**Immuno-protection Device for Hypoxia Reduction in Cellular Therapy**

Chen Yang, Tran Minh Phuong Nam, Pham Hoang Linh Chi, Dang Thuy Tram*
School of Chemical and Biomedical Engineering, Nanyang Technological University, Singapore.

**Team Name**: Our team, **FormaCyte Therapeutics**, consists of an assistant professor and three PhD students. Assistant professor Dang Thuy Tram is a biomedical engineer with expertise in cell-based therapeutics, biomaterials and drug delivery. She is an inventor of an US patent (of another technology platform) licensed by Boston-based Sigilon Therapeutics for development of cellular therapeutics. Chen Yang is the team's technical lead with expertise in designing microfabricated tissues and hydrogel-based macrodevices for improved survival and performance of cellular grafts. He was the winner of Nanyang Technological University's 2020 Entrepreneurship Award. Nam Tran is a biomedical engineer working on device prototyping and scale-up manufacturing. In addition, Chi is a biologist focusing on evaluating functional performance of clinically relevant source of pancreatic beta cells in our device prototype.

**Technology**: We have developed a cell-encapsulating macro-device as an implant to reduce the risk of fatal drop in blood sugar of insulin-dependent diabetic patients. This platform technology is protected by a pending PCT non-provisional patent application (PCT/SG2020/050193, priority date March 2019). Our technology has the potential to protect therapeutic cells from immune rejection to deliver appropriate dosage of insulin for injection-free management of diabetes while avoiding the need for immunosuppressant drugs. The competitive advantages of our technology include prolong survival of the encapsulated cells by adoption of toroidal geometry of microtissues (**Fig. 1A**) and the ability to personalize implant size for individual patients. Currently our technology focused on the treatment of type 1 diabetes (T1D) with potential treatments of other protein-deficiency diseases such as hemophilia A and thyroid disorders. Our result showed that encapsulated microtissues in the macro-device maintained glucose-responsive insulin secretion *in vitro* (**Fig. 1B**). Furthermore, following subcutaneous transplantation of macro-devices containing rat-derived toroid microtissues into immuno-competent diabetic mice for 9 days, no visible adverse effect was observed surrounding the transplanted devices (**Fig. 1C**). Our transplanted macro-device containing a marginal number of insulin-secreting cells lowered the blood glucose a few days (**Fig. 1D**).

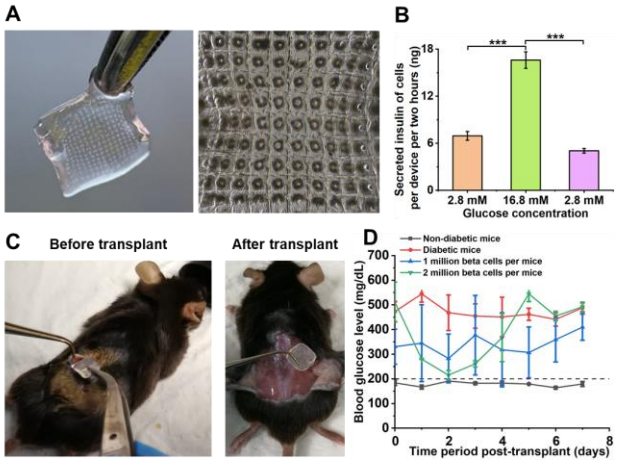


***Fig. 1 In vitro (A, B) and in vivo (C, D) evaluation of glucose-secreting function of encapsulated toroid microtissues in FormaCyte's macrodevice.***

**Market:** T1D is estimated to affect 20 million people aged 20-79 years worldwide. The total addressable market (TAM) of our technology is young adult T1D patient experiencing hypoglycemia accounting for an estimated annual revenue of 94 billion USD. The annual revenues of service available market (SAM) and service obtainable market (SOM) are 6.5 billion USD and 7 million USD respectively. Our beachhead with an annual revenue of 1 million USD comprises patients requiring islet transplantation in the USA with an annual revenue of 1 million USD. For the current and future spending on cell therapy, we based our estimate on the global insulin pen market USD estimated to be 22.15 billion in 2018 and 42.11 billion in 2026 with a compound annual growth rate (CAGR) of 4.82.

**Commercialization Strategy**: Our macrodevice can be classified as cell-device combination product regulated by FDA's Office of Cellular, Tissue and Gene Therapies (OCTGT) and Center for Biologics Evaluation and Research (CBER). We plan to collaborate with local stem cell expert to generate GMP-grade cell source and scaled-up device manufacturing leveraging GMP facility from existing local cell therapy or the Singapore Health Science Authority facility. Customer relationship will be maintained by strong interaction with patient-support groups and training program on our product for nurses and clinicians. For product distribution, we plan to leverage the distribution network of a biopharma partner as channels to deliver our products to clinicians. Fixed costs for manufacturing of our products include rental fee and IP maintenance, manpower cost and in-licensing of IPs to generate iPSC cell sources while variable costs include payment to CROs for preclinical evaluation in large animal models, expenses for in-house R&D activities and cost of regulatory preparation and filing. Our revenue streams include product sale, royalties or licensing fee obtained for non-T1D indications. Currently we estimate our product pricing at 145000 USD/device based on the current cost of islet transplantation, estimating a profit of 30000 USD for each product sold. Our near-term goal is to acquire preclinical data to increase valuation and support regulatory filing for clinical trials. The long-term goal is to obtain FDA approval for our macro-device and achieve an annual sale of 30-50 products in the USA market within the first three years. Our reimbursement strategy is to target countries with medical insurance fully covering cell-based therapy such as the UK. Our exit strategy can be a partnership or acquisition with a large biopharma company on key indications.