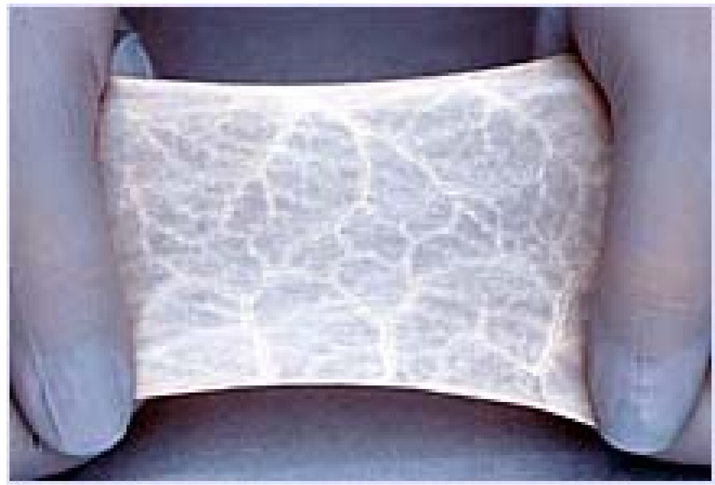
National Institute of Biomedical Imaging and Bioengineering

Bioengineered Tissue Scaffold Promotes Wound Healing

A material developed from the small intestines of pigs is increasingly used by surgeons to restore damaged tissues and support the body's own healing process. Physicians rely on the material, called small intestinal submucosa (SIS), for everything from reconstructing ligaments to treating incontinence. Today, SIS is most commonly used to help the body close hard-to-heal wounds such as second-degree burns, chronic pressure ulcers, diabetic skin ulcers, and deep skin lacerations.

"About half a dozen new tissue engineering companies have capitalized on our findings and have helped translate NIH-funded research into medical devices that are treating patients," says Dr. Stephen Badylak, who helped to discover the healing properties of SIS about 20 years ago.

If researchers magnified SIS a hundred times, it would look like a giant loofah sponge: a wild matrix of loosely intertwined collagen fibers with ample channels and space between the threads. When SIS is placed on a wound, the tissue's anatomic structure acts as an anchor for migrating cells like fibroblasts, which help synthesize collagen, and macrophages, which fight off bacteria. The mesh also supports growing capillaries as they wrap themselves around the collagen fibers like small vines. Once established, these capillaries will eventually ensure a supply of oxygen and nutrients to the new tissue covering the wound. This flurry of activity creates an environment that fosters healing and nurses the skin back to health, totally closing the wound.



Doctors are using this material, made from pigs' intestines, to heal wounds in humans. When moistened, the material, which is called SIS, is flexible and easy to handle.
Image courtesy of Dr. Stephen Badylak, University of Pittsburgh.

An "Accidental" Discovery

SIS was an accidental discovery. In the mid-1980s at Purdue University, Dr. Badylak was searching for naturally occurring substitutes for vascular grafts made of synthetic polymers. Although the polymer grafts were known to work well for larger blood vessels, they had a 50 percent failure rate at five years in smaller vessels.

"I asked myself, 'What body part could substitute as a blood vessel and replace the use of synthetic graft materials?' Our research team discussed many options such as stomach, urinary bladder, and others, but decided to first examine the small intestine because of its natural tubular configuration, its strength, and its abundance in the body," says Dr. Badylak, who is today a professor at the University of Pittsburgh's Department of Surgery.

Dr. Badylak and his team successfully implanted the intestinal tissue in animals. The researchers found that the extracellular matrix (ECM) of the small intestine was the key to successfully creating a biologic scaffold for tissue repair. The ECM consists of structural and functional proteins including many types of collagen, growth factors, and support molecules. Additionally, the team discovered that the ECM not only serves as nature's starting point for tissue healing, but also supplies the foundation for wound repair. For instance, the team learned that ECM-associated molecules generated during wound healing have potent functions, helping to resist infection and recruiting tissue-building molecules for the site of injury.

Hastening the Healing Process

In addition, researchers have discovered ECM sources in the urinary bladder, the liver, and the spleen that can function as biologic scaffolds. “More than 250,000 human patients have been treated with the ECM biologic scaffolds within the past three years, and their use continues to expand,” says Badylak.

SIS, for example, which relies on an extracellular matrix, can be configured into sheets, gels, powders, and multilaminate forms for orthopedic use and hernia repair. In its early stages, scientists engineered SIS primarily from a mechanical perspective. Researchers were looking for a material shaped like a tube, the size of blood vessels, and strong enough to be sutured while also sustaining the contraction and expansion of a pulsating artery. Scientists have since realized that engineering SIS from a biochemical standpoint is paramount. For successful healing to occur, the graft tissue must foster a molecular environment that can speed up the body’s own healing process.

“Through our currently funded NIBIB research, we are trying to understand the biomolecular, immunologic, anatomical, and biomechanical processes of SIS,” says Badylak. “Basically, we are trying to understand all the principles that Mother Nature uses to rebuild tissues.”

Reference

Badylak SF. Xenogenic extracellular matrix as a scaffold for tissue reconstruction. Transplant Immunology 12:367-377, 2004.