McGowan Institute for Regenerative Medicine
A program of the University of Pittsburgh and UPMC

Pitt, Carnegie Mellon Engineers Develop New Method to Explore Mechanical Communication Between Cells

When the body forms new tissues during the healing process, cells must be able to communicate with each other. For years, scientists believed this communication happened primarily through chemical signaling. Now researchers at Carnegie Mellon University and the University of Pittsburgh have found that another dimension – mechanical communication – is equally if not more crucial. The findings, published in the *Proceedings of the National Academy of Sciences*, could lead to advancements in treatments for birth defects and therapies for cancer patients.

"It's like 19th century scientists discovering that electricity and magnetism were the same force," said McGowan Institute for Regenerative Medicine affiliated faculty member Lance Davidson, PhD, associate professor and Wellington C. Carl Faculty Fellow of Bioengineering at the University of Pittsburgh, who co-led the study. "The key here is using mechanical engineering tools and frameworks to reverse-engineer how these biological systems work, thereby giving us a better chance to develop methods that affect this cellular communication process and potentially treat various diseases related to tissue growth."

"We answered this very important biological question by building a new tool that enabled us to see these mechanical processes at the cellular level," said McGowan Institute for Regenerative Medicine affiliated faculty member Philip LeDuc, PhD, professor of Mechanical Engineering at Carnegie Mellon, who co-led the study with Dr. Davidson. The researchers developed a microfluidic control system that delivers chemicals at extremely low flow rates over very small, specific areas, such as integrated collections of individual cells. They hypothesized that in addition to using chemical signals to communicate with each other, embryonic or regenerative cells also used mechanical processes – pushing and pulling on each other – to stimulate and respond.

"In order to identify these mechanical processes, we really had to control small parts of a multi-cellular tissue, which today's technology can finally allow us to do," Dr. Davidson explained. For example, a tissue sample 2 millimeters across may contain up to 8,000 cells. The microfluidic device enables researchers to "touch" as few as three or four and view the mechanical processes using a high resolution laser scanning microscope to view proteins moving in cells.

"We proved that mechanical processes are absolutely important along with chemical," Dr. LeDuc said. When the researchers disabled the mechanical connections between the cells using

microfluidics, the ability of cells to communicate with each other dropped substantially. Although the cells communicated through chemical signaling as well, the cells' mechanical connections – their ability to push and pull on each other – were dominant in transmitting the signals.

Understanding this additional dimension could impact future research in tissue regeneration, from embryonic development to healing to cancer growth.

"If you are dealing with someone who has a birth defect, and their heart didn't form correctly, the question is how do you target it?" Dr. LeDuc asked. "This discovery leads us to believe there is a mechanical way to influence tissue development and one day help the cells better communicate with each other to heal the body."

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Abstract (Mechanochemical actuators of embryonic epithelial contractility. YongTae Kim, Melis Hazar, Deepthi S. Vijayraghavan, Jiho Song, Timothy R. Jackson, Sagar D. Joshi, William C. Messner, Lance A. Davidson, and Philip R. LeDuc. Proceedings of the National Academy of Sciences of the USA; online 09/23/14.)

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