Docket #: S21-284

Localized Drug Delivery Graphene Bioscaffolds for Co-Transplantation of Islets and Mesenchymal Stem Cells

Stanford inventors have developed technologies for improved islet transplantation using a bioscaffold platform that maintains islet health during and after their transplantation.

Islet transplantation is a ?-cell replacement therapy used to treat diabetic patients who lack the ability to secrete insulin. The conventional site for islet transplantation is the liver, however, this is far from optimal given that islets are subjected to hypoxia, toxic metabolites from the liver, a pro-inflammatory environment and an instant blood-mediated inflammatory reaction (IBMIR); together, this results in up to 60-70% of islets being immediately lost following transplantation. Furthermore, given that islet transplantation does not require the creation of a surgical vascular anastomosis, islets therefore need to build and secure a dedicated blood supply, which takes at least 3 weeks. In the interim, islets have to survive by relying on the diffusion of oxygen and nutrients (such as essential amino acids like glutamine and alanine) from the microenvironment of the transplantation site, which results in them enduring significant stress and bioenergetic depletion.

Accordingly, Stanford inventors have addressed several critical problems in the transplantation process with innovative and clinically translatable solutions that will maintain islet health and survival during and following their transplantation. They have developed and validated a novel collagen based cryogel 3D matrix that incorporates an oxygen generator to address the problem of insufficient oxygen which causes islet hypoxia. They also developed a nutrient generator in the form of a mesoporous silica nanoparticle that releases amino acids which can be combined with our bioscaffold. Each of these technologies has been shown to facilitate islet engraftment, function and survival to allow them to reserve hyperglycemia in diabetic animals. They also demonstrate excellent long-term biocompatibility as

tested using our bioscaffold in the subcutaneous space and fat pad (i.e. omentum) in animals. This platform can also be used with stem cell derived beta cells and can be scaled and produced conforming to GMP guidelines for human use.

Applications

- Bioscaffold platform for islet transplantation

Advantages

- Improved biocompatibility
- Reduced inflammatory responses
- More conducive to cells via improved oxygen and nutrient delivery and reduced exposure to toxic metabolites
- Can be used with stem cell-derived islets

Publications

- Razavi, Mehdi, Jing Wang, and Avnesh S. Thakor. *Science advances* 7.47 (2021): eabf9221.

Patents

- Published Application: 20230040370

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