Regenerative Medicine, Cell Manufacturing, and Society
Spring 2023

Thursdays 2:20 to 4:20 Eastern /1:20-3:20 PM Central

This multi-institutional course introduces students working in cell biology and regenerative medicine research to ethical, policy, and social issues relevant to the field of stem cell research and the development of cell therapies. Graduate students at Georgia Institute of Technology (GT), University of Georgia (UGA), University of Puerto Rico – Mayagüez (UPRM) and University of Wisconsin – Madison (UW) who are participating in the NSF Center for Cell Manufacturing Technologies (CMaT) are expected to take it as part of their graduate programs. The course is open to other interested graduate students at each institution and, with permission, advanced undergraduates.

Instructors	**Office Hours / Contact Information**
Aaron Levine, Ph.D. Associate Professor School of Public Policy Georgia Institute of Technology	By appointment 216 DM Smith Building adlevine@gatech.edu
Anita Bhattacharyya, Ph.D. Assistant Professor Department of Cell and Regenerative Biology University of Wisconsin – Madison	By appointment 623 Waisman bhattacharyy@waisman.wisc.edu
James Warnock, Ph.D. Professor & Chair School of Chemical, Materials & Biomedical Engineering University of Georgia	By appointment Driftmier 2126 or Riverbend South 112 james.warnock@uga.edu
Mauricio Cabrera-Ríos, PhD Professor Department of Industrial Engineering University of Puerto Rico – Mayagüez	By appointment mauricio.cabrera1@upr.edu

Learning Outcomes: By the end of the course, students will:

1. Understand current and past legal, political, and social issues related to regenerative medicine. This includes laws and regulations, but also an understanding of clinical ethics issues, translational research and commercialization, and emerging novel techniques requiring careful ethical consideration.
2. Understand more about relations of science, the state, and public, particularly around controversial or novel innovations; and learn how best to address emerging controversies and public concerns ethically in their professional careers.
3. Learn the guidelines for the responsible conduct of research for stem cell science and cell manufacturing, where to access regulatory and oversight documents, and how to apply for research protocols with ethics oversight.
4. Gain analytical skills for addressing policy, legal, and social issues through research and writing exercises. Students will also learn analytical and professional presentation skills through classroom interactions and discussion.

Campus-Specific Details:

Campus	Room	Course Number
GT	EBB 3029 for in-person meetings, Virtual	PUBP 8803 – AL
UGA	Driftmier Engineering Center, Room 1215, Virtual	BIOE 8120
UPRM	Virtual	BING 8995
UW	WIMR 1022 (1/24/23 5001A WIMR), Virtual	CRB 615

The course is designed for the needs of science, engineering and medical students working in stem cell, cellular and molecular biology, and related research as well as social science students interested in learning more about the intersection of biomedical research, ethics and policy. At the University of Wisconsin, it also meets requirements for upper-level undergraduate science majors pursuing the Certificate of Excellence in Stem Cell Science. **Note: Basic fundamentals of stem cell science will not be covered**. For those less familiar with stem cell research, background reading is **suggested before the course begins** (e.g. Stem Cell Basics," available at https://stemcells.nih.gov/info/basics.htm)

Instructional Mode: The course combines lecture and discussion. This includes live, real-time interaction with students from other campuses via videoconferencing. Participation is designed to help students engage with students and faculty from other U.S. universities in real-time. Most class sessions will be recorded and available for students to review in case of technical difficulties.

Requirements: Active participation, completion of all readings and assignments, and attendance are required. A student may have no more than 1 unexcused absence (excused absences are defined as those due to illness or exceptional circumstances and should be approved in advance, whenever possible). In addition to in-class work, students will conduct reading, research, and writing outside of class. Evaluation is based on the following: **participation (25%)**, **reflection papers (30%), group project 1 (15%) and group project 2 (30%)**

Participation evaluation for all students:

▪ Students **must read required material** each week.

▪ Students' input to the discussions should demonstrate engagement with the readings for that day plus material presented in class. We may have lively debates about some topics; this helps to sharpen your skills in identifying issues and arguing a point. At the same time, please be respectful of your colleagues when expressing your point of view.

A = excellent; frequent and thoughtful contributions to discussion; shows engagement with readings; contributes additional insights or critiques

B = good; volunteers summary of readings or offers interpretations; responds to other students' positions or questions

C = minimal; answers questions when directly asked; occasional participation

D = poor; did not participate in discussions or responses reflect that student did not read or engage with readings

F= failure; no participation; does not respond to questions; OR >1 unexcused absence

▪ Students are also expected to contribute to the class Slack site. This is a venue for discussions of class readings among yourselves and your instructors. You can use Slack to raise questions about the reading, highlight news related to class topics, communicate about your group projects, etc. Contributions to the Slack site are one component of your participation in the class. (Students should receive an invitation to the class Slack site the first week of classes and should create an account and join the site as soon as possible.)

Each student will complete three individual **reflection papers**. These are short individual responses to class content (both reading and class discussion). Prompts are provided after class concludes on selected Wednesdays and are due by 5pm the following Monday. Tentative dates for the reflection paper assignments are shown below. (Each is 10% of the final grade.) Reflection papers will be evaluated on accuracy, completeness, and quality of analysis.

