Instructor and Contact Information:

Robin E. Grubs, PhD, LCGC
Office: 3138 Parran Hall
Phone: 412-624-4695
Email: rgrubs@pitt.edu
Office hours: By appointment

Course Description

This course is designed to provide students with the knowledge and skills fundamental to the practice of cancer genetic counseling. The overall goal of the course is to allow students to apply cancer genetics knowledge to clinical situations. The course will cover hereditary cancer syndromes, cancer risk assessment models, and germline and somatic genomic testing.

Learning Objectives:

After completion of this course, each student will be able to:
(1) identify the clinical features and management of hereditary cancer syndromes;
(2) calculate cancer genetic risks using a variety of risk assessment models;
(3) describe different genetic/genomic testing modalities used in clinical cancer genetic counseling; and
(4) Explain genetic/genomic test result interpretation and risk assessment/management.

Prerequisites:

This course builds upon the knowledge and skills covered in HUGEN 2035 and HUGEN 2060 Chromosomes: Structure and Function. For this reason, these two courses are perquisites to this course.

Requirements:

Complete assigned readings
Complete class assignments
Participate in class discussions

Short quizzes
Final exam

Required Texts

None. Readings are drawn from the current literature and classic texts on the course topics.

Student Performance Evaluation and Grading:

Your grade for the course is based upon the grades you receive on the assignments, short quizzes, and cumulative final exam as well as your participation during in-class discussions. The breakdown is as follows:

Variant of uncertain significance (VUS) vetting case presentation—15%
Short quizzes—15%
Cancer syndrome fact sheet—10%
Tumor testing interpretation assignment—10%
Risk model assignment—10%
Class participation—10%
Cumulative final exam—30%

- VUS vetting presentation project—For this project, you will need to vet a VUS result that you have received for a patient who had a hereditary cancer gene panel. You will need to summarize the literature for the particular VUS and use the American College of Medical Genetics variant reclassification guidelines to provide the rationale for why this finding is considered a VUS. There will be a 10-minute class presentation on April 10, 2020. Please send your PowerPoint presentation one week prior to your presentation.
- Short quizzes—You are expected to have read the assigned materials before each class. Short quizzes will be given to assess your understanding of the readings.
- Cancer syndrome fact sheet—Each student will be assigned one inherited cancer predisposition syndrome to research in order to generate a "fact sheet" for their fellow classmates. The expectation is that these fact sheets will aid in studying for the comprehensive examination, which takes place in the Fall semester of your second year of training as well as the American Board of Genetic Counseling certification examination. Fact sheets are due *** (TBD). Please email your fact sheet.
- Tumor testing interpretation assignment—For this project, you will be given the results from a somatic test ordered on a patient's tumor and asked to assess the germline and treatment implications of the result for the patient. This assignment is due *** (TBD).
- Risk Model Assignment—Using the appropriate computer models, you will determine the breast cancer risks and the risks that a BRCA pathogenic will be identified. Case based questions about the risk models will be completed. Risk model exercise is due no later than *** (TBD). Please email the exercise.

- Class participation—you are expected to participate in class each week, through discussion, case-based learning and review of the information from the required readings.
- Cumulative final exam—An exam will be administered the final day of class to assess your understanding of the material presented during the course.

Since you are not graded on a curve, you will not be competing with your classmates for a grade. Therefore, we encourage you to help each other achieve the best work you are capable of producing. Working in a collaborative manner to strive for greater understanding will help you learn the material with more ease and enjoyment.

Grading Scale

97-100%	A+
93-96%	A
90-92%	A-
87-89%	B+
83-86%	B
80-82%	B-
77-79%	C+
73-76%	C
70-72%	C-
67-69%	D+
63-66%	D
60-62%	D-
<60	F

CourseWeb/BlackBoard Instruction

This class utilizes CourseWeb for the class schedule and posting of required readings.

Academic Integrity

All students are expected to adhere to the school's standards of academic honesty. Cheating/plagiarism will not be tolerated. The Graduate School of Public Health's policy on academic integrity, which is based on the University policy, is available online in the Pitt Public Health Academic Handbook www.publichealth.pitt.edu/home/academics/academic-requirements. The policy includes obligations for faculty and students, procedures for adjudicating violations, and other critical information. Please take the time to read this policy.

