Diabetic Complications Consortium

Application Title: microRNA-mRNA interaction networks in arterioles in type 2 diabetes

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1. Project Accomplishments:

We have completed deep sequencing of small RNAs (primarily microRNAs) in resistant arterioles obtained from 20 non-diabetic and 18 diabetic human subjects. We have analyzed the data and identified microRNAs associated with one or more of nearly 30 clinical phenotypes.

2. Specific Aims:

The goal of the pilot project is to identify alternations in the microRNA-target gene network that may contribute to the development of microvascular endothelial dysfunction in type 2 diabetes mellitus (T2DM) in human. Specifically, we will use next-generation sequencing, bioinformatics, and statistical methods to identify alterations in microRNA-mRNA interaction networks in resistance blood vessels in T2DM patients.

A key and most time-consuming aspect of the study is recruitment of a sufficient number of study subjects that meet the inclusion and exclusion criteria. We bring the subjects to the Translational Research Unit at MCW, consent them, phenotype them, and carry out gluteal adipose biopsy. The biopsy samples are then used to isolate resistance blood vessels for vascular function and molecular profile analysis. We recruited, phenotyped, and obtained biopsy samples from 20 normal subjects and 18 T2DM subjects. Resistance blood vessels isolated from these subjects underwent vascular function analysis. RNA was extracted from the vessels, and small RNA libraries prepared, sequenced on a HiSeq2000, and data analyzed using a complete suite of wet lab and dry lab protocols that we have established in our laboratories. The results indicate 37 known human microRNAs and several novel microRNAs were significantly differentially expressed between non-diabetic and diabetic subjects according to a new statistical model that we recently developed for identifying differentially expressed microRNAs based on deep sequencing data. In addition, 23 microRNAs were found to be significantly associated with one or more of 17 clinical or vascular phenotypes.

3. Publications:

A manuscript describing the above results is in the final stage of preparation.