

Scientists discover new method for engineering human tissue regeneration

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If pending clinical trials prove successful, a new discovery published in *The FASEB Journal* could represent a major scientific leap toward human tissue regeneration and engineering. In a research report appearing online, Yale scientists provide evidence to support a major paradigm shift in this specialty area from the idea that cells added to a graft before implantation are the building blocks of tissue, to a new belief that engineered tissue constructs can actually induce or augment the body's own reparative mechanisms, including complex tissue regeneration.

"With the constant growing clinical demand for alternative vessels used for vascular reconstructive surgeries, a significant development for alternative grafts is currently the primary focus of many investigators worldwide," said Christopher K. Breuer, M.D., a researcher involved in the work from Yale University School of Medicine/Yale-New Haven Hospital in New Haven, CT. "We believe that through an understanding of human vascular biology, coupled with technologies such as tissue engineering, we can introduce biological grafts that mimic the functional properties of native vessels and that are capable of growing with the patients." Breuer also says that patients are currently being enrolled in a first-of-its-kind clinical trial at Yale University to evaluate the safety and growth potential of tissue-engineered vascular grafts in children undergoing surgery for [congenital heart disease](#).

To make this discovery, Breuer and colleagues conducted a three-part study, starting with two groups of mice. The first group expressed a gene that made all of its [cells](#) fluorescent green and the second group was normal. Researchers extracted [bone marrow](#) cells from the "green" mice, added them to previously designed scaffolds, and implanted the grafts into the normal mice. The seeded bone marrow cells improved the performance of the graft; however, a rapid loss of green cells was noted and the cells that developed

in the new [vessel wall](#) were not green, suggesting that the seeded cells promoted vessel development, but did not turn into vessel wall cells themselves. These findings led to the second part of the study, which tested whether cells produced in the host's bone marrow might be a source for new cells. Scientists replaced the bone marrow cells of a female mouse with those of a male mouse before implanting the graft into female mice. The researchers found that the cells forming the new vessel were female, meaning they did not come from the male [bone marrow cells](#). In the final experiment, researchers implanted a segment of male vessel attached to the scaffold into a female host. After analysis, the researchers found that the side of the graft next to the male segment developed with male vessel wall cells while the side of the graft attached to the female host's vessel formed from female cells, proving that the cells in the new vessel must have migrated from the adjacent normal vessel.

"There's a very good chance that this study will eventually have a major impact on many disorders that afflict humankind," said Gerald Weissmann, M.D., Editor-in-Chief of *The FASEB Journal*. "These scientists have basically used the body's repair mechanisms to make new tissues through bioengineering. In years to come, starfish and salamanders will have nothing on us!"

More information: Narutoshi Hibino, Gustavo Villalona, Nicholas Pietris, Daniel R. Duncan, Adam Schoffner, Jason D. Roh, Tai Yi, Lawrence W. Dobrucki, Dane Mejias, Rajendra Sawh-Martinez, Jamie K. Harrington, Albert Sinusas, Diane S. Krause, Themis Kyriakides, W. Mark Saltzman, Jordan S. Pober, Toshiharu Shin'oka, and Christopher K. Breuer. Tissue-engineered vascular grafts form neovessels that arise from regeneration of the adjacent blood vessel. *FASEB J.* [doi:10.1096/fj.11-182246](https://doi.org/10.1096/fj.11-182246)

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