DEVELOPING A NOVEL MICROCHANNEL EMULSIFICATION DEVICE FOR DIABETES CELL THERAPY

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Type 1 diabetes is a chronic, autoimmune illness, involving immune rejection of the body's insulin-producing pancreatic beta cells. The reduced insulin production results in a dangerous increase in blood glucose levels. Cell therapy is currently being explored as an attractive long-term treatment option for this disease, whereby pancreatic islet cells are isolated from allogeneic donors, and transplanted into affected patients. Islet transplantation is a minimally invasive treatment that has successfully eliminated the need for exogenous insulin in 50-70% of patients for 5 years (Shapiro, 2017). Limitations to this treatment include the requirement of lifelong immunosuppression that may lead to opportunistic infection, and the limited donor islet supply. To overcome these issues, we are investigating islet immunoisolation in alginate microbeads to eliminate the requirement of immunosuppressive drugs and to improve access to islet transplantation as a therapeutic option.

Compared to conventional nozzle encapsulation processes, emulsification and internal gelation in a stirred vessel is a highly effective and scaleable technique for islet immunoisolation (Hoesli, 2010; Hoesli, 2012). However, the alginate beads produced via stirred emulsification are highly polydisperse. The objective of this project was to determine whether insulin-producing beta cells can be encapsulated in monodisperse alginate beads produced by combining internal gelation and microchannel emulsification technologies.

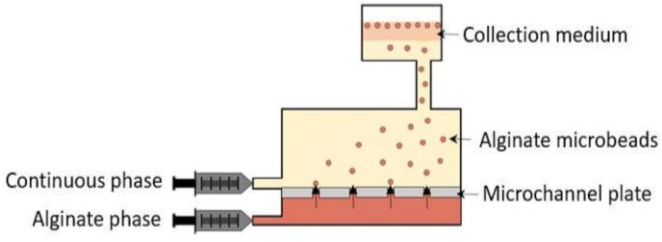

Figure 1 – MCE Encapsulation Device

We developed a novel microchannel emulsification (MCE) device (Figure 1) consisting of an alginate phase flowing below a hydrophobic microchannel plate, with a stagnant continuous oil phase above the plate (Markwick, 2016). Three hydrophobic and non-toxic continuous phase fluids (light mineral oil, glyceryl trioleate, and 3M™ Novec™ 7500 Engineered Fluid) were considered in this study and evaluated based on their density difference with the alginate phase, as well as their surface tensions. Higher density difference between phases and lower continuous phase surface tension both resulted in facilitated droplet formation in the device. Viability assessments of encapsulated mouse insulinoma 6 (MIN6) cells were also conducted via live/dead staining and flow cytometry.

Overall, Novec™ 7500 had the highest density difference with alginate, and the lowest surface tension, compared to the other fluids considered. Using this continuous phase fluid, uniform alginate beads with diameters as low as 1.5 mm were successfully produced with size variations < 10% and production rates of ~100 beads per minute per channel. Preliminary assessments of MIN6 cell survival showed 82 ± 4% viability. Future work will seek to further reduce the minimum bead diameter that can be achieved, to improve cell survival, and to assess encapsulated islet function. The MCE process is a promising low-cost and high-throughput method to encapsulate and transplant a variety of therapeutic cell types.

Hoesli, C.A., Raghuram, K., Kiang, R.L.J. et al. Pancreatic cell immobilization in alginate beads produced by emulsion and internal gelation, Biotechnol. Bioeng. 2010, 108(2) 424-434.

Hoesli, C.A., Kiang, R.L., Mocinecova, D. et al. Reversal of diabetes by βTC3 cells encapsulated in alginate beads generated by emulsion and internal gelation, Journal of Biomedical Materials Research B Applied Biomaterials. 2012, 100(4) 1017-1028.

Markwick, K.E., Dussault, M.A., Bégin-Drolet, A. and Hoesli, C.A. Microchannel emulsification: a novel approach to cell encapsulation, Bioencapsulation Research Group. 2016, 12-13.
Shapiro, A.M.J., Pokrywczynska M., Ricordi C. Clinical pancreatic islet transplantation, Endocrinology. 2017, 13 268-270.