

# miRNAs as Biomarkers of IAPP-induced Inflammation in Type 2 Diabetes

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Type 2 diabetes (T2D) is a chronic disease brought about by metabolic events such as insulin resistance and the progressive dysfunction of insulin-secreting beta cells. Recently, both inflammation and islet amyloid polypeptide (IAPP) - a peptide that aggregates to form amyloid plaques - have been suggested to impair beta cell function. Aggregation of human IAPP (hIAPP) has also been found to drive resident islet macrophages toward a proinflammatory phenotype. In addition, microRNAs (miRNA), which are small, noncoding RNAs, can regulate gene expression and lead to defective insulin secretion and beta cell apoptosis upon exposure to proinflammatory cytokines. For this reason, miRNAs may be upregulated in response to IAPP-induced inflammation in pancreatic islets. More importantly, miRNAs may be potential novel biomarkers of IAPP-induced inflammation in T2D. Thus, in this study, wild-type and hIAPP transgenic islets were cultured for 6 days in high glucose (16.7 mM) to determine whether IAPP promotes upregulation of miR-375, miR-21, and miR-146a through an inflammatory pathway. Quantification of miRNA expression by qRT-PCR revealed that the expression of miR-21 and miR-146a, but not miR-375, was significantly increased in hIAPP transgenic islets compared to wild-type islets. In fact, results from the quantification of immunostaining indicate that miR-21, and miR-146a may be linked to IAPP aggregation in T2D. Collectively, these findings highlight a novel involvement of miR-21 and miR-146a in IAPP-induced inflammation, and identifies miR-21 and miR-146a as potential attractive biomarkers of T2D.

## Awards Won:

Fourth Award of \$500