BIOE 5690: Genetics and Ethics
Summer 2024, Mondays, 5:15 – 7:30pm
BRB 251

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Course description:

Over 30 years have passed since the inception of the Human Genome Project (HGP). Where are we now? The results of the HGP have shaped medical practice and have changed the way people talk about themselves and their relationships. In this course students will be introduced to basic genetics and to recent advances in the genetic and genomic sciences. We will explore the ethical, legal, and social implications of these trends while discussing topics such as whole genome testing, ancestry and race, forensic genetics, and the relationship of genetics to health disparities.

Course objectives:

By the end of the course, students will be able to:

- Discuss the historical and contemporary roots of ethical concerns about genomic technologies
- Analyze the ethical challenges that genetic and genomic technologies pose for medicine, science, and society
- Describe ethically justifiable strategies for minimizing the risks that genomic technologies pose and enhancing the benefits that they offer

Course overview:

Session 1	June 3	Why ELSI?	Joffe
Session 2	June 10	Genetic Interventions	Joffe
Session 3	June 17	Genetics in the Clinic	Joffe/Mueller
Session 4	June 24	Genomics & Research	Joffe/Saylor/LoTempio
Session 5	July 1	Genomics, Ethics, and Pediatrics	Joffe
Session 6	July 8	Ancestry, Race, and Indigenous Communities	Roberts/Joffe (Virtual)
Session 7	July 15	Reproductive Ethics, Disability, and Genomics	Joffe
Session 8	July 22	Precision Medicine	Joffe
Session 9	July 29	Direct-to-Consumer Genetics; Genetics and the Courts	Joffe
Session 10	Aug 5	Sociogenomics	Joffe

Class participation:

This is a discussion-based seminar. I expect you to read and consider the materials before class and to be prepared to thoughtfully discuss them. During class, plan to critically engage with the course materials, identify themes and inconsistencies, and contribute meaningful perspective from your own experience and current events. Some of the material I will discuss is controversial (indeed, one of the take-home messages of this class is that genetics is often controversial). I aim to be respectful of diverse views and ask that you do the same.

Although sessions will be recorded, regular in-person attendance and high-quality class participation are strongly encouraged, both to promote understanding of the course material and to promote student-to-student learning.

I welcome further discussion outside of class and look forward to getting to know you. Please feel free to make an appointment, individually or in groups, to discuss course materials, bioethics in general, career advice, and the like.

Course requirements and grading:

1. Brief Responses

   Each week (except weeks 1, 6, and 10), there will be a prompt that accompanies the readings. Prompts are available on Canvas. Students will be expected to write a brief response (maximum 500 words) for 4 class sessions, referencing at least some of the readings for that day. Writing assignments should be turned in via Canvas by 5 pm on class Mondays. You will be graded only on completion of these assignments—I will not give letter grades. However, I may occasionally ask you to revise one of these

assignments if I believe there is substantial room for improvement or if you have not referenced the readings. Each essay is worth 1.25 points.

2. Midterm Exam

   Students will complete a take-home midterm, worth 45 points, due Monday, July 8 at 11:59pm. The assignment will be available on Canvas at least two weeks prior to the due date. Essays should be 3-5 double-spaced pages.

3. Final Exam

   Students will complete a take-home final, worth 50 points, due Friday, August 9 at 11:59 pm. The assignment will be available on Canvas at least two weeks prior to the due date. Essays should be 4-5 double-spaced pages.

   Both the midterm and the final will be graded on the basis of the following criteria: clearly stated thesis, well-reasoned arguments using principles and themes from class, and appropriate support and references (you are welcome to use references from the readings and/or from other readings that you have found independently; class lectures and slides are not adequate references). I will provide additional instructions with each assignment.

4. Extra credit

   Attendance: While attendance is not mandatory for this class, I strongly encourage it. Students who attend at least 7 classes will receive an extra 2 points towards their final grade. Sign-in sheets will be available during the first half of class. There will be no partial credit for attending fewer than 7 classes. I will consider excused absences on a case by case basis if you notify me in advance.

   Weekly essays: Students who turn in their 4 weekly brief essays *on time* (by 5 pm on the day of class) will receive an extra 2 points towards their final grade. There will be no partial credit for turning in fewer than 4 essays on time.

   Thus, students can get up to 4 extra points towards their final grade, based on a combination of attendance and weekly essay completion. For context, the step between grades (e.g., B+ to A- or A- to A) is 3-4 points.

Accommodations:

I plan to be as flexible as possible. If you need accommodations for any reason, professional or personal, please discuss them with me as soon as you can. I will aim to keep your needs private and will work out an appropriate solution to allow you to achieve the learning goals of this course while maintaining your well-being. I can also help point you towards many university

resources available to students facing a variety of challenges, including mental health issues, housing, child care, writing support, and more.

Academic Integrity:

You are welcome and encouraged to discuss the readings and course topics with your fellow classmates, family, and friends. However, the work you submit for this course must be your work alone. Any plagiarism or other form of cheating will be dealt with according to relevant Penn policies, including Penn's code of academic integrity: https://catalog.upenn.edu/pennbook/code-of-academic-integrity/

I consider use of ChatGPT or other AI/large language models to complete course assignments as a violation of academic integrity. I follow Penn's guidance on the use of AI for class assignments: "*treat the use of AI as you would treat assistance from another person. For example, this means if it is unacceptable to have another person substantially complete a task like writing an essay, it is also unacceptable to have AI to complete the task*."

