MedicalXpress

Researchers make progress engineering digestive system tissues

May 18 2015

New proof-of-concept research at Wake Forest Institute for Regenerative Medicine suggests the potential for engineering replacement intestine tissue in the lab, a treatment that could be applied to infants born with a short bowel and adults having large pieces of gut removed due to cancer or inflammatory bowel disease.

Lead researcher Khalil N Bitar, Ph.D., a professor at the institute, which is part of Wake Forest Baptist Medical Center, reported the results this week at Digestive Diseases Week in Washington, D.C. He also updated attendees on a related project to engineer anal sphincters for patients with fecal incontinence.

"Results from both projects are promising and exciting," said Bitar. "Our latest effort, to find a new solution for the urgent need for gut-lengthening procedures, shows we can meet the basic requirements for regenerating segments of the gastrointestinal tract."

Both projects are based on using a patient's own cells to grow replacement tissue in the lab. Elie Zakhem, a doctoral student in Bitar's lab, is currently working on developing tissue-engineered gut replacements. The researchers use smooth muscle and nerve stem cells from human intestine to engineer innervated muscle "sheets." The sheets are then wrapped around tubular chitosan scaffolds. Chitosan is a natural biomaterial derived from shrimp shells. The material is already approved by the U.S. Food and Drug Administration for certain applications.

The tubular structures were implanted just under the skin of rats for 14 days, a first step in assessing their performance. Researchers found that the implants developed a blood vessel supply and that the tube opening was maintained. In addition, the innervated muscle "remodeled," which means that the cells began the process of releasing their own materials to replace the scaffold.

"It is the combination of smooth muscle and neural cells in gut tissue that moves digested food material through the gastrointestinal tract and this has been a major challenge in efforts to build replacement tissue," said Bitar. "Our preliminary results demonstrate that these cells maintained their function and the implant became vascularized, providing proof of concept that regenerating segments of the gastrointestinal tract is achievable."

The researchers' next steps are to develop the lining of the intestine that is responsible for absorption and secretion. In a study involving research animals, they also plan to surgically connect the replacement segments to native intestine to assess function.

The group's second project, to engineer anal sphincters, also reached a new milestone with the successful implantation of the structures in rabbits.

"These bioengineered sphincters, made with both muscle and nerve cells, restored fecal continence in the animals throughout the six-month follow-up period after implantation," he said. "This provides proof of concept of the safety and efficacy of these constructs."

Sphincters are ring-like muscles that maintain constriction of a body passage, such as controlling the release of urine and feces. There are actually two sphincters at the anus - one internal and one external. A large proportion of fecal incontinence in humans is the result of a

weakened internal sphincter.

"Many individuals find themselves withdrawing from their social lives and attempting to hide the problem from their families, friends and even their doctors," said Bitar. "Many people suffer without little help."

To engineer the internal anal sphincters, researchers used a small biopsy from the animals' sphincter tissue and isolated smooth muscle cells that were then multiplied in the lab. In a ring-shaped mold, these cells were layered with nerve cells isolated from small intestine to build the sphincter. The mold was placed in an incubator, allowing for tissue formation. The entire process took about four to six weeks.

The bioengineered sphincters mimicked the architecture and function of native tissue and there are no signs of inflammation or infection after implantation. The constructs demonstrated the presence of contractile smooth muscle as well as mature nerve-cell populations.

"In essence, we have built a replacement sphincter that we hope can one day benefit human patients," said Bitar. "Because these sphincters are made with both muscle and nerve cells, they are 'pre-wired' to be connected with nerve pathways in the intestine."

Bitar's goal is to eventually conduct studies of the technology in humans. He said the technology could be applied to other diseases of the sphincter muscles, including urinary incontinence.

Provided by Wake Forest University Baptist Medical Center