Abstract

Diabetes mellitus is a metabolic disease associated with a high blood glucose level over a prolonged period of time. Hyperglycemia is caused by the loss of pancreatic insulin producing beta cells. Diabetes mellitus II is linked with insulin resistence, which can indirectly lead to beta cell deficiency. It logically follows that the replacement or regeneration of beta cells could lead to a successful remission of diabetes.

D type cyclins (D1, D2, D3) and cyclin-dependent kinases (Cdk) 4/6 appear to have the potential to induce beta cell proliferation. These proteins are responsible for driving cell mitotic entry. The aim of this bachelor thesis was to verify the possibility of inducing beta cell proliferation via D type and Cdk4/6 synthetic mRNA transfection. *In vitro*-synthesized mRNA induces short-therm protein overexpression. Cyclins harboring mutations are characterized by a higher protein stability and an increased half-life. The presence of D type cyclins and Cdk4/6 after cell transfection was detected using indirect immunofluorescence. Also a Western blot analysis with subsequent immunodetection was performed.

Transfecting rat islet cells with various D type cyclins and Cdk4/6 mRNA combinations has shown to lead to a significant induction of beta cell proliferation. The levels of beta cell replication varied from 40 to 65 % depending on the combination of transfected mRNAs. Whereas only a 5 % level of proliferation was observed in non-transfected rat beta cells. The mutated form of cyclin D1 (D1T286A) with Cdk4 was the most effective combination, where the proliferation rate of rat beta cells reached 65,3 ± 2,9 %.

Key words

beta cells, proliferation, transfection, mRNA, Cdk4, Cdk6, cyclin D, diabetes

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