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GOAP AWARD 2018/9: THE ROLE OF PANCREATIC B CELL SPECIFIC EXOSOMAL MICRORNAS IN THE PATHOGENESIS OF DIABETIC MACULAR EDEMA

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Purpose

There are three types of extracellular vesicles shed from most cell types: (1) microparticles, which originate from the cell membrane; (2) exosomes, created by an intracellular mechanism; and (3) apoptotic bodies, which are formed during cell death. Exosomes, which are 30–200 nm in size, contain nucleic acids, enzymes, cytokines, and other bioactive compounds. In our previous work, we had shown that circulating exosomal miRNA-15a were increased in early stages of diabetic retinopathy. We showed that pancreatic exosomal miR-15a influenced the miR-15a levels in the retina, suggesting that exosomes secreted by the pancreatic cells influence miR-15a expression the retina at the early stages of diabetic retinopathy, and are likely to be involved in the pathogenesis of the disease. Our proposed project is to investigate the role of pancreatic B-cell specific exosomal miR-15a in diabetic macular edema.

Methods

A total of around 150-250 study subjects will be divied accordingly into three groups: control (no DM), T2DM no DR/DME, and patients with DME. Clinical information will include eye findings, and parameters such as HbA1C, renal function and lipid profile. Plasma fraction will be collected and spun separately, and aliquots will be stored in -80°C freezer. Exosomal fractions will be isolated using differential centrifugation including ultracentrifugation. The exosome-enriched fraction will be transported to Johns Hopkins University. Employing ICE, where we will isolate pancreatic β cell specific exosome using immunocapture method. Using single cell qPCR kit from Qiagen, we will isolate microRNA. Using SybrGreen qPCR we will detect expression of mir-15a levels.

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