Page Morton Hunter Distinguished Seminar Series

"ModRNA-Based CRISPR Systems Enable Efficient Gene Knockout and Precise Knockin in Human Pluripotent Stem Cells" Dr. Xiaojun Lance Lian, Ph.D.

Dr. Xiaojun Lance Lian is an Associate Professor of Biomedical Engineering and Biology at Penn State University, where his lab engineers stem cells using modRNA, CRISPR-Cas systems, and small molecules to advance cell-based therapies. He earned his Ph.D. at the University of Wisconsin in 2012, developing novel human stem cell differentiation protocols, and completed postdoctoral research at Harvard University. His work on small-molecule cardiomyocyte differentiation earned the Cozzarelli Prize from the National Academy of Sciences for the best biomedical science paper in PNAS (2012). Dr. Lian has received multiple honors from the Biomedical Engineering Society, including the CMBE Young Innovator Award, BMES Advanced Biomanufacturing Junior Investigator Award, and CMBE Rising Star Award. He is also a recipient of the NIH Trailblazer Award and the NSF CAREER Award, reflecting his contributions to stem cell engineering and regenerative medicine.

Associate Professor of Biomedical Engineering, PennState College of Engineering

Precise genome editing in human pluripotent stem cells (hPSCs) is essential for functional studies and disease modeling, yet plasmid-based CRISPR approaches suffer from low efficiency and risk of genomic integration. We developed non-integrating CRISPR platforms using chemically modified mRNA (modRNA) that enable both gene knockout and knockin with high efficiency and genomic integrity. For knockout, modRNA-encoded Cas9 and base editors achieve rapid, efficient loss-of-function mutations without plasmid delivery. To enable precise gene insertion, we created MAGIK (ModRNA-based Activation for Gene Insertion and Knockin), a two-step platform combining Cas9-2A-p53DD modRNA with a mini-donor plasmid to enhance homology-directed repair, followed by transient transcriptional activation using dCas9 activator modRNA and a dead guide RNA. This approach allows live-cell sorting of correctly edited cells, bypassing drug selection or colony screening. Using MAGIK, we achieved targeted fluorescent reporter knockin at lineage-specifying genes (SOX17, NKX6.1, NKX2.5, and PDX1) across multiple hPSC lines. Finally, we applied these tools to engineer hypoimmune hPSCs via knockout and knockin of immune-modulatory genes, generating a promising cell source for transplantation therapies. Together, these modRNA-based technologies streamline genome editing workflows and expand functional genomics in stem cell biology.

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LOCATION: MUSC Baruch Auditorium - 284 Calhoun St. Charleston, SC 29401

(Zoom link: https://clemson.zoom.us/j/9667360648?omn=91753844103)

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