	Assigned	**Due**
Reflection Paper #1	January 26 (after class)	January 30 by 5pm
Reflection Paper #2	February 16 (after class)	February 20 by 5pm
Reflection Paper #3	March 2 (after class)	March 6 by 5pm

Group Projects: In addition to the individual reflection papers, students will complete two group projects. The first will be a comparative analysis of the policy environment for stem cell research and cell therapy in a country other than the United States. The second will be a mock bioethics commission report, analyzing the scientific, ethical and policy aspects relevant to stem cell science and the development of cell therapies. Teams will be assigned across the universities participating in the course for both projects. These assignments will require reading beyond the requirements listed in the syllabus, and evaluation will be based on the quality of analytical skills displayed as well as the quality of the reports and presentations. Both group project assignments will include written reports and presentations to the class. More details will be provided on the class Dropbox site. For the larger second project, a draft research plan is required as well. Tentative dates relevant to the two group projects are included in the table below:

	Assigned	**Draft Plan**	**Presentation**	**Final Report**
Group Project #1	February 2	N/A	February 23	February 23
Group Project #2	March 10	March 27	April 13 April 20	April 28

Logistics and Communication: All readings are posted on the class Dropbox site**.** The required readings are noted below in the schedule. We will also maintain a class Slack account for discussion of class-related topics, posting of relevant articles, etc. See discussion in "Participation" above.

TENTATIVE CLASS SCHEDULE (Including readings and assignments)

Week	Sites	Subject	Lead Instructor
Jan 12	GT, UGA, UPRM	Class Overview	Levine
	No reading		
Jan 19	GT, UGA, UPRM	Overview of policy landscape – Key institutions Legal, social & ethical backgrounds for regenerative medicine in the U.S.	Levine
	Cossu, G., et al. (2018). Lancet Commission: Stem cells and regenerative medicine. *Lancet* 391(10123): 883-910. **Skim** to identify major issues Warren, M.A. (2000). *Moral Status: Obligations to Persons and Other Living Things* Oxford University Press: Oxford, Chapter 1 Gottweis, H. (2010). "The endless hESC controversy in the United States: history, context, and prospects." *Cell Stem Cell* 7(5): 555-558 Speech by President George W. Bush regarding human stem cell research, August 9, 2001 Speech by President Obama regarding human stem cell research, March 9, 2009 Dickey-Wicker Amendment, Rabb Letter		
Jan 26	All	State and non-governmental policy institutions Policy uncertainty and heterogeneity	Levine
	VonReyn, J., Das, A., and Hogle, L,F. Ch 6 "Beyond the Checkboxes: Research Integrity for Regenerative Medicine Researchers" in Hogle, L. *Regenerative Medicine Ethics*. NY: Springer. **Read section 6.2** "Administrative Organization and Oversight" (p. 133-141), with particular attention to the discussion of stem cells (p. 136-141). Please also familiarize yourself with **6.3** "Essential components of Responsible Conduct of Research" (p. 141-144). Caulfield et al. 2009. The Stem Cell Research Environment: A Patchwork of Patchworks. *Stem Cell Reviews and Reports* 5: 82-88. Levine, AD 2011. Policy Uncertainty and the Conduct of Stem Cell Research" *Cell Stem Cell* 8(2): 132-5. **Reflection Paper #1 released after class, due Monday, January 30 at 5pm**		

Week	Sites	Subject	Lead Instructor
Feb 2	All	Critical issues in preclinical research –Ethical issues of methods & materials (organoids / chimeras)	Bhattacharyya

Bredenoord, A., Clevers, H., and Knoblich, J. 2017. Human tissues in a dish: the research and ethical implications of organoid technology. Science 355:260. https://science.sciencemag.org/content/355/6322/eaaf9414.long

Limit on lab-grown human embryos dropped by stem-cell body. Nature May 26, 2021 https://www.nature.com/articles/d41586-021-01423-y

Reardon, Sara. Human brain cells implanted in rats prompt excitement-and concern. Nature. 2022 Oct;610(7932):427-428. https://www.nature.com/articles/d41586-022-03238-x

VonReyn, J., Das, A., and Hogle, L, F. Beyond the checkboxes: research integrity for regenerative medicine researchers. Read Sec 6.3.2 "Oversight of Research Using Animals Including Chimeras" (p. 22-25).

Group Project #1 Released

Feb 9	All	Clinical issues: patients and practitioners	Capitini

Sanchez, R., Silberstein, L. E., Lindblad, R. W., Welniak, L. A., Mondoro, T. H., & Wagner, J. E. (2013). Strategies for More Rapid Translation of Cellular Therapies for Children: A US Perspective. *Pediatrics*, *132*(2), 351–358.

