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To make old skin cells act young again, boost their surroundings, scientists show

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As we get older, the trillions of cells in our body do too. And like us, they become less resilient and able to weather the stress of everyday life. Our skin especially tells the tale of what's happening throughout our bodies.

But recently, scientists have learned that aging cells bear only part of the blame for this downward spiral. And a new study shows that it might be possible to slow the decline of aging tissue – and even make it act younger—by focusing on the stuff that surrounds those cells.

In an independent study at the University of Michigan Medical School, skin scientists have succeeded in making the skin cells of senior citizens act like younger cells again, simply by adding more filler to the fiber-filled area around the cells.

This extracellulal matrix, or ECM, acts like the scaffold that skin cells roost in. It's made of tiny fibrils of collagen, produced by the cells (fibroblasts). Over time, as skin ages, the ECM becomes fragmented, which causes cells to lose their connections to that scaffold – and the lack of support accelerates their decline further. The same thing may happen in other types of tissue.

In the new study, scientists from the U-M Department of Dermatology injected the skin of 21 volunteers in their 80s with a filler often used cosmetically to reduce facial wrinkles. The filler bolsters the ECM, filling in the spaces left by aging.

The researchers did not receive funding from the product's manufacturer, nor did they get input on the design or results from the company. Rather, they were using the product as a way to increase the mechanical forces within the volunteers' skin.

They also didn't focus on the face, where skin takes a beating over a lifetime of exposure to ultraviolet light and other insults that break down collagen. Instead, they focused on skin that had almost never seen the light of day – the buttocks.

The result: over three months, the fibroblasts began expressing collagen-related genes, producing more collagen, and connecting better to the ECM. The entire layer of skin grew thicker, and more blood vessels, which nourished the cells were seen.

"Fragmentation of the extracellular matrix plays an important role in skin aging, but by altering the matrix using an external filler and increasing the internal pressure, we've shown that we can essentially trigger a signal for cells to wake up," says Gary Fisher, Ph.D., the Harry Helfman Professor of Molecular Dermatology and senior author of the new study, published in the *Journal of Investigative Dermatology*.

He cautions that the new work, done together with U-M associate research professor Taihao Quan, Ph.D., and assistant professor Frank Wang, M.D., and colleagues, does not mean that cosmetic filler should be used throughout the body.

Rather, the importance of the discovery lies in the potential to harness the broader understanding of the ECM for prevention and treatment.

For instance, skin thinning as we age leaves us more prone to skin tearing and interferes with healing after incisions or injury. Better understanding of how the ECM helps support healing could lead to

better strategies for helping patients.

"This shows that skin cells in elderly people have the capacity to respond robustly in a very positive way to alterations in the mechanical property of their environment," says Fisher. "We still need to know more about how cells sense their environment, but in general it appears we have made a real difference in the structural integrity of skin."

More information: *Journal of Investigative Dermatolology*, advance online publication doi:10.1038/jid.2012.364

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