1. Overview/Abstract

Since the kidney is composed of many functionally unique cell types, there is a dire need for tools to investigate the disease mechanisms at the single cell level and identify targets for clinical treatment. Recent sequencing-based single-cell transcriptomic technologies have revolutionized kidney research by their capability of thorough classification of cell subtypes and their varied gene expression. But those technologies don't simultaneously produce surface and intracellular proteome information which represents phenotypes, physiological activities, drug targets, and signaling pathways for cells. Transcriptome and functional proteome are rather complementary to each other, and they present two different layers of cellular regulation. As such, there is a critical need to develop a multiomic technology that can interrogate both transcriptome and proteome at the single-cell level in healthy and diseased conditions in human kidney disease. A multiplex *in situ* tagging (MIST) array developed in the PI's laboratory is naturally suitable for the single-cell functional proteome and transcriptome studies, since any detection on the MIST array is based on selective capture of barcode DNAs. We will integrate the RNA sequencing procedure into the MIST technology and optimize the experimental conditions so both transcriptome and functional proteome can be co-detected for kidney cells on the sections. Spatial MISTomic will uniquely map the tissue-wide transcriptome and functional proteome (including intracellular proteins, surface markers and extracellular proteins) in a spatially resolved manner with the single-cell resolution. It pairs advances in spatial barcoding, molecular biology, and high-throughput imaging to provide spatially resolved profiles of two modalities, enabling new insights into the molecular factors driving regulatory states. The completion of this project will generate an enabling technology and method widely accessible in the kidney research community to investigate kidney diseases in an unprecedented depth. This technology will lay the foundation for future mechanistic studies and identification of potential therapeutic targets.