A New Way to DELIVER PROTEINS

Paul Wotton, Ph.D., CEO of Sigilon Therapeutics, discusses his company's approach for delivering cells that avoid immune detection.

Encapsulated cell therapy is an emerging area of biopharmaceutical research that aims to unleash the therapeutic potential of cells to treat serious diseases without the need for immunosuppression.

While implanted cells have shown the ability to produce therapeutic proteins, the cells are often attacked by the immune system, even if the cells are encapsulated. Researchers have struggled to overcome the problem of fibrosis, where scar tissue forms around cell implants. To stop the body's natural response to a foreign body, patients can be given immunosuppression drugs.

Sigilon Therapeutics has discovered a way to solve the problem of fibrosis and immune response. The company has created water-permeable, polymer beads to encapsulate cells. These "milli" beads allow oxygen and nutrients into the cells without triggering an immune response and being covered by scar tissue. The company's Afibromer technology has led to a new class of implantable cell-based therapies that can avoid detection of the immune system.

"This technology platform produces immune privileged cell factories, which can be implanted in humans without the need for immune suppression," Dr. Wotton says.

The company uses genetically engineered cells, which are put into milli beads, an approach it calls "Living Therapeutics." The milli beads that encapsulate the cells create a cell factory, which enables the programming and control of protein delivery, providing a dose-adjustable approach to delivering protein therapeutics.

"The cells live happily there, and they're able to secrete missing proteins," he says.

The advantage of this technology is control, Dr. Wotton says. "We first engineer cells in the lab, which allows us to control the dose before the cells are implanted. We can engineer the allogeneic cells to produce specific proteins, such as factor VIII and factor IX. This is the difference between our approach, which implants a cell factory into the body, and that of gene therapies, which tries to turn body cells into a factory for proteins."

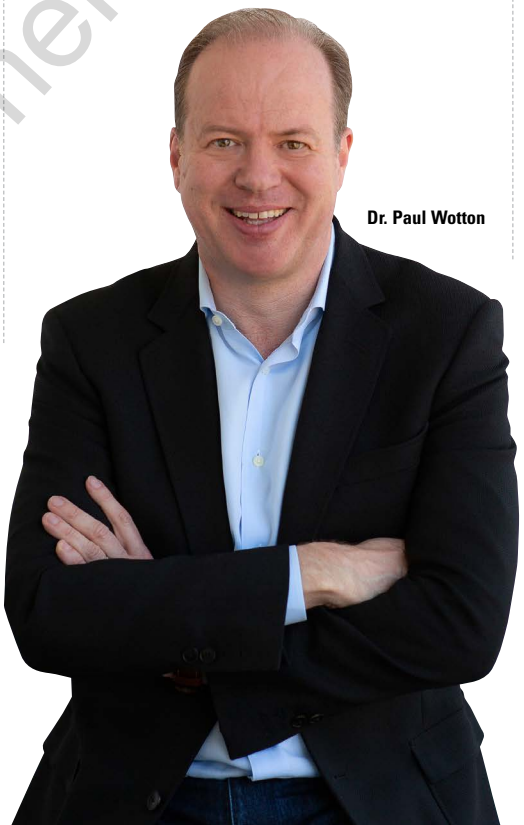
The beads are soft and jelly-like and are about 1 millimeter in diameter. "The beads can contain up to tens of thousands of cells per bead," Dr. Wotton says. "After transplantation, this bead population lives happily inside the body and is able to secrete the proteins they're designed to secrete without being scarred over."

The company's pipeline is focused initially on blood factors, such as VIII and IX, and Dr. Wotton says the company expects to file an IND for one of its hemophilia programs in late 2019.

Dr. Wotton says the technology can be applied to many therapies, and Sigilon is looking at hormone replacement and diabetes. Based on published work done at MIT in both rodent and primate diabetes models, Dr. Wotton is confident the implantation technology can avoid fibrosis in humans.

Sigilon Therapeutics' Afibromer milli beads encapsulate cells creating a cell factory for protein production, which allows for the programming and control of protein delivery and providing a dose-adjustable approach to deliver protein therapeutics.

In April, Sigilon and Lilly began collaborating for the development of encapsulated cell therapies for the potential treatment of type 1 diabetes. In this collaboration, Sigilon will create proprietary products comprised of induced pluripotent stem cells, a type of stem cell derived from adult cells, engineered into differentiated insulin-producing pancreatic beta cells that are encapsulated using Sigilon's Afibromer technology. The goal is to restore insulin production over sustained periods, without triggering any immune reaction.



Dr. Paul Wotton

Lilly will receive an exclusive worldwide license to Sigilon's Afibromer technology for islet cell encapsulation. Sigilon has received an up front payment of $63 million and Lilly will make an undisclosed equity investment in Sigilon. Sigilon is also eligible to receive up to $410 million in development and commercialization milestones, as well as single- to double-digit tiered royalties on future product sales should the collaboration yield a commercially successful product.

Sigilon will be responsible for all development activities and costs related to the collaboration until submission of an investigational new drug application. After an IND is submitted, Lilly will be responsible for all clinical development and commercialization activities and costs related to the collaboration.

Sigilon was founded and created by Flagship Pioneering, a life-sciences innovation firm, which unveiled the company in 2017 with $23.5 million in capital. PV