Accommodation for Students with Disabilities:

If you have a disability for which you are or may be requesting an accommodation, you are encouraged to contact both your instructor and Disability Resources and Services, 140 William Pitt Union, 412-648-7890 as early as possible in the term.

A comprehensive description of the services of that office can be obtained at www.drs.pitt.edu.

Diversity Statement

The University of Pittsburgh Graduate School of Public Health considers the diversity of its students, faculty, and staff to be a strength and critical to its educational mission. Pitt Public Health is committed to creating and fostering inclusive learning environments that value human dignity and equity. Every member of our community is expected to be respectful of the individual perspectives, experiences, behaviors, worldviews, and backgrounds of others. While intellectual disagreement may be constructive, no derogatory statements, or demeaning or discriminatory behavior will be permitted.

If you feel uncomfortable or would like to discuss a situation, please contact any of the following:

- the course instructor;
- the Pitt Public Health Associate Dean for Diversity at 412-624-3506 or nam137@pitt.edu;
- the University's Office of Diversity and Inclusion at 412-648-7860 or https://www.diversity.pitt.edu/make-report/report-form (anonymous reporting form).

Sexual Misconduct, Required Reporting and Title IX Statement

The University is committed to combatting sexual misconduct. As a result, you should know that University faculty and staff members are required to report any instances of sexual misconduct, including harassment and sexual violence, to the University's Title IX office so that the victim may be provided appropriate resources and support options. What this means is that as your professors, we are required to report any incidents of sexual misconduct that are directly reported to us, or of which we are somehow made aware.

There are two important exceptions to this requirement about which you should be aware: A list of the designated University employees who, as counselors and medical professionals, do not have this reporting responsibility and can maintain confidentiality, can be found here: www.titleix.pitt.edu/report/confidentiality

An important exception to the reporting requirement exists for academic work. Disclosures about sexual misconduct that are shared as part of an academic project, classroom discussion, or course assignment, are not required to be disclosed to the University's Title IX office.

If you are the victim of sexual misconduct, Pitt encourages you to reach out to these resources:

- Title IX Office: 412-648-7860
- SHARE @ the University Counseling Center: 412-648-7930 (8:30 A.M. TO 5 P.M. M-F) and 412-648-7856 (AFTER BUSINESS HOURS)

If you have a safety concern, please contact the University of Pittsburgh Police, 412-624-2121.
Other reporting information is available here: www.titleix.pitt.edu/report-0

Schedule of Sessions:

Date	Topics and Assigned Readings
March 25, 2020	**Risk Assessment/ Risk Models** • National Comprehensive Cancer Network (NCCN) v.3.2019 Genetic/Familial High-Risk Assessment: Breast and Ovarian • NCI Cancer Genetics PDQs (http://www.cancer.gov/cancertopics/pdq/genetics) • Amir E, Freedman OC, Seruga B, Evans DG. Assessing women at high risk of breast cancer: a review of risk assessment models. *J Natl Cancer Inst.*2010;102(10):680–691. • Gail MH and Mai PL. Comparing breast cancer risk assessment models. *J Natl Cancer Inst*. 2010;102(10):665-8. • Lee AJ. BOADICEA: a comprehensive breast cancer risk prediction model incorporating genetic and nongenetic risk factors. *Genet Med* 2019;0(0):1-11. PMID:30643217 • Antoniou A, Hardy R, Walker L et al. Predicting the likelihood of carrying a *BRCA1* or *BRCA2* mutation: validation of BOADICEA, BRCAPRO, IBIS, Myriad and the Manchester scoring system using data from UK genetics clinics. *J Med Genet* 2008;45:425-431.
March 27, 2020	**Breast Cancer Surgery/Breast Cancer Risk Management** Screening guidelines: • Saslow D. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin*. 2007;57(2):75-89. PMID: 17392385 Management: • Peters ML. Managing hereditary breast cancer risk in women with and without ovarian cancer. *Gynecol Oncol*. 2017 Jul;146(1):205-214. PMID: 28454658 Chemoprevention: • Nelson HD, Fu R, Zakher B, Pappas M, McDonagh M. Medication use for the risk reduction of primary breast cancer in women: updated evidence report and systematic review for the US Preventive Services Task Force *JAMA*. 2019;322(9):868-886. doi:10.1001/jama.2019.5780

