A team from Columbia University and the Italian Institute of Technology has provided the first direct view of an unusual phenomenon thought to be responsible for the excellent optoelectronic properties of perovskite materials.

Charge carriers in lead halide perovskites last for an unusually long time and travel long distances, resulting in high efficiency despite defects in the material. Columbia's Xiaoyang Zhu and his colleagues had proposed previously that these unique carrier properties are due to polarons—quasiparticles that represent electrons and their self-induced polarization in the lattice—that screen charge carriers and keep them from colliding with defects. But no one had been able to directly observe how, or if, they are formed.

Zhu, Filippo De Angelis, and their colleagues used time-resolved optical Kerr effect spectroscopy to give a time domain view of polaron formation in $CH_3NH_3PbBr_3$ and $CsPbBr_3$ perovskites. The results, reported in *Science Advances* (doi:10.1126/sciadv.1701217), revealed that deformations of the soft $PbBr_3$– lattice are mainly responsible for the polaron formation, and having an organic cation is not essential. Polarons form more than twice as quickly in the methylammonium perovskite than the cesium one because of its higher frequency of $PbBr_3$– vibrations. The researchers also confirmed the formation of the polarons using density functional theory calculations.

A new method to heal defects and make them electronically less reactive in hybrid halide perovskite films could provide a path to further improve the efficiency and stability of perovskite solar cells.

Perovskite surfaces and grain boundaries have a high density of ionic defects, where charges can get trapped and recombine, reducing efficiency. Oxygen or moisture can also seep into perovskite films at defects, setting off degradation, which makes devices less stable. So far, researchers have passivated charged defects in perovskites by adding molecules that act as electron donors or acceptors. But most passivation molecules only passivate one type of defect, either positively or negatively charged.

University of Nebraska–Lincoln's Jinsong Huang reported in *Nature Energy* (doi:10.1038/nenergy.2017.102) that quaternary ammonium halides with the structure $NR^+_4X^-$, where R is an alkyl or aryl group and X is a halide, can efficiently passivate charged defects in mixed-cation halide perovskites with quaternary ammonium and halide ions. With a passivation layer of quarternary ammonium halides—choline chloride or choline iodide—deposited on the perovskite film, the efficiency of $CH_3NH_3PbI_3$ solar cells went up from 17% to a certified value of over 20%.

Bio Focus

Small tissue reprogramming device designed to heal damaged tissues

The advent of cellular reprogramming technologies (those that convert one specific cell type into another) in recent years has opened the possibility for doctors to be able to use on-site, cell-based therapies to treat a range of health issues. For example, these technologies could one day be used to treat Parkinson's disease by converting certain brain cells into nerve cells that produce the chemical messenger dopamine, which helps coordinate body movements. Approaches thus far, however, have numerous hurdles to overcome before becoming viable, such as the risky reliance on viruses to deliver genes that drive the reprogramming process.

Researchers at The Ohio State University (OSU) have now developed a technology called tissue nanotransfection (TNT), which uses a nanochannel device and small electric charge to deliver reprogramming factors that directly transform skin and other adult cells into other types of cells on-site. Described recently in *Nature Nanotechnology* (doi:10.1038/NNANO.2017.134), TNT was used to reprogram skin cells in mice to become vascular (blood vessel) cells in badly injured legs that lacked blood flow, ultimately saving the legs within a short time. In other experiments, researchers used TNT to reprogram skin cells into nerve cells, which they injected into brain-injured mice to help them recover from a stroke.

"We've moved from a stem cell concept to a stem tissue or tissue reprogramming concept that understands that individual cells work with other [cells] in their environment," says study lead author Chandan K. Sen, director of OSU's Center for Regenerative Medicine and Cell-Based Therapies. "Our technology aims at converting tissues as a whole."

The ability to reprogram adult cells to other types of cells is not new. A decade ago, researchers from Japan and the United States showed that they could use gene-carrying viruses to transform adult skin cells into so-called induced pluripotent stem cells (iPS cells)—cells resembling embryonic stem cells that can then develop into other types of cells. While viral vectors are efficient tools for cell reprogramming, they cause inflammation in the body and can even switch on cancer genes, making them unsafe for use in people.

More recently, researchers have devised other nonviral techniques to reprogram cells, but the intermediate step involving iPS cells is still an issue. "Even pluripotent cells themselves can be cancerous," Sen says. A major issue with these techniques, in general, is that they focus on developing and studying cells outside of the body. "But how much of that is relevant to scenarios within the body is questionable," Sen says.

Sen and his team instead wanted to develop a method to reprogram cells *in vivo* without needing viruses or iPS cells. But current *in vivo* transfection technologies deliver genes in a stochastic manner,

which can lead to potentially severe side effects, including inflammation and cell death. The solution was to use nanochannel-based transfection that allows delivery of reprogramming factors with the least injury and highest efficiency. "It's basically a series of nanosized needles that guide the delivery of genetic material," Sen says.

