

The Department of Bioengineering

is please to invite you to our next Bioengineering Seminar Series event featuring:

Dr. Krishanu Saha, PhD,
University of Wisconsin-Madison

“Engineering nanoparticles containing CRISPR for precision gene and cell therapy”



Friday, September 5th, 2025
10:45AM-11:45AM
HST/HE L185

Please contact the bioengineering graduate coordinator, Jay Lomax (jpl316@lehigh.edu),
with any questions or comments.

**Dr. Krishanu Saha, PhD,
University of Wisconsin-Madison**

"Engineering nanoparticles containing CRISPR for precision gene and cell therapy"

Professor of Biomedical Engineering & Retina Research Foundation Kathryn and Latimer Murfee Chair
Program Lead, CRISPR Vision Program
Member, NIH SCGE
Testbed Co-Lead, NSF CMaT
Co-Director, Global Observatory
University of Wisconsin-Madison Professor of Informatics and Radiology

ABSTRACT:

Therapeutic genome editing has tremendous promise for correcting pathogenic mutations and programming cell behavior using genetic circuits. Yet, translating these strategies into approved drugs has only begun, and many diseases remain untreatable in the clinic. Next-generation nonviral genome editing platforms could accelerate progress, as rapid customization of drug candidates to target different genes does not involve the challenges of manufacturing new batches of viral vectors. In this presentation, I will describe two efforts using synthetic nanoparticles, spanning *in vivo* gene therapy and *ex vivo* cell therapy that are in preclinical development and anticipated to initiate first-in-human trials within the next 2-4 years.

The first effort is the CRISPR Vision Program, part of the US National Institutes of Health Somatic Cell Genome Editing Consortium (SCGE). It aims to develop nonviral genome editing platforms to treat inherited retinal channelopathies. For Leber Congenital Amaurosis (LCA16), a severe form of pediatric blindness caused by mutations in the *KCNJ13* gene, we are developing a novel gene therapy using a Crisp adenine-base editor (ABE8e) delivered via subretinal injection of nonviral lipid nanoparticles (LNPs). Our program rigorously evaluates the safety and efficacy of these formulations across various models. Results have been promising: LNP-based delivery of ABE8e mRNA successfully corrected the W53X *KCNJ13* mutation, restoring Kir7.1 channel function. *In vitro*, precise on-target gene correction confirmed by sequencing and functional restoration was demonstrated in retinal pigment epithelial (RPE) cells from patient-derived induced pluripotent stem cells (iPSCs). We also demonstrate high precision and functional rescue in Best disease models.

The second effort is the development of *ex vivo* edited immune cell therapies, exploiting new methods for efficient nonviral integration of large transgenes into human T and natural killer (NK) cells. In T cells, a non-viral method called Cas9-CLIPT allows for nanometer-sized complexing of ribonucleoprotein complexes. These complexes promote the precise and stable integration of therapeutic genes up to 5 kb. This method holds promise for enhancing autologous and allogeneic CAR T and NK cell therapies for cancer and autoimmune diseases. For our first autologous T cell product, the first target is GD2⁺ solid tumors.

For both programs, we will present novel learnings from our correspondence with the US FDA and provide insights into developing nonviral CRISPR platforms to address multiple mutations and indications.

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BIO: Krishanu Saha is a Professor of Biomedical Engineering, Pediatrics, and Bioethics at the University of Wisconsin-Madison. He holds the Retina Research Foundation Kathryn and Latimer Murfee Chair at the McPherson Eye Research Institute. His lab, located at the Wisconsin Institute for Discovery, focuses on gene editing of the retina and cell therapy production through genome editing. Dr. Saha earned his degrees from Cornell University, the University of Cambridge, and the University of California, Berkeley. He was a Branco-Weiss fellow at MIT's Whitehead Institute and Harvard University. He has published over 100 scientific manuscripts, filed several patents, and received numerous awards, including the Biomedical Engineering Society's Rising Star Award. In 2024, Dr. Saha was recognized as one of the top 10 scientists in therapeutic gene editing by STAT's "Who to Know" list. He has co-led large collaborative efforts in cell and gene therapy, including the NSF Center for Cell Manufacturing Technologies (CMT) and the NIH Somatic Cell Genome Editing (SCGE) Consortium. Additionally, Dr. Saha serves on several national and institutional oversight committees related to genome editing and ethics and is actively working to advance therapeutic genome editing programs into clinical trials.

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