	• Kala Visvanathan, MHS et al. Use of Endocrine Therapy for Breast Cancer Risk Reduction: ASCO Clinical Practice Guideline Update *J Clin Oncol.* 2019 Sep 3:JCO1901472. doi: 10.1200/JCO.19.01472.
April 1, 2020	**GI procedures & Surgery/ GI cancer Management** • Syngal S. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol*. 2015; 110(2): 223-62. PMID: 25645574 • Colorectal cancer prevention, screening, and management: https://www.cancer.gov/types/colorectal/hp • Insert reference for PC surveillance review article (should be published in December) • Pancreatic cancer treatment: https://www.cancer.gov/types/pancreatic/hp/pancreatic-treatment-pdq • Le DT. PD-1 Blockade in Tumors with Mismatch-Repair Deficiency. *N Engl J Med*. 2015;372(26):2509-20. PMID: 26028255
April 3, 2020	**Renal/Endocrine syndromes** • Rednam SP , Erez A , Druker H , Janeway KA , Kamihara J , Kohlmann WK , Nathanson KL , States LJ , Tomlinson GE , Villani A , Voss SD , Schiffman JD , Wasserman JD . Von Hippel–Lindau and hereditary pheochromocytoma/paraganglioma syndromes: clinical features, genetics, and surveillance recommendations in childhood. *Clin Cancer Res* 2017;23(12):68–75. • Guilmette J & Nose V. Hereditary and familial thyroid tumors. *Histopathology* 2018;72:70–81. • Deng AT & Izatt L. Inherited Endocrine Neoplasia— A Comprehensive Review from Gland to Gene. *Curr Genet Med Rep* (2019) 7:102–115
April 8, 2020	**Pediatric Cancer Syndromes/Hematologic Syndromes** • Ripperger T. et al. Childhood cancer predisposition syndromes—A concise review and recommendations by the Cancer Predisposition Working Group of the Society for Pediatric Oncology and Hematology. *Am J Med Genet*. 2017;173:1017–1037. • Diets IJ et al. High Yield of Pathogenic Germline Mutations Causative or Likely Causative of the Cancer Phenotype in Selected Children with *CancerClin Cancer Res*; 24(7) April 1, 2018 • Furutani E et al. Germline Genetic Predisposition to Hematologic Malignancy *JCO* 2017;35(9): 1018-

	1028.
April 10, 2020	**VUS Vetting Presentations** • Richards S et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med* 2015;17(5):405-24. • Balmana J et al. Conflicting interpretations of genetic variants and cancer risk by commercial laboratories as assessed by the prospective registry of multiplex testing. *J Clin Oncol*. 2016 Dec;34(34):4071-4078
April 15, 2020	**Somatic Tumor Testing** • Jain R et al. The Relevance of Hereditary Cancer Risks to Precision Oncology: What Should Providers Consider When Conducting Tumor Genomic Profiling. JNCCN Jun;14(6):795-806 • Raymond V et al. Germline Findings in Tumor-Only Sequencing: Points to Consider for Clinicians and Laboratories. *JNCI* 2016;108(4). • Dumbrava EL et al. Expanded Analysis of Secondary Germline Findings From Matched Tumor/Normal Sequencing Identifies Additional Clinically Significant Mutations. *JCO Precis Oncol*. 2019;3. doi: 10.1200/PO.18.00143. Epub 2019 Apr 11 • Meric-Bernstam F. et al. Incidental germline variants in 1000 advanced cancers on a prospective somatic genomic profiling protocol. *Annals of Oncology* 27: 795–800, 2016
April 17, 2020	**Result interpretation (Case Based)** Assigned readings: TBD
April 22, 2020	**Challenging Cases** Assigned readings: TBD
April 24, 2020	**Final**