TISSUE ENGINEERING, INC. (TE)

Prostheses Made of Biomaterials That Regenerate Body Parts

From its beginning, the field of bioengineering has focused on providing the best artificial devices — hearing aids, artificial limbs and other prostheses — to replace body parts that are missing, broken, or dysfunctional. This ATP project with Tissue Engineering (TE), a biotechnology start-up company, takes bioengineering far beyond artificial replacements to a technology that regenerates, rather than replaces, lost or damaged tissues. Although this claim sounds like science fiction, it is in fact quite real. And it promises to produce real medical benefits in the very near future.

COMPOSITE PERFORMANCE SCORE
(based on a four star rating)
* * * *

Technology to Regenerate Lost of Damaged Body Parts

TE is pioneering a new class of biomaterials called ADMAT (animal-derived extracellular matrix). The idea behind the company's ATP project is to use ADMAT materials in collagen-scaffold prostheses to replace damaged or dysfunctional tissues and organs. The prostheses are designed to provide templates that mobilize the body's own cells and induce them to rebuild the lost tissue, gradually replacing the prosthesis itself. Regeneration of body parts requires a biomaterial with a structure, components and chemical signals that allow the body's tissue cells to recognize, respond to, and remodel the material without rejecting it as foreign.

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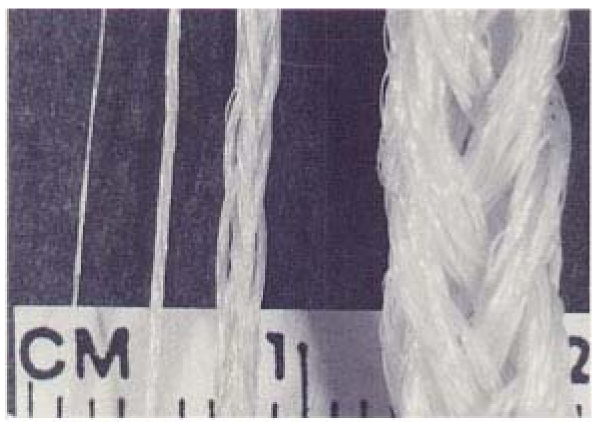
Demand for ADMAT Materials

ADMAT materials are derived from the byproducts of land and marine animals processed for food. The material can be spun into fibers and woven into fabrics using techniques borrowed from the textile industry, or it can be formed into foams, sheets, and films. ADMAT can be used to enhance collagen scaffolds for vascular grafts, ligaments, tendons, periodontal tissue, and similar reconstructions.



Collegen fiber and braided structures from collagen fiber: (a) single collegen fiber, (b) collagen fiber braid, (c) 64-ply collagen fiber braid, (d) 512-ply collagen fiber braid.

During the ATP project, TE successfully developed techniques and procedures for extracting and storing a mixture of collagens and for preserving the desired characteristics of the extracellular matrix. The company

PROJECT HIGHLIGHTS

Project:
To develop techniques and procedures for processing tissue, extracting and storing collagen, and spinning and weaving collagen fibers into fabrics and other forms suitable for human prostheses that could induce the body's own cells to rebuild lost tissue while gradually replacing the prosthesis.

Duration: 3/1/1993 — 2/28/1996
ATP Number: 92-01-0133
Funding (in thousands):

ATP	$1,999	48%
Company	2,128	52%
Total	$4,127	

Accomplishments:
TE accomplished its technical goals. The company developed procedures for processing a tissue-specific extracellular matrix rich in cytokines (cell-generated proteins), extracting and storing type I collagen (a material present in all tissues), and spinning collagen into fibers that can be woven into prosthetic fabrics. The company:

- received two patents for technologies related to the ATP project:"Apparatus and Method for Spinning and Processing Collagen Fiber" (No. 5,562,946: filed 11/2/1994, granted 10/8/1996) and "Bipolymer Foams Having Extracellular Matrix Particulates" (No. 5,709,934: filed 11/22/1994, granted 1/20/1998);

- applied for three other patents related to the technology;

- made several presentations at conferences and workshops; and

- formed a joint venture with Wright Medical Technology, Arlington, Tenn., to develop and distribute products based on the ATP-funded technology for applications involving ligaments, tendons, cartilage, and other musculoskeletal parts

Citations by Others of Project's Patents: See Figure 1.

Commercialization Status:
A commercialization venture has been formed for orthopedic applications. Prototypes are in testing, although no product has yet entered the market. Patent disclosures and a joint venture to commercialize the technology may be providing useful knowledge to other researchers in the field.

Outlook:
This project is on track for market entry in the very near future. The technology is scheduled to be used first in the fabrication of periodontal prostheses and orthopedic applications. Ideas for skin and wound-healing products are also being explored by the company with potential customers.

Number of Employees: 1 at project start, 18 at the end of 1997

Composite Performance Score: * * * *

Company:
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developed new materials for hosting the matrix and a process for adding the matrix to collagen fibers in the course of spinning.

The demand for products the company plans to offer clearly exists. The lag time, however, between technology conception and market availability — particularly for medical treatments — is long. Tissue-engineered products face clinical trials and other regulatory hurdles, in addition to technical and market-introduction barriers. The company is making good progress in navigating these barriers in accord with its technical and business plans.

