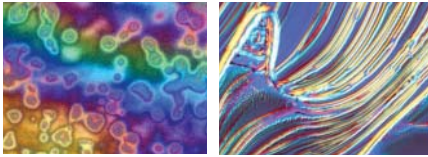


# CELLabration™ Encapsulation System



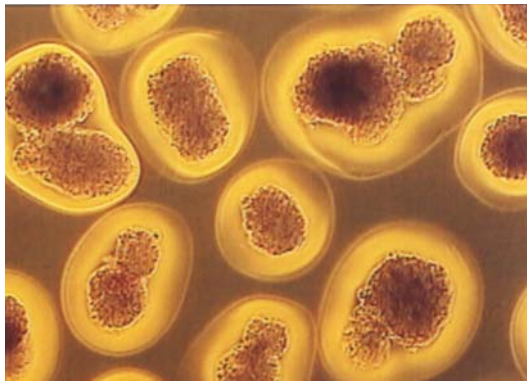
## REGENERATIVE TECHNOLOGIES

### INTRODUCTION

Development of therapeutic protein delivery technologies is the subject of a great deal of research in the pharmaceutical and biotechnology industries. For many clinical conditions, an effective system for delivery of intact and biologically active proteins is unavailable at this time. The use of implanted cells as protein factories is one possible mode to accomplish this goal. The potential advantages of such an approach versus oral administration or injections, include, temporally prolonged expression of the protein, protection of the protein from the proteolytic physiologic environment, and single administration therapy. Protecting the cells while they excrete the proteins is a necessary part of this therapy. The **CELLabration™ Encapsulation System** is a polymeric system designed to conformally coat the surfaces of cells and cell agglomerates, thereby protecting the cells from the body's immune processes, while permitting the passage of nutrients and therapeutic proteins.

### CLINICALLY DEMONSTRATED TECHNIQUE

Novocell, Inc. has demonstrated the effectiveness of the CELLabration technology by the successful encapsulation of islets (cell clusters that produce insulin) from primate donors and transplantation into diabetic primates. The transplants were successful in controlling the blood glucose concentrations in the diabetic recipients. A Phase I/II human clinical trial was initiated by Novocell in December 2005.



**Figure 1.** Encapsulated human islet cells.\* Note the conformal coating surrounding all cell groups. (Photo courtesy of Novocell, Inc.)

### CURRENT TECHNICAL APPROACHES TO CELL THERAPY

There are two methods of providing a therapeutic protein from genetically modified cells: 1) *in vivo* gene therapy wherein the genetic material is introduced directly into the body, typically associated with

a viral component to enhance transfection efficiency, and host cells are transduced to secrete the protein; 2) *ex vivo* gene therapy in which cultured cells are treated with the gene therapy agent, and secreting cells are identified then transplanted into the host.

### BENEFITS OF EX VIVO GENE THERAPY WITH THE CELLABRATION ENCAPSULATION SYSTEM

*Ex vivo* gene therapy may be the preferred method of delivering therapeutic proteins from cells for many reasons, including:

- Cells with secretion of appropriate protein can be selected prior to transplantation.
- Viral transfection of cells, if needed, is performed in a laboratory, thus reducing the risk of live virus transfer to patients.
- Viable and robust cells are prepared by custom engineering instead of targeting degenerating host cells.
- An inducible promoter system can be incorporated to control protein expression.
- Allogeneic cell lines can be used to provide an off-the-shelf product.
- Immune and tumorigenic risks are reduced or eliminated.
- Accommodates all cell types including stem cells.

### POTENTIAL APPLICATIONS

There are many disease states beyond diabetes for which this technology holds promise to provide effective therapies not feasible with current technologies. The proteins potentially delivered include, nerve growth factor for Alzheimer's disease, glial-derived neurotrophic factor for Parkinson's, ciliary neurotrophic factor for ALS, bone morphogenic protein for orthopedic applications, and drug activating enzymes for oncologic applications. The potential of this therapy has only begun to be investigated.

### GOAL

SurModics Regenerative Technologies seeks to partner with visionary medical device and biotechnology companies to commercialize this paradigm-changing technology for the delivery of treatments/therapies as yet not possible. With a focus on strong, synergistic collaborations, SurModics looks to grow the opportunities of these partnerships by bringing innovation together with a team of business and technical leaders committed to accelerated innovation and improved patient outcomes.

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\* Encapsulated islet cells incorporate technology from Novocell, Inc. and SurModics. Islet cell encapsulation is exclusively licensed to Novocell.

9924 West 74th St., Eden Prairie, MN 55344 USA Toll Free: 1-866-SURMODX Phone: 952-829-2700  
Fax: 952-829-2743 www.surmodics.com email: rt@surmodics.com

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