Seminars by Chicago KUH FORWARD

Monday, October 11, 2021
11:00 AM – 12:00 PM Central Time

Host institution: Northwestern University

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

AGENDA

11:00 – 11:05 AM  Welcome and logistics  Aline Martin, PhD
11:05 – 11:55 AM  Presentations
   - Macrophage Phenotype and Function in APOL1 Nephropathy  Esther Liu, BA
   - Endothelial oxygen sensing and metabolic reprogramming in AKI  Ratnakar Tiwari, PhD
   - The role of VEGFR3 Signaling in Glomerular Capillary Loop Development  Michael Donnan, MD
11:55 AM – 12:00 PM  Closing remarks  Aline Martin, PhD

SPEAKERS

Esther Liu, BA
Graduate Student
Driskill Graduate Program at Feinberg School of Medicine
Northwestern University

Bio: I am a graduate student in the lab of Dr. Jennie Lin at Northwestern University. My research interests include macrophage biology, kidney immunology, and genetic basis of kidney disease. Previously I have completed my undergraduate studies at Vanderbilt University where I also researched the role of macrophage inflammation in ovarian and breast cancers. Currently I am working on understanding the role of risk variant APOL1 in chronic kidney disease, specifically on the impact of macrophage-mediated inflammation in the kidney microenvironment.

Abstract: Macrophage Phenotype and Function in APOL1 Nephropathy

Recent discoveries in human genetics have identified 2 variants in the gene encoding for Apolipoprotein L1 (APOL1) which confer increased risk for focal segmental glomerulosclerosis, HIV-associated nephropathy, COVID-19-related kidney injury, and more. Macrophages play an important role in kidney homeostasis and injury, reacting to and relaying inflammation within the tissue and to other immune cells. We used induced pluripotent stem cell-derived macrophages (IPSDM) and bone marrow-derived macrophages (BMDMs) from transgenic APOL1 mice to examine multiple key macrophage pathways and phenotypes to assess the effect of risk variant APOL1 in macrophages functions. We observed that risk variant APOL1 expression results in higher inflammatory gene expression in the macrophages. Additionally there is an increase in glycolytic rate and glycolysis gene expression. Because cellular metabolism is critical to macrophage function, these changes unveil some potential mechanisms that risk variant APOL1 modulates in macrophage inflammatory phenotype and function which are relevant to kidney disease progression.
Ratnakar Tiwari, PhD
Postdoctoral Fellow
Northwestern University

Bio: I am a postdoctoral fellow in the lab of Dr. Pinelopi Kapitsinou. My research interest focuses on understanding the role of the endothelial PHD/HIF axis in acute kidney injury (AKI). Currently, I am working to delineate PHD/HIF axis-driven endothelial metabolic reprogramming and its role in post-ischemic kidney tissue remodeling. By linking PHD/HIF axis-regulated endothelial metabolic alterations with pathophysiological outcomes in post-ischemic AKI, I am trying to identify novel therapeutic targets against AKI.

Abstract: Endothelial Oxygen Sensing and Metabolic Reprogramming in AKI

Dysfunction of renal vasculature has been emerging as a critical process in the pathogenesis of acute kidney injury (AKI) and chronic kidney disease (CKD), but the underlying molecular mechanisms remain unclear. Prolyl-4-hydroxylase domain-containing proteins 1–3 (PHD1–3) act as hypoxia sensors and regulate the abundance of Hypoxia Inducible Factors (HIF)-1 and (HIF)-2, transcription factors that promote adaptation to oxygen deprivation, a critical pathophysiological event in ischemic kidney injury. Besides oxygen sensing, cross-talk between PHD/HIFs signaling and metabolism is emerging. Recently, we have shown that endothelial hypoxic signaling plays a critical role in regulating post-ischemic kidney injury and inflammation. Further, our new findings show that PHD/HIF driven metabolic alterations regulate the angiogenic competence of endothelial cells.

Michael Donnan, MD
Instructor of Medicine
Division of Nephrology and Hypertension
Northwestern University

Bio: I am a physician-scientist with a research focus in the kidney vasculature studying the underlying signaling mechanisms driving healthy vascular development and adaptation in kidney disease. I completed my nephrology fellowship at Northwestern University and I am now continuing my research career at Northwestern under a fellowship award from the American Society of Nephrology. Currently I am investigating how Vascular Endothelial Growth Factor Receptor 3 (VEGFR3) signaling directs both blood and lymphatic vessel development within the kidney with the aim to better define future therapeutic targets for the purpose of treating kidney disease.

Abstract: The Role of VEGFR3 Signaling in Glomerular Capillary Loop Development

Chronic kidney disease is associated with pathological changes to the kidney vasculature which contribute to disease progression. Dysregulation of the growth factor receptor VEGFR3, known primarily for its expression in lymphatic vessels and its role in lymphangiogenesis, is causally linked to the development of kidney diseases making it a potential target for new therapeutics. To investigate the functional role of VEGFR3 signaling, we performed a detailed profile of VEGFR3 expression in the developing mouse kidney and generated new transgenic mouse models to allow conditional and cell-specific deletion of VEGFR3. We found that VEGFR3 expression is not exclusive to lymphatic vessels and undergoes dynamic expression through development in several microvascular beds of the kidney including the endothelial cells of the glomerular capillary loop. Loss of Vegfr3 resulted in both lymphatic defects as well as marked disruption of glomerular capillary development. The mechanisms by which VEGFR3 signaling directs glomerular development will be essential to define prior to the development of therapeutics targeting this pathway.

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

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