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# Combination therapy of multi-layer modification system and immunosuppressive drugs on the survival of transplanted porcine islets

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This study suggested a new combination therapy of using biocompatible polymer to improve the stabilization of islet and prevention of immune cell infiltration and recognition and using diverse immunosuppressive drugs with multi-layer modification to effectively decrease the immune reaction in a porcine to mouse transplantation model. Most of all, the porcine islets were modified with SH-6-arm-PEG-lipid and Gelatin-Catechol (Artificial ECM) for stabilization of fragility. Secondly, stabilized porcine islets were immobilized with three kinds of PEG derivatives (6-arm-PEG-catechol, 6-arm-PEG-SH and linear PEG-SH; PEGylation) for immunoprotection. The artificial ECM and PEG derivatives effectively cover the surface of porcine islets (Artificial ECM + PEGylation group) and help to retain the size of porcine islets. The viability and functionality of porcine islets was not affected. In addition, protein adsorption was measured using artificial ECM and PEG derivatives conjugated on collagen glass, which data has shown that multi-layer modification significantly reduced attachment of human serum albumin, fibronectin and IgG compared to control collage glass. The combined effect of multi-layer modified porcine islet and cocktailed immunosuppressive drugs on the survival time of grafted islet was assessed in a xenogeneic porcine-to-mouse model (control group, artificial ECM + PEGylation group, control + drug group, and artificial ECM + PEGylation + drug group). The median survival time (MST) of artificial ECM + PEGylation group was 4-fold increased compared to that of control group. In addition, the MST of artificial ECM+ PEGylation + drug group was 2.16-fold increased compared to control + drug group. Therefore, we proposed new porcine islet transplantation protocol using surface multi-layer modification and immunosuppressive drugs for stabilization and immunoprotection.

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