Lab-engineered muscle implants restore function in animals

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New research shows that exercise is a key step in building a muscle-like implant in the lab with the potential to repair muscle damage from injury or disease. In mice, these implants successfully prompt the regeneration and repair of damaged or lost muscle tissue, resulting in significant functional improvement.

"While the body has a capacity to repair small defects in skeletal muscle, the only option for larger defects is to surgically move muscle from one part of the body to another. This is like robbing Peter to pay Paul," said George Christ, Ph.D., a professor at Wake Forest Baptist Medical Center's Institute for Regenerative Medicine. "Rather than moving existing muscle, our aim is to help the body grow new muscle."

In the current issue of Tissue Engineering *Part A*, Christ and team build on their prior work and report their second round of experiments showing that placing cells derived from muscle tissue on a strip of biocompatible material – and then "exercising" the strip in the lab – results in a muscle-like implant that can prompt muscle regeneration and significant functional recovery. The researchers hope the treatment can one day help patients with muscle defects ranging from cleft lip and palate to those caused by traumatic injuries or surgery.

For the study, small samples of muscle tissue from rats and mice were processed to extract cells, which were then multiplied in the lab. The cells, at a rate of 1 million per square centimeter, were placed onto strips of a natural biological material. The material, derived from pig bladder with all cells removed, is known to be compatible with the body.

Next, the strips were placed in a computer-controlled device that slowly expands and contracts – essentially "educating" the implants on how to perform in the body. This cyclic stretching and relaxation occurred three times per minute for the first five minutes of each hour for about a week. In the current study, the scientists tried several different protocols, such as adding more cells to the strips during the exercise process.

The next step was implanting the strips in mice with about half of a large muscle in the back (latissimus dorsi) removed to create functional impairment. While the strips are "muscle-like" at the time of implantation, they are not yet functional. Implantation in the body – sometimes referred to as "nature's incubator" – prompts further development.

The goal of the project was to speed up the body's natural recovery process as well as prompt the development of new muscle tissue. The scientists compared four groups of mice. One group received no surgical repair. The other groups received implants prepared in one of three ways: one was not exercised before implantation, one was exercised for five to seven days, and one had extra cells added midway through the exercise process. The results showed that exercising the implants made a significant difference in both muscle development and function.

"The implant that wasn't exercised, or pre-conditioned, was able to accelerate the repair process, but recovery then stopped," said Christ. "On the other hand, when you exercise the implant, there is a more prolonged and extensive functional recovery. Through exercising the implant, you can increase both the rate and the magnitude of the recovery."

A variety of laboratory tests were used to measure results. A test of muscle force at two months, for example, showed that animals who received the implants with extra cells added had a threefold increase in absolute force compared to animals whose muscle damage was not repaired. The force-producing capacity of muscle is what determines the ability to perform everyday tasks.

"If these same results were repeated in humans, the recovery in function would clearly be considered significant," said Christ. "Within two months after implantation, the force generated by the repaired muscle is 70 percent that of native tissue, compared to 30 percent in animals that didn't receive repair."

The results also showed that new muscle tissue developed both in the implant, as well as in the area where the implant and native tissue met, suggesting that the implant works by accelerating the body's natural healing response, as well as by prompting the growth of new muscle tissue.

The researchers hope to evaluate the treatment in patients who need additional surgery for cleft lip and palate, a relatively common birth defect where there is a gap in muscle tissue required for normal facial development. These children commonly undergo multiple surgeries that involve moving muscle from one location to another or stretching existing muscle tissue to cover the tissue gap. The implant used in the current research is almost exactly the size required for these surgeries.

"As a surgeon I am excited about the advances in tissue-engineered muscle repair, which have been very promising and exciting potential in the surgical correction of both functional and cosmetic deformities in cleft lip and cleft palate" said Phillip N. Freeman, M.D., D.M.D., associate professor of Oral and Maxillofacial Surgery at the University of Texas Health Science Center at Houston. "Current technology does not address the inadequate muscle volume or function that is necessary for complete correction in 20 percent to 30 percent of cases. With this innovative technology there is the potential to make significant advances in more complete corrections of cleft lip and cleft palate patients."

The technology was originally developed under the Armed Forces Institute of Regenerative Medicine (AFIRM) with funding from the Department of Defense and the National Institutes of Health. The sponsor of the current research was the Telemedicine & Advanced Technology Research Center. A longer-term goal is to use the implant – in combination with other tissue-engineered implants and technologies being developed as part of AFIRM -- to treat the severe head and facial injuries sustained by military personnel. For example, AFIRM-sponsored projects under way to engineer bone, skin and nerve may one day be combined to make a "composite" tissue.

Provided by Wake Forest University Baptist Medical Center