Class Recordings:

To facilitate access for all class members, class sessions, including your participation, will be audio recorded and the recordings will be made available to the class for the duration of this course. These recordings, as well as previously recorded lectures and other course materials, are made available solely for your personal, educational use and may not be shared, copied, or redistributed without my permission and that of Penn. You are not permitted to record class sessions yourselves. Unauthorized sharing or recording is a violation of the Code of Academic Integrity.

Readings:

All information for this course, including readings, can be found on the Canvas site, which you can access with a PennKey and password. There is no textbook. Readings average 40-50 pages per week and include a mix of academic articles and newspaper or magazine-style narratives. I have also included many optional readings as additional resources. I encourage you to download them and save them for your files; you may also find them helpful for the weekly essays and the exam essays (and of course, I hope you'll choose to read many of them).

Session 1, June 3, 2024
Why do we need an ELSI of genomics?
Joffe

Objectives:

By the end of the class, you will be able to:

- Define the concept of eugenics and its relevance to contemporary genomic medicine and science
- Describe the Human Genome Project and the ethical issues it raises
- Identify and critique the concept of genetic exceptionalism

Readings:

1. Buck v. Bell, 274 U.S. 200 (1927)
2. Lombardo, P. A. The power of heredity and the relevance of eugenic history. *Genet Med* 20, 1305–1311 (2018).
3. Collins, F. S. Medical and ethical consequences of the human genome project. *J Clin Ethics* 2, 260–7 (1991).
4. Jones, K. M. *et al.* Complicated legacies: The human genome at 20. *Science* 371, 564–569 (2021).
5. Green, M. J. & Botkin, J. R. "Genetic exceptionalism" in medicine: clarifying the differences between genetic and nongenetic tests. *Annals of Internal Medicine* 138, 571–575 (2003).
6. Sabatello, M. & Juengst, E. Genomic Essentialism: Its Provenance and Trajectory as an Anticipatory Ethical Concern. *Hastings Cent Rep* **49**, S10–S18 (2019).
7. Hudson, K. L. Genomics, health care, and society. 365, 1033–1041 (2011).

Optional Readings:

1. Zimmer, C. Chapter 3: This Race Should End with Them. In *She Has Her Mother's Laugh*. New York:Dutton, 2018, pgs 67-106.
2. Knoppers, B. M. & Chadwick, R. The Human Genome Project: under an International Ethical Microscope. *Science* 265, 2035–2036 (1994).
3. Lombardo, P. A. Medicine, eugenics, and the Supreme Court: from coercive sterilization to reproductive freedom. *J Contemp Heal Law Policy* 13, 1–25 (1996).

Session 2, June 10, 2024
Genetic interventions
Joffe

Objectives:

By the end of this class, you will be able to:

- Describe the use of somatic gene therapy to prevent or treat human disease and the ethical issues it raises
- Analyze the ethical controversies surrounding germline genetic modification
- Discuss the ethics of using genetic technologies to intervene on the natural environment

Readings:

1. Puthumana J, Egilman AC, Ramachandran R, Naushad N, Shah N, Ross J. Early experience with the FDA's regulatory review of novel gene therapies. BMJ Evid Based Med. 2021.
2. Thomas K. This New Treatment Could Save the Lives of Babies. But It Costs $2.1 Million. New York Times. 2019 May 25;Sect. B.
3. Berg P, Baltimore D, Brenner S, Roblin RO, 3rd, Singer MF. Asilomar conference on recombinant DNA molecules. Science. 1975;188(4192):991-4.
4. Lanphier E, Urnov F, Haecker SE, Werner M, Smolenski J. Don't edit the human germ line. Nature. 2015;519(7544):410-1.
5. Cohen IG, Savulescu J, Adashi EY. Medicine. Transatlantic lessons in regulation of mitochondrial replacement therapy. Science. 2015;348(6231):178-80.
6. Hynes RO, Coller BS, Porteus M. Toward Responsible Human Genome Editing. JAMA. 2017;317(18):1829-30.
7. Claiborne AB, English RA, Kahn JP. Finding an ethical path forward for mitochondrial replacement. Science. 2016;351(6274):668-70.
8. Yong E. A Reckless and Needless Use of Gene Editing on Human Embryos. The Atlantic. 2018 November 25, 2018.
9. Baltimore D, Berg P, Botchan M, Carroll D, Charo RA, Church G, et al. Biotechnology. A prudent path forward for genomic engineering and germline gene modification. Science. 2015;348(6230):36-8.
10. Kahn J. The Gene Drive Dilemma: We Can Alter Entire Species, but Should We? New York Times. 2020 January 12;Sect. Sunday Magazine.
11. Zimmer C. 'Gene Drives' Are Too Risky for Field Trials, Scientists Say. New York Times. 2017 November 21.

Optional Readings:

1. Lander ES, Baylis F, Zhang F, Charpentier E, Berg P, Bourgain C, et al. Adopt a moratorium on heritable genome editing. Nature. 2019;567(7747):165-8.

2. Hacein-Bey-Abina S, Pai SY, Gaspar HB, Armant M, Berry CC, Blanche S, et al. A modified gamma-retrovirus vector for X-linked severe combined immunodeficiency. N Engl J Med. 2014;371(15):1407-17.
3. Esrick EB, Lehmann LE, Biffi A, Achebe M, Brendel C, Ciuculescu MF, et al. Post-Transcriptional Genetic Silencing of BCL11A to Treat Sickle Cell Disease. N Engl J Med. 2021;384(3):205-15.
4. Gillmore JD, Gane E, Taubel J, Kao J, Fontana M, Maitland ML, et al. CRISPR-Cas9 In Vivo Gene Editing for Transthyretin Amyloidosis. N Engl J Med. 2021;385(6):493-502.

