Seminars by Chicago KUH FORWARD

Monday, January 31, 2022
11:00 AM – 12:00 PM Central Time

Host institution: University of Illinois at Chicago

Join Zoom Meeting: https://northwestern.zoom.us/j/98284850748
Meeting ID: 982 8485 0748

AGENDA

11:00 – 11:05 AM  Welcome and logistics  Victor Gordeuk, MD
11:05 – 11:55 AM  Presentations
  The application of transgenic mice to investigate sickle cell nephropathy  Santosh Saraf, MD
  Epigenetic Regulation of Hemoglobin Switching in Non-Human Primates: A Review of Basic and Translational Studies  Donald Lavelle, PhD
  Animal models to study normal and malignant hematopoietic stem cells  Nadim Mahmud, MD, PhD
11:55 AM – 12:00 PM  Closing remarks  Victor Gordeuk, MD

SPEAKERS

The faculty host for this seminar is Victor Gordeuk, MD, a professor of medicine and director of the Sickle Cell Center at the University of Illinois at Chicago. He has extensive experience leading multi-center clinical and translational research projects and training candidates in translational research related to sickle cell disease and other hematologic conditions.

Santosh Saraf, MD
Associate Professor of Medicine
Division of Hematology/Oncology, Department of Medicine
University of Illinois College of Medicine

Bio: Dr. Saraf received his medical degree from the Temple University School of Medicine and completed an internal medicine residency and hematology & oncology fellowship at the University of Illinois at Chicago (UIC). Dr. Saraf joined the Division of Hematology & Oncology at UIC in 2012 and completed a Master of Science in Clinical and Translational Research through the UIC School of Public Health in 2014. He currently serves as the Director of Translational Research for the Sickle Cell Center and the Fellowship Program Director for Hematology & Oncology. Dr. Saraf focuses his clinical care and research on understanding the mechanisms of kidney disease in patients with sickle cell disease and on developing curative therapies through hematopoietic stem cell transplantation for patients with clinically aggressive sickle cell disease.

Title: The application of transgenic mice to investigate sickle cell nephropathy

Abstract: Kidney disease is a common complication in people with sickle cell disease which leads to increased morbidity and early mortality. The pathophysiology of kidney damage and targeted therapies to treat sickle cell disease-related kidney disease are urgently needed. Animal models may provide insight into the mechanisms of kidney damage and allow a careful examination of whether specific therapies can lead to improvements in biomarkers of kidney injury and function as well as histopathologic and gene expression changes occurring in the kidney.
Title: Epigenetic Regulation of Hemoglobin Switching in Non-Human Primates: A Review of Basic and Translational Studies

Abstract: Human hemoglobin switching describes the highly regulated, sequential expression of the five β-like globin genes (HBE, HBG2, HBG1, HBD and HBB) of the human β-globin gene complex. The sequential activation of these β or β-like globin genes during human development from early embryonic through late fetal (‘adult’) stages, and during erythroid maturation, occurs in an order corresponding to their 5’ to 3’ location on chromosome 11. The β-hemoglobinopathies are the most common inherited diseases in humans, and are diseases of mutated HBB or its altered regulation. Since the other β-like globin genes can potentially substitute for defective HBB, much translational research is directed toward understanding and manipulating sequential activation at the human β-globin gene complex to treat β-hemoglobinopathies. Non-human primates provide a vital contribution to such efforts because of their recapitulation of the developmental/maturational switch in hemoglobin production as observed in humans (mice do not model this switch). Valuable insights into druggable epigenetic forces that mediate the switch have been thereby gained. We review important lessons learned in non-human primates, complemented by other studies, and suggest rational next steps.
identification of critical signaling pathways governing hematopoiesis. Utilization of advanced murine models has also allowed spatial and temporal controls of genes. Several immunodeficient mouse models with further genetic engineering are being used as humanized mouse model to study functional potency of HSC/LSC. The humanized mouse model serves as an in vivo assay tool to study efficacy of pharmacologic agents or genetic manipulation to target LSC. In such models, patient derived primary leukemia cells are often used, termed as PDX (patient derived xenotransplantation). Although bone marrow transplantation was started almost 50 years ago and several animal models exist to test functional potency of blood/marrow derived hematopoietic or mesenchymal stem cells, experiments to determine genotoxicity of ex vivo expanded or manipulated cell based products are still limited. This is particularly important if cell based therapy manufacturing involves gene manipulation (gene therapy, use of CRISPR technology) or use of geneotoxic pharmacologic agents. Despite major advancements in mouse models to study human diseases yet incomplete fidelity of the mouse system points a shift towards studies focused directly on human cells.

Chicago KUH FORWARD is a NIDDK-funded interdisciplinary training program for pre- and postdoctoral trainees in basic, translational, or clinical research in the fields of kidney, benign urologic, and benign hematologic diseases across Chicago. Partnering institutions include Northwestern University, Loyola University, Lurie Children’s Hospital, Rush University, University of Chicago, and University of Illinois at Chicago. NIH U2CDK129917 and TL1DK132769

Seminars by Chicago KUH FORWARD is a forum that brings together our city-wide KUH research community to learn about new and existing cross-cutting tools and promote cross talk among scientists at Chicago KUH FORWARD institutions. Seminars are virtual and open to all levels of researchers interested in advancing KUH training and research. Seminar recordings may be made available upon request.

Your participation in Chicago KUH FORWARD seminars and events helps us maximize integration and promote a true trainee community that engages, recruits, prepares, and sustains the next generation of kidney, urology, and hematology researchers. Any predoctoral or postdoctoral fellow or early career investigator interested in presenting at a future KUH Seminar can let us know by sending a message to chicago.kuhforward@northwestern.edu.

Please take the time to provide your feedback on Chicago KUH FORWARD programs. Seminar attendees will be given the opportunity to complete a brief survey at the end of the seminar.

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