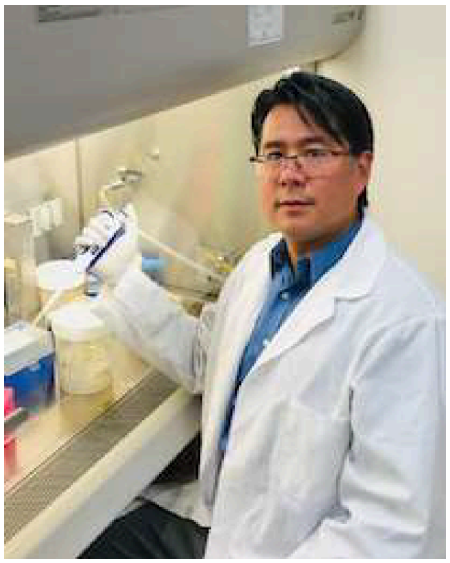

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Project Title: Micro vessels-on-a-chip to model diabetic microangiopathy and to advance precision medicine in diabetes

Scientific Summary: Diabetes mellitus is a major health problem affecting nearly half a billion people worldwide and contributes to approximately 11% of all deaths. Diabetes results in hyperglycemia that damages micro vessels throughout the body. This is known as diabetic microangiopathy and can lead to dysfunction of multiple organs including the brain, eyes, heart, kidneys, and nerves. Proper micro vessel function is critical for oxygenation and nutrient delivery. The mechanisms that drive diabetic microangiopathy are clearly complicated and incompletely understood. A significant barrier is cause by the complex organization of micro vessels, which are made of endothelial cells and mural pericyte supporting cells. Interactions between the two cell types and the surrounding matrix are critical to disease pathogenesis and new disease models that capture these interactions are clearly needed. Completion of the study proposed will increase understanding of the biological processes driving diabetes, generate new biomarkers to track disease, and establish a platform to potentially test new therapeutics.

What area of diabetes research does your project cover and what role will it play in preventing, treating and/or curing diabetes? Diabetes results in high sugars that damage small blood vessels throughout the body. This can lead to dysfunction of multiple organs including the brain, eyes, heart, kidneys, and nerves. Proper small vessel function is critical for oxygenation and nutrient delivery. The mechanisms that drive small vessel damage are clearly complicated and incompletely understood. A significant barrier is cause by the complex organization of small vessels, which are made of two different cell types. Interactions between the two cells and the surrounding tissues are critical to disease pathogenesis and new disease models that capture these interactions are clearly needed. This proposal describes a plan to develop a microfluidic platform that incorporates human blood vessel cells that self-assemble into perusable small vessel networks for modeling diabetic small vessel disease outside of the body. The specific aims are: 1) to develop, characterize, and utilize a microfluidic model of diabetic small vessel disease and 2) to utilize gene expression and protein analyses to investigate pathogenesis and to identify new biomarkers to track the progression of diabetic small vessel disease. In addition, advanced microscopy and biochemical assays will be used to characterize morphology, function, and signaling pathways in our temporally and spatially controlled system.