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Microfluidic encapsulation of pancreatic islets with improved biopolymers for type1 diabetes cell therapy

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Cell therapy is defined as the administration of living cells to a patient. Type1 diabetes (around 40million people worldwide) can require this treatment, for patients whose blood glucose levels are difficult to control with the usual insulin treatment. These patients can be transplanted with allogeneic pancreatic islets that provide a stable normoglycaemia. However, this requires the administration of immunosuppressant that leads to many side effects and complications. Islet microencapsulation presents an alternative to immunosuppressive treatment. In this project, islets are encapsulated using microfluidics. This technology produces microcapsules of 10-1000µm in diameter with a low size dispersion and better control in shape (compared to the commonly used air dripping nozzle encapsulation technology). The better control in size and low size dispersion in microfluidics enables to produce capsules which size is adapted to that of the islets, reducing the biopolymer volume and therefore increasing the chances of the viability of the islets. The good shape control enables to avoid protrusions, hence reducing the risks of detection by the immune system. Regarding the encapsulation polymer, the most common is alginate, because of its biocompatibility, permeability and jellifying conditions (pH 7, 37°C). We use here alginates with improved mechanical properties, synthesized by adding different chemical functions on normal alginate. In order to find the system parameters that enable the production of capsules with the different biopolymers, their physicochemical properties (rheology, surface tension and contact angle) and the fluidic behavior were characterized (micro-Particle Image Velocimetry). Thanks to these data, we were able to encapsulate for the first time human and neonatal pig pancreatic islets using very viscous improved biopolymers, with a size dispersion lower than 5%. These encapsulated islets were first tested *in vitro* for viability and insulin secretion and finally implanted in mice, in order to check for diabetes reversal after 30days.

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