Session 3, June 17, 2024
Genetics in the Clinic
Joffe

Objectives:

By the end of the class, you will be able to:

- Identify the ethical issues raised by the use of genetic testing in the clinic
- Describe the process and challenges of genetic counseling and informed consent for genetic testing
- Define the concepts of genetic privacy, genetic screening, duty to warn, and duty to recontact

Readings:

1. Elmore SNC. p53 and Me. N Engl J Med. 2018;378(21):1962-3.
2. Miller, D. T., Lee, K., Abul-Husn, N. S., Amendola, L. M., Brothers, K., Chung, W. K., ... & ACMG Secondary Findings Working Group. (2023). ACMG SF v3.2 list for reporting of secondary findings in clinical exome and genome sequencing: A policy statement of the American College of Medical Genetics and Genomics (ACMG). *Genetics in Medicine*, *25*(8), 100866.
3. Rich K. Genetic Information Nondiscrimination Act and the Affordable Care Act: When Two Is Better Than One. Genet Test Mol Biomarkers. 2018;22(6):331-2.
4. Wade CH. What Is the Psychosocial Impact of Providing Genetic and Genomic Health Information to Individuals? An Overview of Systematic Reviews. Hastings Cent Rep. 2019;49 Suppl 1:S88-S96.
5. Burgess MM. Beyond consent: ethical and social issues in genetic testing. Nat Rev Genet. 2001;2(2):147-51.
6. Jamal, L., Schupmann, W., & Berkman, B. E. (2020). An ethical framework for genetic counseling in the genomic era. *Journal of Genetic Counseling*, *29*(5), 718-727.
7. Parens E. Drifting Away from Informed Consent in the Era of Personalized Medicine. Hastings Cent Rep. 2015;45(4):16-20.
8. Manchanda R, Loggenberg K, Sanderson S, Burnell M, Wardle J, Gessler S, et al. Population testing for cancer predisposing BRCA1/BRCA2 mutations in the Ashkenazi-Jewish community: a randomized controlled trial. J Natl Cancer Inst. 2015;107(1):379.
9. Rothstein, M. A. (2018). Reconsidering the duty to warn genetically at-risk relatives. *Genetics in Medicine*, *20*(3), 285-290.

Optional Readings:

1. Spector-Bagdady K, Prince AER, Yu JH, Appelbaum PS. Analysis of state laws on informed consent for clinical genetic testing in the era of genomic sequencing. American journal of medical genetics Part C, Seminars in medical genetics. 2018;178(1):81-8.
2. Clayton EW, Appelbaum PS, Chung WK, Marchant GE, Roberts JL, Evans BJ. Does the law require reinterpretation and return of revised genomic results? Genet Med. 2021;23(5):833-6.

3. Ormond KE. From genetic counseling to "genomic counseling". Mol Genet Genomic Med. 2013;1(4):189-93.
4. Burke W, Tarini B, Press NA, Evans JP. Genetic screening. Epidemiol Rev. 2011;33:148-64.
5. Ray T. Quest Diagnostics Win in Wrongful Death Case Reveals Ongoing Challenges for Variant Classification. GenomeWeb, November 12, 2020.
6. Werner-Lin, A., McCoyd, J. L., & Bernhardt, B. A. (2019). Actions and uncertainty: How prenatally diagnosed variants of uncertain significance become actionable. *Hastings Center Report*, *49*, S61-S71
7. Lauerman, J. My DNA Results Spur Alzheimer's Anxiety at $12,000 Cost. Bloomberg, November 5, 2012.
8. Kolker, R. The Vanishing Family. New York Times, July 20, 2023.

Session 4, June 24, 2024
Genomics and Research
Joffe/Saylor/LoTempio

Objectives:

By the end of the class, you will be able to:

- Identify and critique models of consent for and governance of genomic research
- Analyze the challenges raised by return of results and secondary findings from genomic research
- Discuss the ethical issues associated with identifiability of genomic data and with genomic data sharing

Readings:

1. Grady C, Eckstein L, Berkman B, Brock D, Cook-Deegan R, Fullerton SM, et al. Broad Consent for Research With Biological Samples: Workshop Conclusions. Am J Bioeth. 2015;15(9):34-42.
2. Appelbaum PS, Parens E, Waldman CR, Klitzman R, Fyer A, Martinez J, et al. Models of consent to return of incidental findings in genomic research. Hastings Cent Rep. 2014;44(4):22-32.
3. Burke W, Evans BJ, Jarvik GP. Return of results: ethical and legal distinctions between research and clinical care. American journal of medical genetics Part C, Seminars in medical genetics. 2014;166C(1):105-11.
4. Koenig BA. Have we asked too much of consent? Hastings Cent Rep. 2014;44(4):33-4.
5. Wadman M. Conflict flares over incidental genetic findings. Science. 2021;373(6555):610.
6. Fullerton SM, Anderson NR, Guzauskas G, Freeman D, Fryer-Edwards K. Meeting the governance challenges of next-generation biorepository research. Sci Transl Med. 2010;2(15):15cm3.
7. Gymrek M, McGuire AL, Golan D, Halperin E, Erlich Y. Identifying personal genomes by surname inference. Science. 2013;339(6117):321-4.
8. Rodriguez LL, Brooks LD, Greenberg JH, Green ED. The complexities of genomic identifiability. Science. 2013;339(6117):275-6.
9. Paltoo DN, Rodriguez LL, Feolo M, Gillanders E, Ramos EM, Rutter JL, et al. Data use under the NIH GWAS data sharing policy and future directions. Nat Genet. 2014;46(9):934-8.
10. Dyke SO, Philippakis AA, Rambla De Argila J, Paltoo DN, Luetkemeier ES, Knoppers BM, Brookes AJ, Spalding JD, Thompson M, Roos M, Boycott KM, Brudno M, Hurles M, Rehm HL, Matern A, Fiume M, Sherry ST. Consent Codes: Upholding Standard Data Use Conditions. PLoS Genet. 2016 Jan 21;12(1):e1005772.

