NewsBytes

Studying Force in 3-D

Mechanical forces drive many processes in the human body, from organ and tissue formation during development, to stem cell differentiation, to wound healing. Until recently, scientists could only study these forces at the single cell level in two-dimensional experimental models. Now, researchers have developed a new tool and computer model to study forces generated by cells in 3-D contexts at a very small scale.

"This is the first time we have been able to measure three-dimensional forces in very small structures or with a small number of cells," says **Christopher Chen, PhD**, bioengineering professor at the University of Pennsylvania and senior author of the work that appeared in a June 2009 issue of *Proceedings of the National Academy of Sciences*.

Chen's group measured forces exerted by human and mouse fibroblasts, a type of cell that is abundant in connective tissue in the body. Fibroblasts secrete proteins to form an extra-cellular matrix that binds cells together into tissues. "All cells aside from blood cells are adhered to this matrix, sort of like a carpeting that they're embedded in, and they're pulling against that matrix," Chen says. "When they feel those forces, there's a fair amount of data to suggest that they change their behavior."

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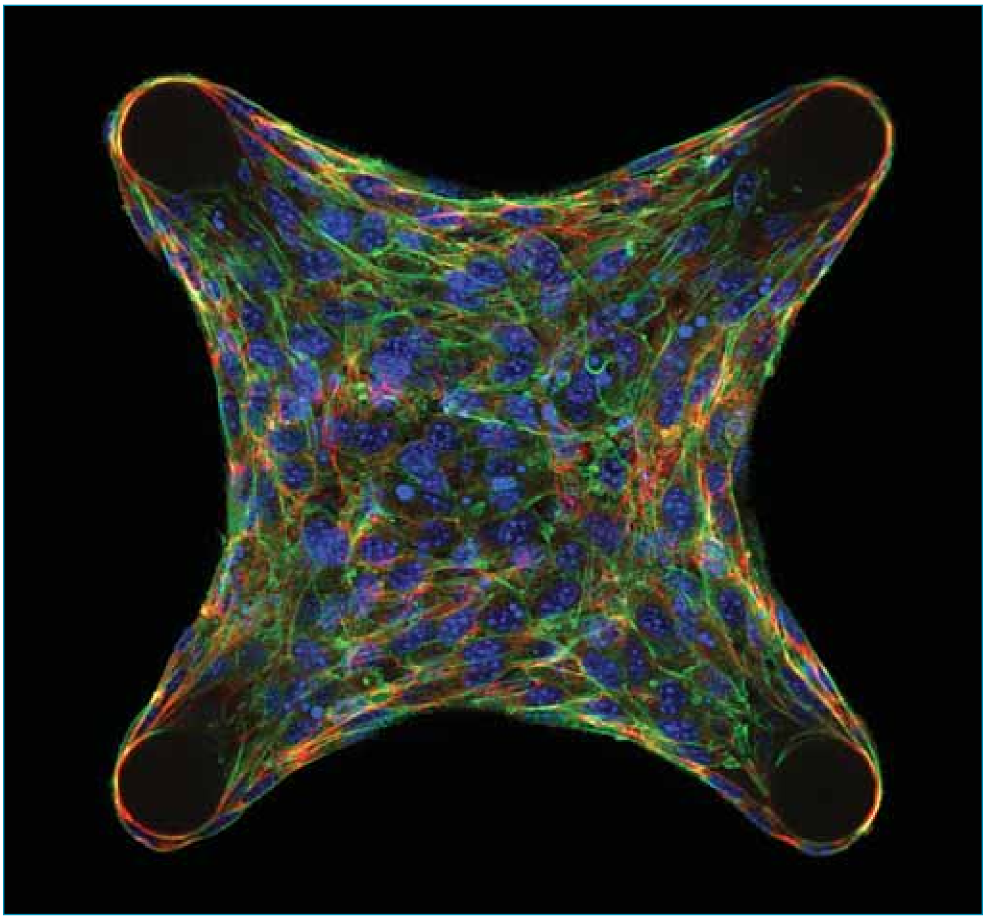

Fluorescent image of fibroblast cells embedded in a collagen matrix suspended between four small rods. Chen's study measured the force exerted by these cells using sensors at the small rods, and used computational models to predict the patterns of force throughout the microtissue. Cell nuclei are shown in blue, the cytoskeleton protein actin in green, and structural matrix proteins in red. Image courtesy of Wesley R. Legant.

The measurement tool Chen's group constructed contains two tiny cantilevers connected to a sensor with a collagen gel between them. Chen's group then put fibroblasts into the collagen goo. When fibroblasts hit collagen, they contract and reorganize the collagen fibers, Chen says, and this results in a mix of collagen and cells suspended between the cantilever rods, like a hammock. The scientists then measured the force from that contraction. They also varied conditions in the set up, such as the thickness of the collagen and the stiffness of the cantilever springs, and looked at how the cells reacted. The stiffer the springs, the more the fibroblasts contracted. And the more contractile forces the cells encountered, the more extra-cellular matrix they pumped out. In the body, this reaction to force is useful. For example in wound healing, the fibroblasts sense the tension from the wound edges pulling apart and secrete more matrix to form scar tissue.

Chen and his group then constructed a computational model to better understand the distribution of force within the collagen mass. They found that the points in the structure where their model predicted the highest stress correlated with the most production of extracellular matrix. The model can also be useful for predicting forces in more complicated geometrical structures, more like those found in the body, Chen says.