Regenerative Medicine, Cell Manufacturing, and Society
Fall 2019

Mondays 2:20 to 4:25 Eastern /1:20-3:25 PM Central

This multi-institutional course is designed primarily to introduce advanced 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 (in-person or virtual) 216 DM Smith Building adlevine@gatech.edu, 404-385-3329
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 james.warnock@uga.edu
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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	Krone Engineered Biosystems Building (EBB) 3029	PUBP 8803 – AL
UGA	Driftmier Engineering Center, Room 103	BIOE 8120
UPRM	L-241	BING 8995
UW	330 Waisman Center	MHB/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. 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 classroom 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.

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 classroom 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 Mondays and are due by **5pm** on Friday of the same week. 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	September 16 (after class)	September 20 by 5pm
Reflection Paper #2	October 7 (after class)	October 11 by 5pm
Reflection Paper #3	November 4 (after class)	November 8 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 an analysis of social, ethical, and policy issues in an integrated case study. 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 final 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 due October 28. Tentative dates relevant to the two group projects are included in the table below:

	Assigned	**Draft Plan**	**Presentation**	**Final Report**
Group Project #1	September 16	N/A	October 7	October 7
Group Project #2	October 14	October 28	December 2	December 9

Logistics and Communication: All readings are posted on the class Dropbox site**.** The required readings are noted below in the schedule. Official course communication will be conducted via email using the class listserv (cmat_ethics_class@lists.gatech.edu). We will also maintain a class Slack account for discussion of class-related topics, posting of relevant articles, etc. See discussion in "Participation" above.

Electronic Etiquette Policy: Students are not allowed to use laptops, tablets, or phones (except during emergencies) during class meetings for any purpose other than **to take notes and access materials related to the course.** Surfing the internet and/or text messaging is not appropriate and will reduce participation grades.

TENTATIVE CLASS SCHEDULE (Including readings and assignments)

Week	Sites	Subject	Lead Instructor
Aug 12	UPRM	Welcome / Introductory Discussion	Levine
	No readings		
Aug 19	GT, UGA, UPRM	Class Overview / Introductory Discussion	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		
Aug 26	GT, UGA, UPRM	Workplace issues: diversity & inclusion, successful professional conduct	Benton-Johnson
	Ong, M., Wright, C., Espinosa, L., & Orfield, G. (2011). Inside the Double Bind: A Synthesis of Empirical Research on Undergraduate and Graduate Women of Color in Science, Technology, Engineering, and Mathematics. *Harvard Educational Review*, *81*(2), 172–209.		
Sept 2		NO CLASS-LABOR DAY	
Sept 9	All	Overview of policy landscape – Key institutions Legal, social & ethical backgrounds for regenerative medicine in the U.S.	Levine
	Gottweis, H. (2010). "The endless hESC controversy in the United States: history, context, and prospects." *Cell Stem Cell* 7(5): 555-558 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). Dickey-Wicker Amendment, Rabb Letter **Skim and use as reference**		
Sept 16	All	FDA / Regulatory Policy	Levine
	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 #1 due September 20 at 5pm**		

Week	Sites	Subject	Lead Instructor
Sept 23	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		
	Hyun, Wilkerson, and Johnston. Embryology policy: Revisit the 14-day rule. Nature. 2016 May 12;533(7602):169-71. doi: 10.1038/533169a. https://www.nature.com/news/embryology-policy-revisit-the-14-day-rule-1.19838		
	Loike and Kadish, Ethical rejections of xenotransplantation? The potential and challenges of using human-pig chimeras to create organs for transplantation. *EMBO Rep*. 2018 Aug;19(8). https://www.embopress.org/doi/full/10.15252/embr.201846337		
	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).		
Sept 30	All	CRISPR-Cas9 and gene editing ethics International Policy Environment	Saha
	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.		
Oct 7	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.		
	Group Project #1 Report / Presentations due October 7		
	Reflection Paper #2 due October 11 at 5pm		

Week	Sites	Subject	Lead Instructor
Oct 14	UW (UGA TBA)	Workplace issues: diversity & inclusion, successful professional conduct	Fitzpatrick
	Ong, M., Wright, C., Espinosa, L., & Orfield, G. (2011). Inside the Double Bind: A Synthesis of Empirical Research on Undergraduate and Graduate Women of Color in Science, Technology, Engineering, and Mathematics. *Harvard Educational Review*, *81*(2), 172–209.		
Oct 21	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. Piscopo, N. J., Mueller, K. P., Das, A., Hematti, P., Murphy, W. L., Palecek, S. P., Capitini, C. M. and Saha, K. (2018), Bioengineering Solutions for Manufacturing Challenges in CAR T Cells. *Biotechnol. J.*, 13: 1700095. 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).	
Oct 28	All	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 **Group Project #2 Research Plan Due**		
Nov 4	All	Unproven Therapies & Medical Crowdfunding	Levine
	Sipp D., et al. (2017). Marketing of unproven stem cell–based interventions: A call to action. *Science Translational Medicine*. 9(397): eaag0426 Turner, Leigh. (2018). The US Direct-to-Consumer Marketplace for Autologous Stem Cell Interventions. *Perspectives in Biology and Medicine* 61(1): 7-24. Young MJ, Scheinberg E. The Rise of Crowdfunding for Medical Care: Promises and Perils. *JAMA.* 2017;317(16):1623–1624. Snyder J, Turner L, Crooks VA. Crowdfunding for Unproven Stem Cell–Based Interventions. *JAMA.* 2018;319(18):1935–1936. **Reflection Paper #3 due November 8 at 5pm**		
Nov 11	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.		

Week	Sites	Subject	Lead Instructor
Nov 18	All	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.		
Nov 25	All	Emerging social, ethical and policy issues in cell manufacturing	Levine
	Readings TBA		
Dec 2	All*	Student presentations of Group Project #2 Course wrap-up and discussion	N/A
Dec 9	UW	Course wrap-up and discussion **Group Project #2 Final Reports Due**	Bhattacharyya

* = UPRM not in session but students will try to join the group in their normal classroom. Students can also connect directly from home, if necessary.