Optional Readings:

1. Carmichael M. Newborn screening: a spot of trouble. Nature. 2011;475(7355):156-8.
2. Greely HT. The uneasy ethical and legal underpinnings of large-scale genomic biobanks. Annual review of genomics and human genetics. 2007;8:343-64.
3. Henderson GE, Edwards TP, Cadigan RJ, Davis AM, Zimmer C, Conlon I, et al. Stewardship practices of U.S. biobanks. Sci Transl Med. 2013;5(215):215cm7.
4. Holm IA, Yu TW, Joffe S. From Sequence Data to Returnable Results: Ethical Issues in Variant Calling and Interpretation. Genet Test Mol Biomarkers. 2017;21(3):178-83.
5. Presidential Commission for the Study of Bioethical Issues. Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct to Consumer Contexts. Washington, DC; 2013. (***Chapter 5 only***)
6. Presidential Commission for the Study of Bioethical Issues. Privacy and Progress in Whole Genome Sequencing. Washington, DC; 2012. (***Chapter 3 only***)
7. Koplin JJ, Savulescu J, Vears DF. Why genomics researchers are sometimes morally required to hunt for secondary findings. BMC Med Ethics. 2020;21(1):11.
8. Lyon GJ. Personalized medicine: Bring clinical standards to human-genetics research. Nature. 2012;482(7385):300-1.
9. Maxson Jones K, Ankeny RA, Cook-Deegan R. The Bermuda Triangle: The Pragmatics, Policies, and Principles for Data Sharing in the History of the Human Genome Project. J Hist Biol. 2018 Dec;51(4):693-805. doi: 10.1007/s10739-018-9538-7. PMID: 30390178; PMCID: PMC7307446.
10. McGuire AL, Beskow LM. Informed consent in genomics and genetic research. Annual review of genomics and human genetics. 2010;11:361-81.
11. Raymond MB, Cooper KE, Parker LS, Bonham VL. Practices and Attitudes toward Returning Genomic Research Results to Low-Resource Research Participants. Public health genomics. 2021;24(5-6):241-52.
12. Shabani M, Knoppers BM, Borry P. From the principles of genomic data sharing to the practices of data access committees. EMBO Mol Med. 2015;7(5):507-9.
13. All of Us Research Program I, Denny JC, Rutter JL, Goldstein DB, Philippakis A, Smoller JW, et al. The "All of Us" Research Program. N Engl J Med. 2019;381(7):668-76.

Session 5, July 1, 2024
Genomics, Ethics, and Pediatrics
Joffe

Objectives:

By the end of the class, you will be able to:

- Discuss the ethics of newborn screening using genomic technologies
- Identify the ethical dilemma raised by predictive genetic testing of children for adult-onset conditions
- Describe what we know about the psychosocial consequences of testing children for genetic conditions

Readings:

1. Moyer VA, Calonge N, Teutsch SM, Botkin JR, United States Preventive Services Task F. Expanding newborn screening: process, policy, and priorities. Hastings Cent Rep. 2008;38(3):32-9.
2. Berg JS, Agrawal PB, Bailey DB, Jr., Beggs AH, Brenner SE, Brower AM, et al. Newborn Sequencing in Genomic Medicine and Public Health. Pediatrics. 2017;139(2).
3. Rochman, B. Will My Son Develop Cancer? The Promise (and Pitfalls) of Sequencing Children's Genomes. Time.com, October 22, 2012. Available at https://healthland.time.com/2012/10/22/will-my-son-develop-cancer-the-promise-and-pitfalls-of-sequencing-childrens-genomes/.
4. Botkin JR, Belmont JW, Berg JS, Berkman BE, Bombard Y, Holm IA, et al. Points to Consider: Ethical, Legal, and Psychosocial Implications of Genetic Testing in Children and Adolescents. Am J Hum Genet. 2015;97(1):6-21.
5. Evans JP. Return of results to the families of children in genomic sequencing: tallying risks and benefits. Genet Med. 2013;15(6):435-6.
6. Wakefield CE, Hanlon LV, Tucker KM, Patenaude AF, Signorelli C, McLoone JK, et al. The psychological impact of genetic information on children: a systematic review. Genet Med. 2016;18(8):755-62.
7. Ondrasik, D. Genetic testing is crucial for children with developmental delays. Stat News, April 10, 2023. https://www.statnews.com/2023/04/10/developmental-delays-genetic-testing-cacna1a/

Optional Readings:

1. American Academy of Pediatrics Committee On Bioethics. Ethical and policy issues in genetic testing and screening of children. Pediatrics. 2013 (reaffirmed 2018);131(3):620-2
2. Ross LF, Saal HM, David KL, Anderson RR, American Academy of P, American College of Medical G, et al. Technical report: Ethical and policy issues in genetic testing and screening of children. Genet Med. 2013;15(3):234-45.

