'Origami organs' can potentially regenerate tissues

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Northwestern Medicine scientists and engineers have invented a range of bioactive "tissue papers" made of materials derived from organs that are thin and flexible enough to even fold into an origami bird. The new biomaterials can potentially be used to support natural hormone production in young cancer patients and aid wound healing.

The tissue papers are made from structural proteins excreted by cells that give organs their form and structure. The proteins are combined with a polymer to make the material pliable.

In the study, individual types of tissue papers were made from ovarian, uterine, kidney, liver, muscle or heart proteins obtained by processing pig and cow organs. Each tissue paper had specific cellular properties of the organ from which it was made.

The article describing the tissue paper and its function will be published Aug. 7 in the journal *Advanced Functional Materials*.

"This new class of biomaterials has potential for tissue engineering and regenerative medicine as well as drug discovery and therapeutics," corresponding author Ramille Shah said. "It's versatile and surgically friendly."

Shah is an assistant professor of surgery at the Feinberg School of Medicine and an assistant professor of materials science and engineering at McCormick School of Engineering. She also is a member of the

Simpson Querrey Institute for BioNanotechnology.

For wound healing, Shah thinks the tissue paper could provide support and the cell signaling needed to help regenerate tissue to prevent scarring and accelerate healing.

The tissue papers are made from natural organs or tissues. The cells are removed, leaving the natural structural proteins - known as the extracellular matrix - that then are dried into a powder and processed into the tissue papers. Each type of paper contains residual biochemicals and protein architecture from its original organ that can stimulate cells to behave in a certain way.

In the lab of reproductive scientist Teresa Woodruff, the tissue paper made from a bovine ovary was used to grow ovarian follicles when they were cultured in vitro. The follicles (eggs and hormone-producing cells) grown on the tissue paper produced hormones necessary for proper function and maturation.

"This could provide another option to restore normal hormone function to young cancer patients who often lose their hormone function as a result of chemotherapy and radiation," Woodruff, a study coauthor, said.

A strip of the ovarian paper with the follicles could be implanted under the arm to restore hormone production for cancer patients or even women in menopause.

Woodruff is the director of the Oncofertility Consortium and the Thomas J. Watkins Memorial Professor of Obstetrics and Gynecology at Feinberg.

In addition, the tissue paper made from various organs separately supported the growth of adult human stem cells. Scientists placed human

bone marrow stem cells on the tissue paper, and all the stem cells attached and multiplied over four weeks.

"That's a good sign that the paper supports human stem cell growth," said first author Adam Jakus, who developed the tissue papers. "It's an indicator that once we start using tissue paper in animal models it will be biocompatible."

The tissue papers feel and behave much like standard office paper when they are dry, Jakus said. Jakus simply stacks them in a refrigerator or a freezer. He even playfully folded them into an origami bird.

"Even when wet, the tissue papers maintain their mechanical properties and can be rolled, folded, cut and sutured to tissue," he said.

Jakus was a Hartwell postdoctoral fellow in Shah's lab for the study and is now chief technology officer and cofounder of the startup company Dimension Inx, LLC, which was also cofounded by Shah. The company will develop, produce and sell 3-D printable materials primarily for medical applications. The Intellectual Property is owned by Northwestern University and will be licensed to Dimension Inx.

An Accidental Spill Sparked Invention

An accidental spill of 3-D printing ink in Shah's lab by Jakus sparked the invention of the tissue paper. Jakus was attempting to make a 3-D printable ovary ink similar to the other 3-D printable materials he previously developed to repair and regenerate bone, muscle and nerve tissue. When he went to wipe up the spill, the ovary ink had already formed a dry sheet.

"When I tried to pick it up, it felt strong," Jakus said. "I knew right then I could make large amounts of bioactive materials from other organs.

The light bulb went on in my head. I could do this with other organs."

"It is really amazing that meat and animal by-products like a kidney, liver, heart and uterus can be transformed into paper-like biomaterials that can potentially regenerate and restore function to tissues and organs," Jakus said. "I'll never look at a steak or pork tenderloin the same way again."

Provided by Northwestern University