SYLLABUS **Spring 2025**

CAMB 633 – *Advanced Seminar in Cell and Gene Therapy*

Perelman SCHOOL OF MEDICINE UNIVERSITY of PENNSYLVANIA

Time	Thursdays 3.30 PM – 5.00 PM
Dates	2025, Jan 23 – May 1
Location	TBD

Course Director

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Co-Directors

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Course Coordinator

Anna Kline | CAMB/GTV
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COURSE GOALS:

The course provides students with a conceptual framework for the critical appraisal of current cell and gene therapy landscape through review of the literature and seminar presentations. The course will critically review select articles from the scientific literature, exploring key aspects of experimental design and data interpretation, scientific rigor and reproducibility. There are several specific goals for this course. One is to introduce students to current approaches in the field of gene therapy, with emphasis on key techniques for delivery as well as laboratory and translational endpoint metrics. A second goal is to review the relevant disease physiology and translational challenges in matching treatment approach and disease context. Throughout, students will learn to consider both technical limitations and ethical boundaries of these novel approaches. A final goal is to convene with experts to better understand the role of intellectual property protection, industry partnerships and the requirements to bring a novel drug to the FDA for approval. These goals will be achieved through paper reviews, lectures and class discussions.

COURSE DESCRIPTION:

Prerequisites: CAMB 633 is open to students at all levels, but students will benefit from foundational knowledge in the molecular basis of gene therapy and basic immunology.

Structure of the course: The course comprises a mix of student-led Journal Club classes and Expert Seminar lectures.

Perelman SCHOOL OF MEDICINE UNIVERSITY of PENNSYLVANIA

Class: Students will be responsible for leading a group discussion of assigned scientific manuscripts in the field of cell and gene therapy selected by course faculty. At the beginning of the course, students select from faculty selected primary research papers, with each student co-leading between 2 and 4 Journal Clubs, depending on the number of enrolled students. Student co-leads will collaboratively prepare slides covering background and paper figures. They will each cover a portion of the article result section with corresponding figure (-s). Emphasis in review will be placed on technical rigor and reproducibility, as well as the broader scientific context and disease pathophysiology. Each class will last 90 minutes, including presentation and discussion of the manuscripts with Q&A. Each class will cover one manuscript, with all paper presentations led by a given student contributing in aggregate to the student grade (50%).

Lectures: 3-4 lectures are spread throughout the semester. During each lecture, a faculty member or external speaker will lecture for ~45-60 minutes followed by ~30 minute discussion. Students are expected to ask questions during or at the end of the lecture. Course faculty will moderate lecture and discussion.

Evaluation:

Students are expected to actively participate in all aspects of the course and come prepared for class. Together, the lead student and faculty will guide and moderate the discussion of papers, their impacts on the field of gene therapy, including potential future outcomes. Class grades will be based on: 50% on paper presentations and 50% on discussion participation (in class and seminars). Absences should be cleared with course directors ahead of time. More than two absences will impact the attendance grade portion.

SELECTION OF ARTICLES BY FACULTY

Peter Kurre (Perelman SOM, Department of Pediatrics, Division of Hematology)

- *In vivo macrophage engineering reshapes the tumor microenvironment leading to eradication of liver metastases. Kerzel et al., Cancer Cell 2023;* **PMID: 37863068**
- *Suprachoroidal gene transfer with nonviral nanoparticles in large animal eyes*; **PMID: 38457512**
- *Durable and efficient gene silencing in vivo by hit-and-run epigenome editing:*; **PMID: 38418872**
- *Intra-tumoral administration of CHST15 siRNA remodels tumor microenvironment and augments tumor-infiltrating T cells in pancreatic cancer.* **PMID: 38799652**

Norbert Pardi (Perelman SOM, Department of Medicine, Division of Infectious Diseases)

- *IL-1 and IL-1ra are key regulators of the inflammatory response to RNA vaccines;* **PMID: 35332327**
- *Modified mRNA Vaccines Protect against Zika Virus Infection;* **PMID: 28222903**
- *mRNA A phase 1 trial of lipid-encapsulated mRNA encoding a monoclonal antibody with neutralizing activity against Chikungunya virus;* **PMID: 34887572**
- *Biocompatible, Purified VEGF-A mRNA Improves Cardiac Function after Intracardiac Injection 1 Week Post-myocardial Infarction in Swine*; **PMID: 30038937**
- *CAR T cells produced in vivo to treat cardiac injury*; **PMID: 34990237**

Stefano Rivella (Perelman SOM, Department of Pediatrics, Division of Hematology)

- *In vivo editing of lung stem cells for durable gene correction in mice.* PMID: 38870301
- *Engineered virus-like particles for efficient in vivo delivery of therapeutic proteins*. PMID: 35021064
- *Nanoblades allow high-level genome editing in murine and human organoids.* PMID: 37435135
- *GP64-pseudotyped lentiviral vectors target liver endothelial cells and correct hemophilia A mice.* PMID: 38684862

Rebecca Ahrens-Nicklas (Perelman SOM, Department of Pediatrics, Division of Human Genetics and Metabolism)

- *Gene therapy augments the efficacy of hematopoietic cell transplantation and fully corrects mucopolysaccharidosis type I phenotype in the mouse model;* Visigali et al., Blood 2010; **PMID 20847202**
- *Hematopoietic Stem- and Progenitor-Cell Gene Therapy for Hurler Syndrome;* Gentner et al., NEJM 2021; **PMID 34788506**
- *Longhurst HJ, et al. CRISPR-Cas9 In Vivo Gene Editing of KLKB1 for Hereditary Angioedema.* **PMID: 38294975.**
- *Single-Dose Gene-Replacement Therapy for Spinal Muscular Atrophy;* Mendell et al., NEJM 2017; **PMID 29091557**

LECTURES (Provisional, July 2024)

Industry perspective- Spark Therapeutics
Speakers: Katherine High
Dr. High will discuss how do you create an integrated gene therapy company, from discoveries in an academic environment to production of gene therapy drugs.

Gene Therapy and Ethical Issues
Speaker: Kiran Musunuru
Recently, the birth of twin girls whose genomes were altered before birth using CRISPR gene-editing techniques was announced. The feat wasn't necessarily a technical breakthrough, but raised ethics and scientific concerns about the application of this technology. Dr. Musunuru will discuss the potential applications of this technology, but also the potential abuses in absences of clear guidelines.

Going to the FDA: From Bench to Bedside: Regulatory Pathway to IND Submission for Cell and Gene Therapy products.
Speaker: Nancy Robinson Garvin
The lecture will discuss the FDA governing body for cell and gene therapy products (CBER), the various types of FDA meetings available to researchers and how to request each meeting type, data needed to support the request, and timeline from submission to approval/clinical trial. The lecture will also review the various types of FDA applications focusing primarily on the IND submission. The lecture will conclude with a discussion of the new four distinct FDA approaches (Priority Review, Breakthrough Therapy, Accelerated Approval, & Fast Track) for new breakthrough/first in human therapies and how this can apply to novel cell and gene therapy drug products and the timelines for each.