3. Callahan KP, Flibotte J, Skraban C, Wild KT, Joffe S, Munson D, et al. Influence of Genetic Information on Neonatologists' Decisions: A Psychological Experiment. Pediatrics. 2022;149(3).
4. Ceyhan-Birsoy O, Murry JB, Machini K, Lebo MS, Yu TW, Fayer S, et al. Interpretation of Genomic Sequencing Results in Healthy and Ill Newborns: Results from the BabySeq Project. Am J Hum Genet. 2019;104(1):76-93.
5. Johnston J, Lantos JD, Goldenberg A, Chen F, Parens E, Koenig BA, et al. Sequencing Newborns: A Call for Nuanced Use of Genomic Technologies. Hastings Cent Rep. 2018;48 Suppl 2:S2-S6.
6. McConkie-Rosell A, Spiridigliozzi GA. "Family matters": a conceptual framework for genetic testing in children. Journal of genetic counseling. 2004;13(1):9-29.
7. Meng L, Pammi M, Saronwala A, Magoulas P, Ghazi AR, Vetrini F, et al. Use of Exome Sequencing for Infants in Intensive Care Units: Ascertainment of Severe Single-Gene Disorders and Effect on Medical Management. JAMA Pediatr. 2017;171(12):e173438.
8. Rhodes R. Why test children for adult-onset genetic diseases? Mt Sinai J Med. 2006;73(3):609-16.
9. Smith HS, Swint JM, Lalani SR, de Oliveira Otto MC, Yamal JM, Russell HV, et al. Exome sequencing compared with standard genetic tests for critically ill infants with suspected genetic conditions. Genet Med. 2020;22(8):1303-10.
10. Whole-genome sequencing of newborn babies presents ethical quandaries. Economist. 2022 May 13.

Session 6, July 8, 2024
Ancestry, Race, and Indigenous Communities
Roberts/Joffe

This class will be held virtually on Zoom

Objectives:

By the end of the class, you will be able to:

- Describe why race is not a biological or genetic concept
- Analyze the role of genetics and other factors in health disparities
- Discuss best practices for conducting contemporary and ancient DNA-based research involving Indigenous communities

Readings:

1. Duster T. Medicine. Race and reification in science. Science. 2005;307(5712):1050-1.
2. Yudell M, Roberts D, DeSalle R, Tishkoff S. Taking race out of human genetics. Science. 2016;351(6273):564-5.
3. Lewis ACF, Molina SJ, Appelbaum PS, Dauda B, Di Rienzo A, Fuentes A, et al. Getting genetic ancestry right for science and society. Science. 2022;376(6590):250-2.
4. West KM, Blacksher E, Burke W. Genomics, Health Disparities, and Missed Opportunities for the Nation's Research Agenda. JAMA. 2017;317(18):1831-2.
5. Wilkins CH, Schindler SE, Morris J C. Addressing Health Disparities Among Minority Populations. JAMA Neurol 77, 1063–1064 (2020).
6. Borrell LN, Elhawary JR, Fuentes-Afflick E, Witonsky J, Bhakta N, Wu AHB, et al. Race and Genetic Ancestry in Medicine - A Time for Reckoning with Racism. N Engl J Med. 2021;384(5):474-80.
7. National Academies of Science, Engineering, and Medicine. Using Population Descriptors in Genetics and Genomics Research, 2023. Chapter 4, “Requisites for Sustained Change.”
8. Mello MM, Wolf LE. The Havasupai Indian tribe case--lessons for research involving stored biologic samples. N Engl J Med. 2010;363(3):204-7.
9. Claw KG, Anderson MZ, Begay RL, Tsosie KS, Fox K, Garrison NA, et al. A framework for enhancing ethical genomic research with Indigenous communities. Nat Commun. 2018;9(1):2957.
10. Fleskes RE, Bader AC, Tsosie KS, Wagner JK, Claw KG, Garrison NA. Ethical Guidance in Human Paleogenomics: New and Ongoing Perspectives. Annu Rev Genomics Hum Genet. 2022.
11. South African San Institute. San Code of Research Ethics. 2017

Optional Readings:

1. Dobzhansky T. Genetics and equality: equality of opportunity makes the genetic diversity among men meaningful. Science. 1962;137(3524):112-4.

2. National Academies of Science, Engineering, and Medicine. Using Population Descriptors in Genetics and Genomics Research, 2023.
3. Baharian S, Barakatt M, Gignoux CR, Shringarpure S, Errington J, Blot WJ, et al. The Great Migration and African-American Genomic Diversity. PLoS Genetics. 2016;12(5):e1006059.
4. Birney, E., Inouye, M., Raff, J., Rutherford, A. & Scally, A. The language of race, ethnicity, and ancestry in human genetic research. *Arxiv* (2021).
5. Bonham VL, Green ED, Perez-Stable EJ. Examining How Race, Ethnicity, and Ancestry Data Are Used in Biomedical Research. JAMA. 2018;320(15):1533-4.
6. Bryc K, Durand EY, Macpherson JM, Reich D, Mountain JL. The genetic ancestry of African Americans, Latinos, and European Americans across the United States. Am J Hum Genet. 2015;96(1):37-53.
7. Lee SS, Mountain J, Koenig B, Altman R, Brown M, Camarillo A, et al. The ethics of characterizing difference: guiding principles on using racial categories in human genetics. Genome Biol. 2008;9(7):404.
8. Sankar P, Cho MK, Mountain J. Race and ethnicity in genetic research. Am J Med Genet A. 2007;143A(9):961-70.
9. Khamsi R. A more-inclusive genome project aims to capture all of human diversity. Nature. 2022;603(7901):378-81.
10. Lipphardt V, Surdu M, Ellebrecht N, Pfaffelhuber P, Wienroth M, Rappold GA. Europe's Roma people are vulnerable to poor practice in genetics. Nature. 2021;599(7885):368-71.
11. Alpaslan-Roodenberg S, Anthony D, Babiker H, Banffy E, Booth T, Capone P, et al. Ethics of DNA research on human remains: five globally applicable guidelines. Nature. 2021;599(7883):41-6.
12. Kennett DJ, Plog S, George RJ, Culleton BJ, Watson AS, Skoglund P, et al. Archaeogenomic evidence reveals prehistoric matrilineal dynasty. Nat Commun. 2017;8:14115.
13. Cortez, A. D., Bolnick, D. A., Nicholas, G., Bardill, J. & Colwell, C. An ethical crisis in ancient DNA research: Insights from the Chaco Canyon controversy as a case study. *J Soc Archaeol* **21**, 157–178 (2021).
14. Nakatsuka, N. *et al.* Genetic continuity and change among the Indigenous peoples of California. *Nature* **624**, 122–129 (2023). (*Note: see especially ethics and inclusion statement*)
15. Kowal, E. *et al.* Community partnerships are fundamental to ethical ancient DNA research. *Hum. Genet. Genom. Adv.* **4**, 100161 (2023).