Commercialization is in progress. TE has placed periodontal prosthesis prototypes with potential customers for testing. It has created other products for research, testing and diagnostic applications. These activities are not regulated, so commercialization can happen more speedily. In addition, it has formed a venture with Wright Medical Technology for commercialization of orthopedic applications. TE is also in discussions with several other companies to commercialize other applications, such as a line of skin and wound-healing products.

Large Potential Benefits for Society

The eventual successful commercial introduction of the ATP-funded technologies will bring large health gains to patients with many forms of medical problems, ranging from dental to cardiovascular. Procedures and materials that would enable the regrowth of ligaments and cartilage in knees and enable dental tissue to regenerate with a single surgery — at costs lower than those offered by alternative medical approaches today, and that one day may even facilitate organ regeneration — would have great benefits for society.

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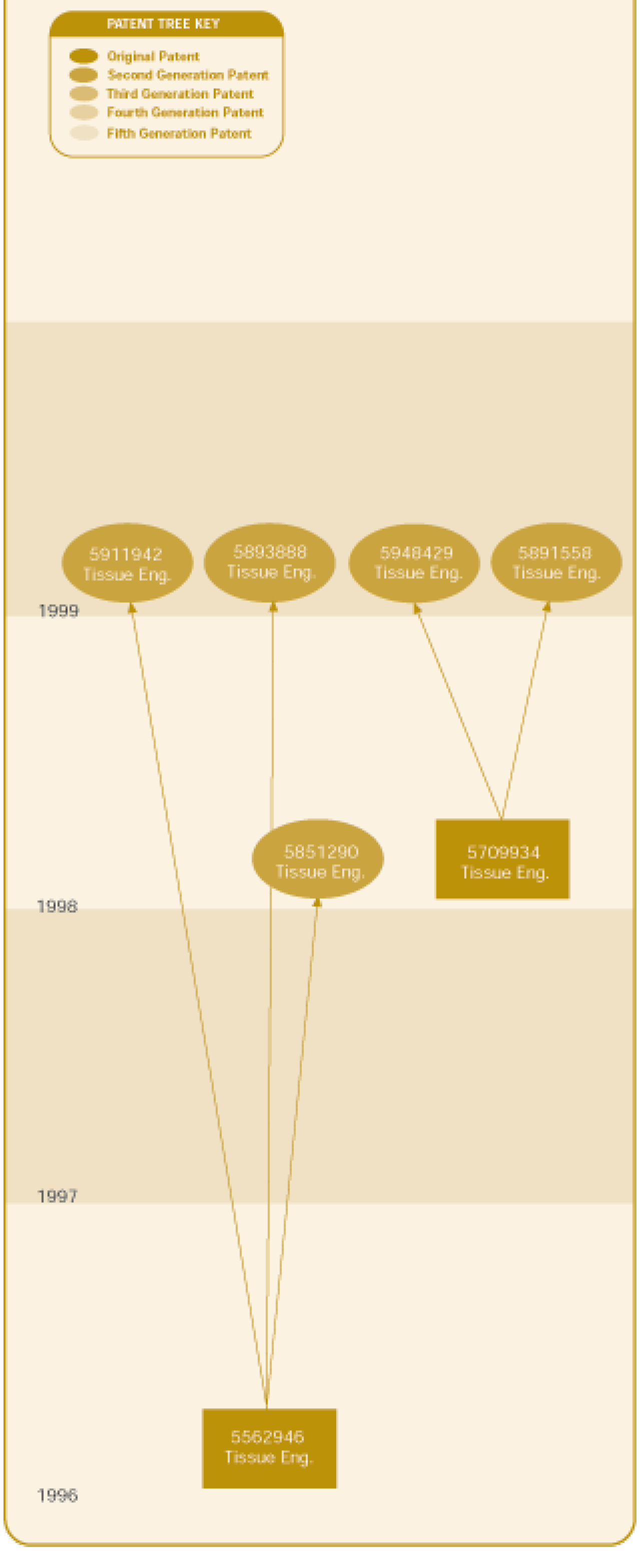
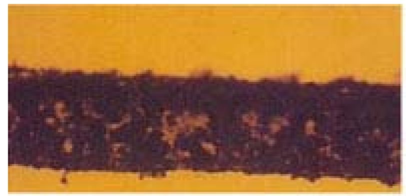
Figure 1 Patent Tree for Project Led by Tissue Engineering, Inc.: Citations by Others of Tissue Engineering, Inc. Patents





Collagen fiber decorated with ADMAT micro-particulates via ATP-funded patended process.

These potential benefits are likely to be huge because of the large number of patients who could use these prostheses, the advantages the TE approach has over currently available alternatives, and improvements in the ability of patients to function as a result of using the new technology. The ATP award is playing an important role in bringing these benefits to society, because applications of the new technology are about two years ahead of where they would have been without ATP funding.

A recent detailed case study by the Research Triangle Institute# estimated that TE's ADMAT technology could be expected to generate about $33 billion (in present value dollars) in net benefits for society in a single medical application area: anterior cruciate ligament repair. The study estimated that about 100,000 patients per year with ligament damage would be eligible for the new treatment, that the number using the Tissue Engineering technology would start at 9,000 in the first year of availability and grow to 72,000 ten years later, supplanting an increasing percentage of alternative technologies currently in use. The study incorporated

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estimated benefits from quality-of-life improvements, using a "quality-adjusted-life-years" index value. It estimated that about $15 billion of the expected benefits would be attributable to ATP's accelerating the technology development by two years.