**HUMGEN 803: Advanced Topics in Genetics**

Winter 2022

**Meeting Time:** Wednesdays 3pm-5pm, 2 credits

**Room:** TAUB LIB 5360

**Course Director**: Jeffrey Kidd, Ph.D. [jmkidd@umich.edu](mailto:jmkidd@umich.edu)

**Overview:** HUMGEN 803 is a discussion course for graduate students in the Human Genetics M.S. and the Genetics and Genomics Ph.D. degree programs. The course involves in-depth discussion of papers from the primary literature and covers a diverse range of topics relevant to genetics and genomics research with a focus on methods and approaches. Each week, a faculty member will lead a discussion of 2-3 papers. A student will be assigned to give an introductory overview of each paper with a focus on the relevant background and the question that the paper seeks to address. This should be brief (~5 minutes) and given as a spoken oral overview without using PowerPoint slides. The overview is followed by a guided discussion focused on the methods, results, and conclusions of the study where students may be randomly called on to explain each figure or other aspects of the paper. For each class session, a student will also be assigned to act a summarizer. At the end of the class period the summarizer will offer a high-level overview of what was revealed by the papers and during the discussion, how the papers relate to each other, and how they relate to concepts covered in the genetics curriculum or to larger issues in the fields of genetics and genomics. This summary may also include how understanding of the papers changed as a result of the group discussion. Grades will be assigned based on class participation and the level of engagement of each student.

**Course logistics:** The assignment of students to give an overview of the papers and discussion will be posted on Canvas. This course is planned for in person instruction in the Winter 2022 term. The health of our community is of primary concern. Please do not attend class if you are unwell or are under investigation for symptoms based on the UM Covid screening policies. Please contact that weeks’ instructor and the course director (Dr. Kidd) if you are unable to attend in person. In such a scenario, options for remote discussion (Zoom) will be activated. If a student is unable to participate for a given week an alternative assignment will be offered.

**Expectations:** All students are expected to read and understand all of the papers for each week. Students are encouraged to discuss the papers with each other prior to class with a focus on aspects that may be unfamiliar. The students assigned to give the introduction and final summary may be called upon to assist in explaining aspects of the paper that are particularly confusing. The paper leaders are encouraged to confer with the faculty leader each week about aspects that may be unclear.

**Instructors:**

Stephanie Bielas, Ph.D. sbielas@umich.edu

Shigeki Iwase, Ph.D. siwase@umich.edu

Catherine Keegan, M.D., Ph.D. keeganc@umich.edu

Jeffrey Kidd, Ph.D. jmkidd@umich.edu

Jacob Kitzman, Ph.D. kitzmanj@umich.edu

Miriam Meisler, Ph.D. meislerm@umich.edu

Ryan Mills, Ph.D. remills@umich.edu

Stephanie Moon, Ph.D. smslmoon@umich.edu

Jacob Mueller, Ph.D. jacobmu@umich.edu

Goutham Narla, M.D., Ph.D. gnarla@umich.edu

Week 1 Wednesday, January 5 **Kidd**

**1. Genomic responses in mouse models poorly mimic human inflammatory diseases**

Seok J, et al. (2013) *PNAS* 110(9):3507-12 PMID: 23401516

**2 Genomic responses in mouse models greatly mimic human inflammatory diseases**

Takao K and Miyakawa T (2015) *PNAS* 112(4):1167-72 PMID: 25092317

Week 2 Wednesday, January 12 **Kidd**

**1. The structure of haplotype blocks in the human genome** Gabriel SB, et al. (2002) *Science* 296(5576):2225-9 PMID: 12029063

**2. A Fine-Scale Map of Recombination Rates and Hotspots Across the Human Genome** Myers S, et al. (2005) *Science* 310(5746):321-4 PMID: 16224025

Week 3 Wednesday, January 19 **Kidd**

**1. PRDM9 Is a Major Determinant of Meiotic Recombination Hotspots in Humans and Mice** Baudat F. et al, (2010) *Science* 327(5967):836-40 PMID: 20044539

**2. Repeated losses of PRDM9-directed recombination despite the conservation of PRDM9 across vertebrates** Baker Z, et al. (2017) *eLife* 6: e24133 PMID: 28590247

Week 4 Wednesday, January 26 **Kidd**

**1.** **Genetic Dissection of Complex Traits** Lander ES and Schork NJ (1994) *Science* 30;265(5181):2037-48 PMID: 8091226