Session 7, July 15, 2024
Reproductive Ethics, Disability, and Genomics
Joffe

Objectives:

By the end of the class, you will be able to:

- Identify the genetic technologies used in reproductive medicine
- Discuss the ethical challenges raised by genetic testing in reproductive contexts
- Describe the disability rights critiques of preimplantation and prenatal genetic testing

Readings:

1. Committee Opinion No. 693: Counseling About Genetic Testing and Communication of Genetic Test Results. Obstet Gynecol. 2017 (reaffirmed 2020);129(4):e96-e101.
2. Committee Opinion No. 690: Carrier Screening in the Age of Genomic Medicine. Obstet Gynecol. 2017 (reaffirmed 2023);129(3):e35-e40.
3. Whitten CF. Sickle-cell programming--an imperiled promise. N Engl J Med. 1973;288(6):318-9.
4. Morain S, Greene MF, Mello MM. A new era in noninvasive prenatal testing. N Engl J Med. 2013;369(6):499-501.
5. Parens E, Asch A. The disability rights critique of prenatal genetic testing. Reflections and Recommendations. Hastings Cent Rep. 1999;29(5):S1-22.
6. Reingold RB, Gostin LO. Banning Abortion in Cases of Down Syndrome: Important Lessons for Advances in Genetic Diagnosis. JAMA. 2018;319(23):2375-6.
7. Becker AJ. I'm Thankful Every Day for the Decision I Made After My Prenatal Tests. New York Times. 2022 February 2, 2022;Sect. A.
8. Johnston J, Matthews LJ. Polygenic embryo testing: understated ethics, unclear utility. Nat Med. 2022;28(3):446-8.

Optional Readings:

1. Bayefsky MJ, Berkman BE. Implementing Expanded Prenatal Genetic Testing: Should Parents Have Access to Any and All Fetal Genetic Information? Am J Bioeth. 2022;22(2):4-22.
2. Access to reproductive options after prenatal diagnosis-patient access and physician responsibilities: an updated position statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2020;22(1):3.
3. Norton ME, Jacobsson B, Swamy GK, Laurent LC, Ranzini AC, Brar H, et al. Cell-free DNA analysis for noninvasive examination of trisomy. N Engl J Med. 2015;372(17):1589-97.
4. Preterm-Cleveland v. McCloud, No. 18-3329 (6th Cir. 2019)
5. National Council on Disability. Genetic Testing and the Rush to Perfection: Part of the Bioethics and Disability Series. October 23, 2019.
6. Nuffield Council on Bioethics. Non-invasive prenatal testing: ethical issues. March 2017.
7. Massie J, Castellani C, Grody WW. Carrier screening for cystic fibrosis in the new era of medications that restore CFTR function. Lancet. 2014;383(9920):923-5.

8. Bell CJ, Dinwiddie DL, Miller NA, Hateley SL, Ganusova EE, Mudge J, et al. Carrier testing for severe childhood recessive diseases by next-generation sequencing. Sci Transl Med. 2011;3(65):65ra4.

Session 8, July 22, 2024
Precision Medicine
Joffe

Objectives:

By the end of the class, you will be able to:

- Define the concept of precision medicine
- Discuss the tension between precision medicine and population health
- Describe why genomic diversity poses challenges for precision medicine

Readings:

1. Jameson, J. L. & Longo, D. L. Precision Medicine — Personalized, Problematic, and Promising. *New Engl J Medicine* **372**, 2229–2234 (2015).
2. Hey SP, Kesselheim AS. Countering imprecision in precision medicine. Science. 2016;353(6298):448-9.
3. Joyner MJ, Paneth N. Seven Questions for Personalized Medicine. JAMA. 2015;314(10):999-1000.
4. Khoury MJ, Galea S. Will Precision Medicine Improve Population Health? JAMA. 2016;316(13):1357-8.
5. McCarthy M, Birney E. Personalized profiles for disease risk must capture all facets of health. Nature. 2021;597(7875):175-7.
6. Popejoy, A. B. & Fullerton, S. M. Genomics is failing on diversity. *Nature* **538**, 161–164 (2016).
7. Manrai AK, Funke BH, Rehm HL, Olesen MS, Maron BA, Szolovits P, et al. Genetic Misdiagnoses and the Potential for Health Disparities. N Engl J Med. 2016;375(7):655-65.
8. Huntington SF, Davidoff AJ, Gross CP. Precision Medicine in Oncology II: Economics of Targeted Agents and Immuno-Oncology Drugs. J Clin Oncol. 2020;38(4):351-8.