Weber, E.W., Maus, M.V., Mackall, C.L. (2020). The Emerging Landscape of Immune Cell Therapies. Cell 181, April 2, 2020.https://doi.org/10.1016/j.cell.2020.03.001

VonReyn, J., Das, A., and Hogle, L,F. Beyond the checkboxes: research integrity for regenerative medicine researchers. Read Sec 6.3.1 "Human subjects: protecting research participants and tissue donors in regenerative research" (p. 14 -19).

Feb 16	All	Critical issues in preclinical research – Authentication, Purity, Quality Control	Bhattacharyya

Barker RA, Carpenter MK, Forbes S, Goldman SA, Jamieson C, Murry CE, Takahashi J, Weir G. The Challenges of First-in-Human Stem Cell Clinical Trials: What Does This Mean for Ethics and Institutional Review Boards? *Stem Cell Reports*. 2018 May 8;10(5):1429-1431

Barazzetti, G., Hurst, S.A., and Mauron A. (2016). Adapting Preclinical Benchmarks for First-in-Human Trials of Human Embryonic Stem Cell-Based Therapies. *Stem Cells Transl. Med*. 5(8), 1058–1066.

Reflection Paper #2 released after class, due Monday, February 20 at 5pm

Week	Sites	Subject	Lead Instructor
Feb 23	All	CRISPR-Cas9 and gene editing ethics International Policy Environment	Saha and Levine

Hurlbut, J. B., Jasanoff, S., Saha, K., Ahmed, A., Appiah, A. et al (2018). Building Capacity for a Global Genome Editing Observatory: Conceptual Challenges. *Trends in Biotechnology*, *36*(7), 639–641.

Jasanoff, S., & Hurlbut, J. B. (2018). A global observatory for gene editing. *Nature*, *555*(7697), 435–437.

Lundberg, A. S., & Novak, R. (2015). CRISPR-Cas Gene Editing to Cure Serious Diseases: Treat the Patient, Not the Germ Line. *The American Journal of Bioethics: AJOB*, *15*(12), 38–40.

Saha, K., Hurlbut, J. B., Jasanoff, S., Ahmed, A., Appiah, A., et al (2018). Building Capacity for a Global Genome Editing Observatory: Institutional Design. *Trends in Biotechnology,* 36(8): 741-43

Charo, R. A. (2016). On the Road (to a Cure?) — Stem-Cell Tourism and Lessons for Gene Editing. *New England Journal of Medicine*, *374*(10), 901–903.

Group Project #1 Report / Presentations due

Mar 2	All	FDA / Regulatory Policy & Unproven Therapies	Levine and Chandnani

Marks, P. and Gottlieb, S. 2018. Balancing Safety and Innovation for Cell-Based Regenerative Medicine. *New England Journal of Medicine*. 378(10): 954-959.

Hogle, L. F. and A. Das (2017). "The social production of evidence: regenerative medicine and the 21st Century Cures Act." *Regenerative Medicine* 12(6): 581-586.

Michael Mendicino, Yong Fan, Deborah Griffin, Kurt C. Gunter, Karen Nichols (2019). Current state of U.S. Food and Drug Administration regulation for cellular and gene therapy products: potential cures on the horizon, *Cytotherapy*, 21(7): 699-724. **Skim and use as reference for specific policies**

Reflection Paper #3 released after class, due Monday, March 6 at 5pm

Mar 9	GT, UPRM, UW	Spring Break – No Class Meeting	

Group Project #2 released

Week	Sites	Subject	Lead Instructor
Mar 16	GT, UGA, UPRM	Academic – industry relations	Murphy
	Ornstein, Charles and Thomas, Katie. (2018). Top Cancer Researcher Fails to Disclose Corporate Financial Ties in Major Research Journals. *New York Times*. https://www.nytimes.com/2018/09/08/health/jose-baselga-cancer-memorial-sloan-kettering.html Additional readings TBA		
Mar 23	UGA, UPRM, UW	Technology transfer, material transfer agreements, patenting, and intellectual property debates	Levine & Walsh
	AUTM White Paper (2007) "In the Public Interest: Nine Points to Consider in Licensing University Technology." Walsh, J.P., Cho, C., and Cohen, W.M. (2005). View from the Bench: Patents and Material Transfers *Science* 309: 2002-2003.		
Mar 30	All	Insurance, reimbursement and the economics of cell therapies	Howard
	Howard, D. H., et al. (2015). Pricing in the Market for Anticancer Drugs. *Journal of Economic Perspectives* 29(1): 139-162. Bach, P. B., et al. (2017). FDA approval of tisagenlecleucel: Promise and complexities of a $475 000 cancer drug. *JAMA* 318(19): 1861-1862.		
Apr 6	GT, UGA, UW	Bioethics in industry / Emerging issues	Levine & Childers
	Readings TBA		
Apr 13	All	**Student presentations of Group Project #2**	N/A
	None		
Apr 20	All	**Student presentations of Group Project #2**	N/A
Apr 27	UGA, UPRM, UW	Course wrap-up and discussion	TBA
	Readings TBA		

Week	Sites	Subject	Lead Instructor
May 4	UPRM, UW	Course wrap-up and discussion	TBA
	Readings TBA		

Group Project #2 Final Reports Due Friday, April 28 at 5pm