

The influence of miR-125b in pancreatic β -cell apoptosis

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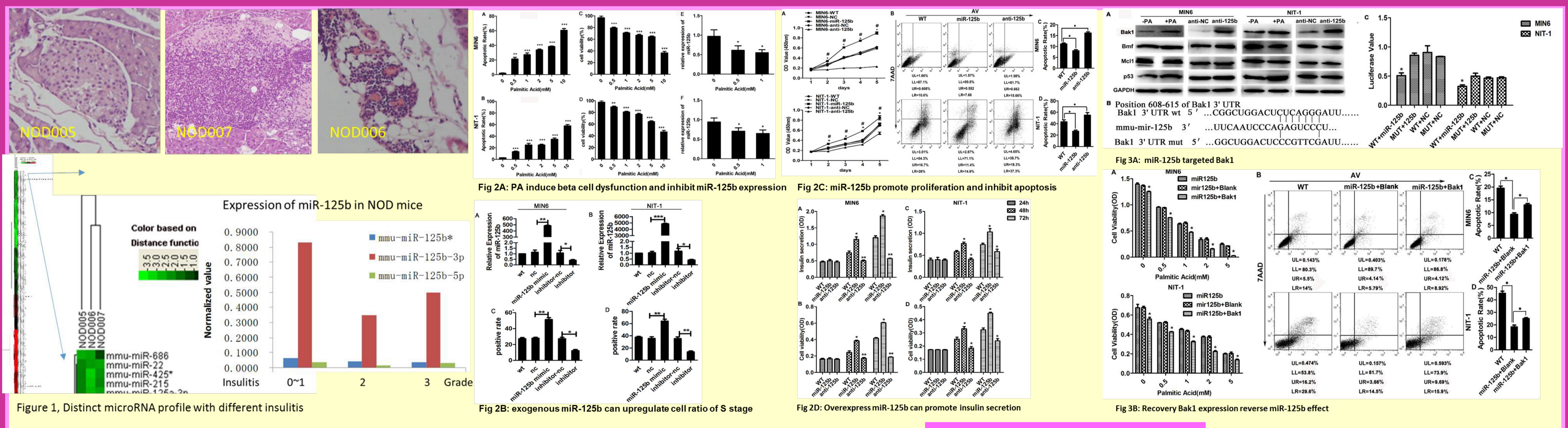
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Objectives:

Type 1 diabetes is characterized by autoimmune insulinitis and islet cell apoptosis. Recent study indicate miRNA may have role in the development of type 1 diabetes. This study analysed the miRNA expression profile in the pancreas of type 1 diabetes model NOD mouse, and investigated the influence of miR-125b in pancreatic β -cell dysfunction.

Methods:

20 NOD mice are raised, pancreas sample are collect for pathological analysis, microarray were used to analyze miRNA expression profile, which found miR-125b have significant alteration. In PA (palmitic acid) induced apoptosis model with islet cell line. MiR-125b expression were measured. Transient transfection with mimics and inhibitor of miR-125b in islet cells, Bak1, Cytochrome C and caspase-3 expression were measured. Dual luciferase reporter assay was to validate if Bak1 is target gene of miR-125b. The effect of miR-125b on proliferation, apoptosis and insulin secretion in β -cells were analyzed through flow cytometry, CCK8 assay and ELISA.



Results:

13/20 NOD mice developed diabetes by 25 weeks. By microarray analysis, microRNA profile can distinguish insulinitis with no insulinitis; miR-125b have significant alteration, which is validated by qRT-PCR. In addition to low viability and increased apoptosis rate, prolonged exposure of the β -cell lines to palmitate caused a dose-dependent decrease of miR-125b. After transient transfection with mimics and inhibitor of mir-125b in NIT-1 cell cells, we found mir-125b inhibit Bak1 expression, then subsequently downregulate Cytochrome C and caspase-3 expression, contribute to its inhibition effects on apoptosis. Dual luciferase reporter assay validate Bak1 as target gene of miR-125b. High miR-125b level also promoted insulin secretion by increasing cell viability.

Conclusions:

Our findings suggest that miR-125b may participate in pancreatic β -cell dysfunction, and involve in the molecular mechanism of type 1 diabetes, by maybe as a novel target for the treatment of this disease.

References:

Bang-Berthelsen CH, Pedersen L, Fløyl T, et al. Independent component and pathway-based analysis of miRNA-regulated gene expression in a model of type 1 diabetes. BMC Genomics. 2011 4; 12:97

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