Speaker: Rohit N. Kulkarni MD PhD

Title: Role of mRNA modifications in regulation of islet cell biology

Summary: A defect in the secretory function of beta cells is central to the pathogenesis of all forms of diabetes. While a reduced beta cell mass secondary to an autoimmune attack is characteristic of type 1 diabetes, the inability of beta cells to compensate for the ambient insulin resistance by an appropriate increase in insulin secretion and enhanced mass is a typical observation in type 2 diabetes. The precise mechanisms and signaling pathways that regulate insulin secretion and modulate beta cell proliferation and death continue to be major areas of research.

This presentation will focus on exploring how the modifications in messenger RNA (mRNA) can influence the expression of proteins that directly modulate secretory function and cellular growth of beta cells. A major focus will be on the proteins that serve as writers, erasers and readers of methylation of N-adenosine at position 6 (also termed as m^6A) and its relevance for regulating beta cell biology. Results on the regulation of human beta cell function and the creation of genetically engineered models will be presented in the context of the development of diabetes and progression of the disease. The link between mRNA modifications and signaling pathways, especially the insulin/insulin-like growth factor network will be discussed.

The results from these series of studies provide a novel approach to understanding the pathogenesis of defects of the beta cells and point to potential new targets that can be exploited to promote beta cell survival, growth and secretory function in the long-term goals of improving therapeutic options for patients with diabetes.

Relevant References:

De Jesus DF, Zhang Z, Kahraman S, Brown N, Chen M, Hu J, Gupta MK, He C, **Kulkarni RN**. m^6A methylation regulates human islet biology and plays a role in the β-cell failure of type 2 diabetes. Nature Metabolism 1(8):765-774, 2019. PMID: 31867565; PMCID: PMC6924515.