Optional Readings:

1. Bertier, G., Carrot-Zhang, J., Ragoussis, V. & Joly, Y. Integrating precision cancer medicine into healthcare—policy, practice, and research challenges. *Genome Med* **8**, 108 (2016).
2. Landry, L. G., Ali, N., Williams, D. R., Rehm, H. L. & Bonham, V. L. Lack Of Diversity In Genomic Databases Is A Barrier To Translating Precision Medicine Research Into Practice. *Health Affair* **37**, 780–785 (2018).
3. Topol EJ. Individualized medicine from prewomb to tomb. Cell. 2014;157(1):241-53.
4. Hirsch FR, Scagliotti GV, Mulshine JL, Kwon R, Curran WJ, Jr., Wu YL, et al. Lung cancer: current therapies and new targeted treatments. Lancet. 2017;389(10066):299-311.
5. Burgener EB, Moss RB. Cystic fibrosis transmembrane conductance regulator modulators: precision medicine in cystic fibrosis. Curr Opin Pediatr. 2018;30(3):372-7.

6. Pregelj L, Hwang TJ, Hine DC, Siegel EB, Barnard RT, Darrow JJ, et al. Precision Medicines Have Faster Approvals Based On Fewer And Smaller Trials Than Other Medicines. Health Aff (Millwood). 2018;37(5):724-31.
7. Subbiah V, Kurzrock R. Universal Genomic Testing Needed to Win the War Against Cancer: Genomics IS the Diagnosis. JAMA Oncol. 2016;2(6):719-20. (*counterpoint to West*)
8. West HJ. No Solid Evidence, Only Hollow Argument for Universal Tumor Sequencing: Show Me the Data. JAMA Oncol. 2016;2(6):717-8. (*counterpoint to Subbiah*)
9. Petrovski S, Goldstein DB. Unequal representation of genetic variation across ancestry groups creates healthcare inequality in the application of precision medicine. Genome Biol. 2016;17(1):157.
10. Bayer R, Galea S. Public Health in the Precision-Medicine Era. N Engl J Med. 2015;373(6):499-501.
11. Precision medicine needs an equity agenda. *Nat Med* **27**, 737–737 (2021).

Session 9a, July 29, 2024
Direct-to-Consumer Genomics
Joffe

Objectives:

By the end of the class, you will be able to:

- Identify the potential benefits and risks of direct-to-consumer genetic testing for medical conditions
- Discuss the regulation of direct-to-consumer genetic testing
- Describe the implications of direct-to-consumer genetic testing for conceptions of ancestry

Readings:

1. Bloss CS, Schork NJ, Topol EJ. Effect of direct-to-consumer genomewide profiling to assess disease risk. N Engl J Med. 2011;364(6):524-34.
2. Majumder MA, Guerrini CJ, McGuire AL. Direct-to-Consumer Genetic Testing: Value and Risk. Annu Rev Med. 2021;72:151-66.
3. Direct-to-consumer genetic testing: a revised position statement of the American College of Medical Genetics and Genomics. Genet Med. 2016;18(2):207-8.
4. Phillips KA, Trosman JR, Douglas MP. Emergence of Hybrid Models of Genetic Testing Beyond Direct-to-Consumer or Traditional Labs. JAMA. 2019;321(24):2403-4.
5. Moneer O, Miller JE, Shah ND, Ross JS. Direct-to-consumer personal genomic tests need better regulation. Nat Med. 2021;27(6):940-3.
6. Fox M. Now you can buy a home DNA test for 10 different diseases. NBC.com. 2017. Available from: https://www.nbcnews.com/health/health-news/fda-approves-23andme-s-home-dna-tests-10-diseases-n743416.

Optional Readings:

1. Tandy-Connor S, Guiltinan J, Krempely K, LaDuca H, Reineke P, Gutierrez S, et al. False-positive results released by direct-to-consumer genetic tests highlight the importance of clinical confirmation testing for appropriate patient care. Genet Med. 2018;20(12):1515-21.
2. U.S. Food and Drug Administration. FDA allows marketing of first direct-to-consumer tests that provide genetic risk information forcertain conditions 2017 [Available from: https://www.fda.gov/news-events/press-announcements/fda-allows-marketing-first-direct-consumer-tests-provide-genetic-risk-information-certain-conditions.
3. U.S. Food and Drug Administration. FDA authorizes, with special controls, direct-to-consumer test that reports three mutations in the BRCA breast cancer genes 2018 [updated March 6. Available from: https://www.fda.gov/news-events/press-announcements/fda-authorizes-special-controls-direct-consumer-test-reports-three-mutations-brca-breast-cancer.
4. McGuire AL, Burke W. An unwelcome side effect of direct-to-consumer personal genome testing: raiding the medical commons. JAMA. 2008;300(22):2669-71.

5. Ostergren JE, Gornick MC, Carere DA, Kalia SS, Uhlmann WR, Ruffin MT, et al. How Well Do Customers of Direct-to-Consumer Personal Genomic Testing Services Comprehend Genetic Test Results? Findings from the Impact of Personal Genomics Study. Public Health Genomics. 2015;18(4):216-24.
6. Guerrini CJ, Robinson JO, Bloss CC, Bash Brooks W, Fullerton SM, Kirkpatrick B, et al. Family secrets: Experiences and outcomes of participating in direct-to-consumer genetic relative-finder services. Am J Hum Genet. 2022;109(3):486-97.
7. Laestadius LI, Rich JR, Auer PL. All your data (effectively) belong to us: data practices among direct-to-consumer genetic testing firms. Genet Med. 2017;19(5):513-20.
8. Larmuseau MHD. Growth of ancestry DNA testing risks huge increase in paternity issues. Nat Hum Behav. 2019;3(1):5.
9. Padawer R. Sigrid Johnson was Black. A DNA test said she wasn't. New York Times. 2018 November 18.

