Novel Enzymatic Crosslinking-based Hydrogel Nanofilm Caging System

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Efficacy of pancreatic β-cell therapy for type 1 diabetes is limited by low cell survival rate owing to physical stress, and aggressive host immune response. To overcome such limitations, a multilayer hydrogel nanofilm caging strategy is demonstrated, which protects cells from high shear stress and reduce immune response by interfering cell-cell interaction. A tough and elastic hydrogel nanofilm is fabricated by monophenol modified glycol chitosan and hyaluronic acid that crosslink each other to form nano-thin hydrogel film on the cell surface via tyrosinase mediated reactions. Enzymatic crosslinking-based hydrogel nanofilm caged cells were characterized by measuring fluorescence intensity, ζ-potential, and transmission electron microscopy imaging. Furthermore, thin, uniform, and compact nanofilm formation were conducted on mouse β-cell spheroids for the application in the field of islet transplantation. The cytoprotective effect against physical stress and the immune protective effect was evaluated *in vitro*. Finally, hydrogel nanofilm caged mouse β-cell spheroids were injected into the type 1 diabetes mouse model and regulated its blood glucose level more significantly compare to the non-caged spheroids group. Overall, expectation of our novel enzymatic crosslinking-based hydrogel nanofilm caging method will provide a new platform for clinical applications of β-cell-based therapy.