

In Vitro and in Vivo Evaluation of Nano Collagen Molecules to Enhance Mesenchymal Stem Cells Differentiate into Insulin Producing Cells

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Abstract : The use of specific molecules including nutrients and pharmacological agents has been tried in modulation of stem cells differentiation (MSCs) to insulin producing cells. The aim of this study is to investigate the ability of nano collagen molecules (nutrient or scaffold) to enhance the MSCs differentiation into insulin-producing cells in combination with nicotinamide and exendin-4 (pharmacological agents) in vitro and in vivo. The results demonstrated that the cells exhibit morphologically islet-like clusters after treatment with nano collagen molecules, nicotinamide and exendin-4. MSCs extra treated with nano collagen molecules showed significant increases in Nkx6.1 and insulin mRNA expression at 14-d and 21-d culture compared with those merely treated with nicotinamide and exendin-4. Early 7-day elevation in PDX-1 mRNA expression was observed. Furthermore, the MSCs exposed to nano collagen molecules produced the highest secretion of insulin ($p \leq 0.05$). Type-2 diabetes induced by high-fat diet and low dose of streptozotocin in rat model was built in this study. This rat exhibited higher food intake, water intake, lower glucose tolerance, lower-insulin tolerance, and higher HbA1C (significant increases, $p \leq 0.01$) as compared with the normal rat that demonstrated the model of type-2 diabetes was successfully built. Biopsy examinations also showed that obvious destruction of islet. After injection of differentiated MSCs into the destructed pancreas of diabetes rat, more regenerated islet were observed at the rats that treated with nano collagen molecules and exhibited much lower HbA1C as compared with the normal rat and diabetes rat after 4 weeks (significant decreases, $p \leq 0.001$). These results indicate that the culturing MSCs with nano collagen molecules, nicotinamide, and exendin-4 are beneficial for MSCs differentiation into islet-like cells. These nano collagen molecules may lead to alternations or up-regulation of gene expression and influence the differentiated outcomes induced by nicotinamide and exendin-4.

Keywords : nano collagen molecules, nicotinamide, MSCs, diabetes

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