**2. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls** Wellcome Trust Case Control Consortium (2007) *Nature* 447, 661–678 PMID: 17554300

**3. Exome sequencing identifies the cause of a mendelian disorder** Ng SB, et al. (2010) Nature Genetics 42(1):30-5 PMID: 19915526

Week 5 Wednesday, February 2 **Mueller**

**1. Mammalian Y chromosomes retain widely expressed dosage-sensitive regulators.** Bellott DW, et al. (2014) *Nature* Apr 24;508(7497):494-9 PMID: 24759411

**2. Two genes substitute for the mouse Y chromosome for spermatogenesis and reproduction.** Yamauchi Y, et al. (2016) *Science* 351:514–16 PMID: 26823431

Week 6 Wednesday, February 9 **Keegan**

**1. Interruption of progerin-lamin A/C binding ameliorates Hutchinson-Gilford progeria syndrome phenotype.** Lee S-j et al. (2016) *J Clinical Investigation* 126: 3879-3893. PMID: 27617860

**2.** **Development of a CRISPR/Cas9-based therapy for Hutchinson-Gilford progeria syndrome.** Santiago-Fernández et al. (2019) *Nat. Medicine* 25: 423-426 (including extended data). PMID: 30778239

Week 7 Wednesday, February 16 **Keegan**

**1. Somatic mosaic activating mutations in *PIK3CA* cause CLOVES syndrome.** Kurek KC et al. (2012). *Amer J Hum Genet* 90: 1108-1115. PMID: 22658544

**2. Targeted therapy in patients with PIK3CA-related overgrowth syndrome.** Venot Q et al. (2018). *Nature* 558: 540-546.

Week 8 Wednesday, February 23 **Iwase**

**1. The histone H3-H4 tetramer is a copper reductase enzyme.** N Attar et al. (2020) *Science* 369(6499):59-64 PMID: 32631887

**2. Histone serotonylation is a permissive modification that enhances TFIID binding to H3K4me3.** LA Farrelly *et al.* (2019) *Nature* 567: 535.

Wednesday, March 2. No class – Winter Break

Week 9 Wednesday, March 9 **Moon**

**1. GTPBP1 resolves paused ribosomes to maintain neuronal homeostasis**. Terrey M et al. (2020) *eLife* Nov 13;9:e62731 PMID: 33186095

**2. Ribosome Collisions Trigger General Stress Responses to Regulate Cell Fate.** Wu CC et al. (2020) *Cell* Jul 23;182(2):404-416 PMID: 32610081

Week 10 Wednesday, March 16 **Bielas**

**1. Assembly of functionally integrated human forebrain spheroids.** Birey F et al., (2017) *Nature* 545: 54-59. PMID: 28445465

**2. Induction of expansion and folding in human cerebral organoids.** Li Y et al. (2017) *Cell Stem Cell* 20: 385-396. PMID: 28041895

Week 11 Wednesday, March 23 **Kitzman**

**1. Accurate classification of BRCA1 variants with saturation genome editing.** GM Findlay et al., (2018) *Nature* 562:217-222. PMID: 30209399

**2. Mutations primarily alter the inclusion of alternatively spliced exons** Baeza-Centurion P, et al. (2020) *Elife* 9:e59959. PMID: 33112234

Week 12 Wednesday, March 30 **Meisler**

**1. Antisense oligonucleotides increase *Scn1a* expression and reduce seizures and SUDEP incidence in a mouse model of Dravet syndrome** Han Z et al. (2020) *Science Translational Medicine* 12(558):eaaz6100 PMID: 32848094

**2. Scn8a Antisense Oligonucleotide Is Protective in Mouse Models of SCN8A Encephalopathy and Dravet Syndrome** Lenk G et al., *Annals of Neurology* (2020) (3):339-346 PMID: 31943325

Week 13 Wednesday, April 6 **Mills**

**1. Haplotype-resolved diverse human genomes and integrated analysis of structural variation** Ebert P et al. (2021) *Science* 2;372(6537) PMID: 33632895

**2. Dissecting the causal mechanism of X-linked dystonia-parkinsonism by integrating genome and transcriptome assembly.** T Aneichyk et al., (2018) *Cell* 172(5): 897-909. PMID: 29474918

Week 14 Wednesday, April 13 **Narla**