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The Promise of Cell Therapy Realized

Single molecule therapeutics target single pathways and have been limited in success when treating complex diseases. By contrast, cell therapy harnesses the natural properties of cells to interact with, and react to, pathophysiological stimuli arising from multiple pathways in parallel, providing multifactorial support in an unprecedented way. Mesenchymal stem cells (MSCs) are on the brink of becoming the first stem cell product on the market for anti-inflammatory indications. MSCs have been shown to modulate the immune system, protect endogenous tissues from injury, and promote regeneration in a variety of diseases.

The Sentien Approach: Engineered Delivery

The therapeutic mechanism of action of MSC transplants is directly related to the cell's ability to metabolize and secrete molecules into the bloodstream, which causes systemic effects on immune and tissue cells. We have engineered a system to maximize delivery of therapy from these cells and overcome the pharmacological barriers that constrain MSC transplantation.



Figure 1 – Bioreactor delivery of MSC secreted factors harnesses the power of mesenchymal stem cells with the greatest control and longest duration of therapeutic activity. MSCs naturally secrete hundreds of potent therapeutic molecules, but in vivo studies have revealed MSCs only secrete these molecules for a few short hours upon transplantation. Our MSC bioreactors ensure efficient, consistent and reproducible delivery of these factors over many hours of administration.

Our system consists of a bioreactor seeded with mesenchymal stem cells that is designed to connect directly to the bloodstream of a patient. We have optimized manufacturing processes to control device seeding and cell performance with minimized lot-to-lot variability in preparation for clinical use.



Figure 2 – Seeding of MSC bioreactors (SentinelsTM) and lot-to-lot consistency of device performance. We have developed proprietary protocols for control of seeding and distribution of cells on hollowfibers for successful and consistent delivery of potent secreted molecules such as sTNFR1 and VEGF.

The SentinelTM: Mesenchymal Stem Cell Bioreactor Therapy

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> Sentien Biotechnologies, Inc. was formed to translate our flagship product, the Sentinel, into clinical use as an add-on to dialysis. The Sentinel is a mesenchymal stem cell bioreactor that is designed to connect to a patient's bloodstream via an extracorporeal circuit and deliver a diverse array of therapeutic factors secreted by the cells.



Figure 3 – Schematic diagram of the Sentinel bioreactor circuit. Patient blood is routed outside the body with a pump, and into the intracapillary space of a hollow-fiber bioreactor. This bioreactor is seeded with MSCs, and the cells respond to the blood by secreting molecules that are collected in the extracapillary space of the reactor and rejoined with the blood that is returned to the patient.

The Sentinel



Figure 4 – Therapeutic Testing of MSC Devices in Canine Ischemia-Reperfusion Injury. MSC devices were seeded with 500M human allogeneic cells and administered one day after 90 mins of I/R injury for a 12 hour perfusion time. One week survival of dogs shows clear delineation of Sentinel treated animals compared to acellular devices and untreated controls.



Phase I & II SBIR Awards

NIH/NIDDK - R44DK085766 "Mesenchymal Stem Cell Bioreactor for the Active Treatment of Acute Renal Failure"

Phase I SBIR Awards

NIH/NIDDK - R43DK093285 "A Cellular Device for the Treatment of Acute Liver Failure"

DoD (Army) - W81XWH-12-C-0034 "Blood Purification for Organ Failure"

NSF – NSF1013320 "Assembly and Storage of Cell-Derived Drug Delivery Devices"



Lead Program: Acute Kidney Injury

The Sentien lead program is in Acute Kidney Injury, an enormous unmet need:

>2.5M patients develop AKI annually >50% mortality among patients with severe AKI

Funding Sources