Targeted Microbubble Regenerative Medicine to Treat Type 1 Diabetes

Dr. Paul Grayburn, a cardiologist at Baylor Research Institute (BRI), is a pioneer in the use of ultrasound targeted microbubble destruction (UTMD) technology to deliver therapeutic genes and proteins to the desired cells and tissues.

Dr. Grayburn and his team have shown that UTMD technology can potentially lead to new treatments for type 1 diabetes both directly, by enabling delivery of genes, and indirectly, by enabling testing of innovative treatments in preclinical models. In pilot studies in baboons, the researchers have shown that UTMD-delivered genes result in normalization of blood sugar, insulin levels and glucose tolerance tests. Moreover, this was associated with in vivo regeneration of normally functioning islet cells.

Targeted Microbubble Regenerative Medicine to Treat Cardiac Disease

Recently, Dr. Grayburn and colleagues have leveraged UTMD-mediated delivery of therapeutics for treating cardiac disease. By using UTMD to deliver a therapeutic gene (and separately, the corresponding protein), the researchers successfully treated adriamycin cardiomyopathy in an in vivo rat model. They showed that they could not only stimulate myocardial regeneration, but also reverse the cardiomyopathy itself. This UTMD-mediated therapy approach is potentially a breakthrough for treating cardiomyopathy, in addition to other cardiac diseases.
**Improvement of Islet Cell Transplantation to Treat Type 1 Diabetes and Chronic Pancreatitis**

Researchers at BRI were the first to report that when pancreatic islet cells are injected into patients to treat type 1 diabetes, they are subject to a severe inflammatory reaction, which can damage the islet cells. Molecular analysis revealed that the inflammatory reaction occurs within hours of the transplant. The BRI scientists have discovered a means to counter this destructive inflammatory response. They showed that withaferin A, a plant-derived compound with strong anti-inflammatory and anti-oxidant properties, is a strong inhibitor of inflammation in pancreatic beta islets, protecting them against cytokine-induced cell damage while improving the survival of transplanted islets. Using a mouse model of Type 1 diabetes, the BRI team showed that mice receiving withaferin treatment 30 days after islet transplantation (closed circles) had sufficient islet mass to be functional compared with control mice (open circles), as evidenced by significantly better blood glucose metabolism.

![Graph showing restoration of blood glucose metabolism in withaferin-treated mice after islet cell transplantation](image)

This discovery has important therapeutic implications in islet transplantation, whereby withaferin A could be incorporated as an adjunctive treatment to current immunosuppressive therapies to improve islet transplant outcomes in patients with type 1 diabetes or chronic pancreatitis.

**Opportunities**

BRI has issued patents and pending patent applications for each of these innovations that are available for licensing. In addition, opportunities exist for partnering and collaboration to further advance these technologies.

**Selected Publications:**


SoRelle et al. (2013). Withaferin A inhibits pro-inflammatory cytokine-induced damage to islets in culture and following transplantation. Diabetologia., v. 56, pp. 814-824
