PROGRESS IN TISSUE

By Ali Khademhosseini, Joseph P. Vacanti and Robert Langer

Pioneers in building living tissue report important advances over the past decade

KEY CONCEPTS

- Efforts to build living tissue replacements have progressed over the past decade, and some simple engineered tissues are already used in humans.
- Advances have come from a greater understanding of cell behavior and sophisticated new building materials.
- More tissue-engineered products are close to commercial readiness but must undergo the complex regulatory scrutiny given to living materials.

—The Editors

When two of us (Langer and Vacanti) last wrote in this magazine 10 years ago about prospects for tissue engineering, the very idea that living flesh could be "constructed" by following engineering principles and combining nonliving materials with cells sounded fantastical to many. Yet the need for such transplantable human tissues to replace, restore or enhance organ function was, and remains, urgent. Today nearly 50 million people in the U.S. are alive because of various forms of artificial organ therapy, and one in every five people older than 65 in developed nations is very likely to benefit from organ replacement technology during the remainder of their lives.

Current technologies for organ substitution, such as whole-organ transplants and kidney dialysis machines, have saved many lives, but they are imperfect solutions that come with heavy burdens for patients. Engineered biological tissues are customizable and immune-compatible and can therefore potentially make a significant difference in the lives of people with failing organs. They can fill other human needs as well, for example, serving as "organs on a chip" for testing the toxicity of candidate drugs.

Engineered tissues can take many forms, from aggregations or thin sheets of cells to thick constructs of complex tissue and, the ultimate engineering challenge, an entire functioning organ. Since we initially presented the obstacles involved in creating these implantable tissues [see "Tissue Engineering: The Challenges Ahead," by Robert S. Langer and Joseph P. Vacanti; SCIENTIFIC AMERICAN, April 1999], scientists have made considerable progress. Products such as skin substitutes and cartilage replacements have already helped thousands of patients. Artificial tissues such as bladder, cornea, bronchial tubes and blood vessels are in clinical trials. And laboratory work on building more complex tissue structures is producing encouraging results.

Although some of the obstacles we described 10 years ago remain, significant advances over the past decade have come from new insights into the way the body naturally builds tissues, during both embryonic development and natural wound healing. And engineering approaches to assembling tissue structures have become more sophisticated, as have the chemical, biological and mechanical properties of the materials available for the task. As a result, the field is coming of age, and tissue-engineered products are increasingly a realistic option for medical treatment.

Delivering Life's Blood

One reason that tissues such as skin and cartilage were among the first to be ready for human testing is that they do not require extensive internal vasculature. But most tissues do, and

TISSUE CULTURE DEVICE containing microfabricated "blood vessels" is one of the advances made possible by novel materials and technologies available to tissue engineers. A membrane containing nanoscale pores separates the artificial vessels from a layer of liver cells.

"MICROFABRICATION OF THREE-DIMENSIONAL ENGINEERED SCAFFOLDS," BY JEFFREY T. BORENSTEIN, ELI J. WEINBERG, BRIAN K. ORRICK, CATHRYN SUNDBACK, MOHAMMAD R. KAAZEMPUR-MOFRAD AND JOSEPH P. VACANTI, IN *TISSUE ENGINEERING*, VOL. 13, NO. 8, 2007