Researcher says microchannels could advance tissue engineering methods

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Utilizing fractal patterns similar to those created by lightning strikes, Victor Ugaz, associate professor in the Artie McFerrin Department of Chemical Engineering at Texas A&M University, has created a network of microchannels that could advance the field of tissue engineering by serving as a three-dimensional vasculature for the support of larger tissue constructs, such as human organs.

Ugaz's work, which was undertaken with colleague Arul Jayaraman and appears in the July online version of "Advanced Materials," is funded by the National Institutes of Health.

The findings detail the construction of an elaborate network of fractal channels that mimic the naturally occurring vasculatures found in trees as well as in the human body. The controlled manufacturing of these networks, which are capable of supporting transport of fluid, is the first step in translating this work to a tissue engineering application where it potentially stands to make a significant impact, Ugaz says.

"I think we've learned how to make these 3-D channels, and we can make them in the kinds of materials that people would use for tissue-engineering applications, in biomaterials," says Ugaz. "We've also looked at characteristics of the network, and we've shown that there are similarities to natural-occurring vasculature."

Providing man-made replacement parts to people in need of organ transplants (and bypassing the need for suitable donors) has been a chief aim of tissue engineering, but so far the field's biggest successes have been the production of skin and cartilage. This is largely due to the fact that tissue engineers have yet to effectively produce a three-dimensional vasculature that can serve as a network of artificial arteries, veins and capillaries. This network of channels is needed to support larger structures such as kidneys, Jayaraman explains.

"Developing scaffolds for tissue engineering with built-in vasculature is a high priority area in tissue engineering as the ability to provide nutrients to all depths of growing tissue is extremely critical," says Jayaraman, assistant professor in the department. "Typically, as the tissue grows, the inner regions tend to be nutrient-limited, which affects the overall viability of the tissue-engineered product. The development of 3-D vascular networks in bio-compatible materials addresses this specific need in the tissue engineering community."

Without such a network in place, the tissue created by engineers is dependent upon diffusion for the transport of nutrients and waste products. Diffusion, however, is a slow process, taking about 17 minutes to traverse a span of 200 microns, or about twice the thickness of a human hair. Increase that distance to an inch, and it takes close to four months for diffusion to occur. That length of time won't support cell growth, Ugaz notes.

"That's just a fundamental limit of this diffusion mechanism - the timescale," Ugaz says. "If your aim is to manufacture artificial organs, you'll need a network that has the ability to supply all of the cells in a three-dimensional volume with nutrients while moving waste products out and keeping these processes going in a certain timescale.

"The way this is all accomplished [in nature] is with a type of branched network, similar to how a tree is naturally structured. There is a trunk, and distribution occurs throughout a large volume by branches of various lengths and thicknesses that emanate from that trunk. This allows transport to penetrate inside a large volume, until the distance between branches and stems is minimized. It's all really an issue of transport."

Framing the challenge in those terms, Ugaz began contemplating how such a complex architecture could be artificially mimicked. He was well aware of a phenomenon known as the Lichtenberg effect. Named after German physicist Georg Christoph Lichtenberg, the effect is responsible for the creation of a fractal pattern as a stored electrical charge is released. This branching pattern occurs on the surface or interior of insulating materials during an electric discharge.

The patterns are similar to the branching patterns seen in a lightning strike. They also can be seen on the skin of lightning-strike victims or on the ground at the point where a lightning strike occurred. A more common example of this effect can be seen in crystal blocks that are often sold as decorative pieces.

Observing these patterns, Ugaz saw the similarities to the artificial network he envisioned creating and wondered if liquid could be transported through these branching pathways, similar to the way nutrients are transported through a tree's vasculature.

He went to work, teaming with Texas A&M's National Center for Electron Beam Research to implant a high level of electric charge inside an acrylic block using electron beam irradiation. When a point of release for the charge was created, Ugaz was left with the expected fractal patterns.

In his laboratory, he and his research group continue to account for such variables as size, range of size, angles, average area ratios and diameters, as well as how all of this relates to the intensity and frequency of charge. Together with Jayaraman, Ugaz is working to translate these microchannels into a biomedical application.

Their work appears promising. So far, the team has found that these fractal pathways can indeed serve as an elaborate vasculature that is capable of sustaining transport in manner suited for tissue engineering purposes. What's more, by adjusting certain variables, Ugaz can reliably reproduce these architectures not only in acrylic blocks but in biodegradable porous materials that allow for cell cultures to be embedded in the area surrounding the vasculature. He's even begun widening the vascular channels to facilitate flow through them and interconnecting separate networks to form larger vasculatures.

And unlike other methods of creating artificial vasculatures, Ugaz's method enables large, complex, three-dimensional networks to be instantaneously constructed in a way that enables them to be mass-produced.

Ugaz emphasizes that his findings thus far are simply the first step in a lengthy process of applying his work to tissue engineering applications. There's still much work to be done, including developing a means of lining his microchannels with cells that would help preserve the network while directing the surrounding material to break down.

Source: Texas A&M University

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