The team created their TNT platform chip by first spin-coating a photoresist layer onto thinned, double-sided-polished silicon wafers. They then patterned nanoscale openings onto the photoresist via lithography. Using the openings as etch masks, they used deep reactive ion etching to drill nanochannels in the silicon. On the backside of the wafers, they used contact photolithography to pattern microscale reservoirs. As a final step, they deposited an insulating and protective layer of silicon nitride onto the TNT platform surface.

When an intense, focused electric field is applied through the arrayed nanochannels, tissue cell membranes in contact with the device are benignly nanoporated (exposed to nanosecond electric pulses that reversibly increase membrane permeability) and reprogramming factors are electrophoretically driven into the cells. Importantly, the researchers needed to identify reprogramming factors that could directly turn adult connective tissue (fibroblasts and keratinocytes) into other types of tissues. Through the study of fetal biology and how blood vessels develop, they identified genetic factors—*Etv2*, *Foxc2*, and *Fli1*, or *EFF*—that could turn skin cells into a type of vascular cell (induced endothelial cells) *in vitro*.

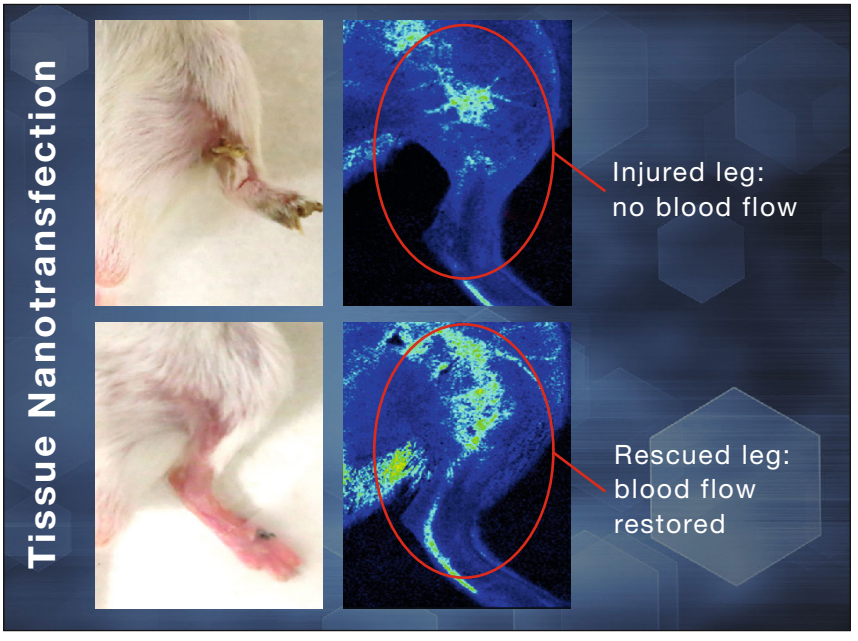
The researchers tested their device on mice that had damaged femoral arteries preventing blood from flowing throughout their legs. They placed the penny-sized TNT chip onto the animal's skin, applied the electric field to the device for less than a second, and removed it. After one week, imaging tests showed that new blood vessels were growing in the leg—the skin tissues converted to functioning blood vessels, and the process even extended into deeper regions of the limb. This process was likely mediated by extracellular vesicles, released from the skin cells, that carry the genetic material encoding the reprogramming factors, which then get taken up by a second line of cells. In effect, the reprogramming process built an extensive network of blood vessels and after two weeks, blood flowed throughout the whole leg again, saving the limb.

In other tests, the research team used the TNT chip to inject the well-established reprogramming factors *Ascl1*/*Brn2*/*Myt1l* (ABM)—protein-encoding genes—into the skin of mice that suffered from stroke. The cells developed into neurons (nerve cells), which the researchers harvested and implanted into the mice brains to help them recover. Physiological brain readings suggested improvements three weeks after implantation. Importantly, the reprogramming process did not set off the immune system so TNT did not require immunosuppression.

"I think this is a real interesting new technology which may facilitate *in vivo* reprogramming in the future," says Benedikt Berninger, who researches adult neurogenesis and cellular reprogramming at the Johannes Gutenberg-Universität Mainz in Germany. "The key achievements are the improved delivery of reprogramming factors (plasmids encoding transcription factors) by the topical nanoporation of skin cells compared to classical bulk electroporation which causes more damage." Similar to nanoporation, bulk electroporation increases cell membrane permeability, but the technique is far less precise due to the way the electric field is applied. But Berninger is curious about whether the technique can be applied to deep tissues (such as the heart or pancreas) and about the target cell specificity of the extracellular vesicles. "Ideally, the extracellular vesicles should only be taken up by cells that one would like to reprogram, but there is currently no way to direct this process," he says.

On the former point, Sen says the TNT platform is not limited to reprogramming skin cells and can be used on any type of fibroblast. The team is currently working on identifying reprogramming factors to turn fibroblasts into other types of cells; they have already found several, including factors to make insulin-producing islet cells (for diabetes treatment) and brown adipose tissue (for obesity treatment).

Joseph Bennington-Castro



Introducing a technique called tissue nanotransfection, researchers are able to reprogram skin cells into vascular cells, allowing a badly injured mouse leg to heal in two weeks. Credit: The Ohio State University.