Session 9b, July 29, 2024
Genomics and the Courts
Joffe

Objectives:

By the end of this class, you will be able to:

- Identify major sources of law that may constrain law enforcement's use of genetic data
- Explain how investigative genetic genealogy differs from traditional investigative uses of genetic data by law enforcement
- Articulate and defend at least one policy change you would support

Readings:

1. Kroll-Zaidi R. Your DNA test could send a relative to jail. New York Times. 2021 December 27, 2021;Sect. Magazine.
2. Hazel JW, Clayton EW, Malin BA, Slobogin C. Is it time for a universal genetic forensic database? Science. 2018;362(6417):898-900.
3. Ram N, Murphy EE, Suter SM. Regulating forensic genetic genealogy. Science. 2021;373(6562):1444-6.
4. Ram N. Investigative genetic genealogy and the future of genetic privacy. The SciTech Lawyer. 2020;16(4):19-22.
5. McSwiggan S, Elger B, Appelbaum PS. The forensic use of behavioral genetics in criminal proceedings: Case of the MAOA-L genotype. Int J Law Psychiatry. 2017;50:17-23.

Optional Readings:

1. Maryland v. King. 133 S. Ct 1958, 2013.
2. United States v. Kincade. United States Court of Appeals for the Ninth Circuit, 2004. 379 F.3d 813.
3. Ram N. You can't hide your genes. Slate [Internet]. 2018 May 7, 2022. Available from: https://slate.com/technology/2018/05/consumer-genetic-databases-arent-the-only-side-door-for-police-to-get-your-dna.html.
4. Guerrini CJ, Wickenheiser RA, Bettinger B, McGuire AL, Fullerton SM. Four misconceptions about investigative genetic genealogy. J Law Biosci. 2021;8(1):lsab001.

Session 10, August 5, 2024
Social and Behavioral Genomics
Joffe

Objectives:

By the end of this class, you will be able to:

- Describe the use of polygenic risk scores in social and behavioral genomics
- Analyze the ethics of genomic research to predict social and behavioral traits
- Discuss whether it is ever appropriate to prohibit some scientific research due to social risks

Readings:

1. Marchant GE, Bird SJ. Editors' overview: forbidding science? Sci Eng Ethics. 2009;15(3):263-9.
2. Harden KP. Why progressives should embrace the genetics of education. New York Times. 2018 July 28;Sect. Opinion.
3. Tabery J. Why Is Studying the Genetics of Intelligence So Controversial? Hastings Cent Rep. 2015;45(5 Suppl):S9-14.
4. Roberts D. Can Research on the Genetics of Intelligence Be "Socially Neutral"? Hastings Cent Rep. 2015;45(5 Suppl):S50-3.
5. Meyer, M. N. *et al.* Wrestling with Social and Behavioral Genomics: Risks, Potential Benefits, and Ethical Responsibility. *Hastings Cent. Rep.* **53**, S2–S49 (2023). (***Executive summary, pgs S2 to S7, only***)
6. Savulescu J, Earp BD, Schuklenk U. Ethics of genetic research on same-sex sexual behaviour. Nat Hum Behav. 2021;5(9):1123-4.
7. Ganna A, Verweij KJH, Nivard MG, Maier R, Wedow R, Busch AS, et al. Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior. Science. 2019;365(6456). (***See note at top of first page re: sections to read***)
8. Docherty A, Kious B, Brown T, Francis L, Stark L, Keeshin B, et al. Ethical concerns relating to genetic risk scores for suicide. Am J Med Genet B Neuropsychiatr Genet. 2021;186(8):433-44.
9. Martschenko, D. O. "The elephant in the room": social responsibility in the production of sociogenomics research. *Biosocieties* 1–19 (2021) doi:10.1057/s41292-021-00239-3.
10. Kozlov, M. The controversial embryo tests that promise a better baby. *Nature* **609**, 668–671 (2022).

Optional Readings:

1. Meyer, M. N. *et al.* Wrestling with Social and Behavioral Genomics: Risks, Potential Benefits, and Ethical Responsibility. *Hastings Cent. Rep.* **53**, S2–S49 (2023). (***Full article***)
2. Ganna A, Verweij KJH, Nivard MG, Maier R, Wedow R, Busch AS, et al. Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior. Science. 2019;365(6456). (***Full article***)

3. Lee JJ, Wedow R, Okbay A, Kong E, Maghzian O, Zacher M, et al. Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals. Nat Genet. 2018;50(8):1112-21.
4. Okbay A, Wu Y, Wang N, Jayashankar H, Bennett M, Nehzati SM, et al. Polygenic prediction of educational attainment within and between families from genome-wide association analyses in 3 million individuals. Nat Genet. 2022;54(4):437-49.
5. Zietsch BP, Sidari MJ, Abdellaoui A, Maier R, Langstrom N, Guo S, et al. Genomic evidence consistent with antagonistic pleiotropy may help explain the evolutionary maintenance of same-sex sexual behaviour in humans. Nat Hum Behav. 2021;5(9):1251-8.
6. Ball P. The IQ trap: how the study of genetics could transform education. New Statesman. 2018 April 16, 2018.
7. Belluck P. Many Genes Influence Same-Sex Sexuality, Not a Single 'Gay Gene'. New York Times. 201 August 29, 2019.