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## Down-regulation of miR-139-5p contributes to the anti-apoptotic effect on diabetic rat islets and INS1 cells induced by Liraglutide via targeting Irs1

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Diabetes is a chronic metabolic disease characterized with elevated glucose and lipid disturbance, which pathogenesis involves beta cell dysfunction and insulin resistance. Liraglutide is administered as GLP-1 receptor agonist on patient with diabetes mellitus and shows protective effect on beta cell function by inhibiting its apoptosis and promoting its proliferation and regeneration. MicroRNAs (miRNAs) are a category of endogenous non-coding small RNA, which inhibit the translation by binding to the 3' untranslated region (3' UTR) of their target mRNAs. It has become increasingly clear that miRNAs are not only involved in regulation of cell differentiation and apoptosis, but also in the pathogenesis of a variety of diseases. In our study, we aim to investigate the miRNA level differentially expressed in the pancreatic tissues of normal or diabetic SD rats without or with administration of Liraglutide, screen intended miRNA and predict its target gene, and explore the mechanism by which miRNA contributes to the anti-apoptotic effect of Liraglutide on pancreatic beta cells. We revealed differential expression of miRNAs and validated the increased expression of miR-139-5p in diabetic rats, while which decreased in diabetic rats with administration of liraglutide. We verified the direct regulatory effect of miR-139-5p on insulin receptor substrate 1(Irs1), a key player in insulin signal transduction pathway, through the target sequence ACTGTAG by using double luciferase report experiments. We also found palmitic acid can increase the expression of miR-139-5p and reduce IRS1 expression at both mRNA level and protein level in INS1 cells. Furthermore, administration of Liraglutide decreased the expression of miR-139-5p and enhanced the expression of IRS1, which protected both pancreatic tissues of SD rats and INS1 cells from apoptosis. Our data demonstrates that increased expression of miR-139-5p, which targets Irs1, prompts apoptosis in both pancreatic tissue of diabetic SD rats and INS1 cells treated with palmitic acid, down-regulation of miR-139-5p contributes to the anti-apoptotic effect induced by Liraglutide via targeting Irs1.

### Biography

Haipeng Xiao, MD, PhD is the Professor of Endocrine, Chief Expert President at the First Affiliated Hospital of Sun Yat-sen University. He is the member of American Thyroid Association (ATA), member of Continuing Medical Education (CME) Committee, American Endocrine Society, member of Association for Medical Education in Europe (AMEE), and the Vice Secretary General, Clinical Teaching Committee of Medical Education, Ministry of Education, P R China. He is the Editorial Board Member of *Chinese Medical Journal*, *Chinese Journal of Endocrinology and Metabolism*, *Chinese Journal of Diabetes* and *Cardiovascular Endocrinology*. As a long-term Researcher in endocrine and metabolic diseases, he has published over 50 papers in core Chinese and foreign periodicals such as *Journal of Clinical Endocrinology & Metabolism (JCEM)*, *Brain Research*, etc. Moreover, he took the lead in treating Graves' diseases by introducing thyroid arterial embolization, and for the first time ever, he reported relevant findings of using innovative methods to treat Graves' diseases in the prestigious *Journal of JCEM*. In June of 2012, he published another academic thesis "Circulating MicroRNA Profiles as Potential Biomarkers for Diagnosis of Papillary Thyroid Carcinoma" in JCEM which has received high attention and positive response among medical scientists home and abroad.

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