Cells communicate by doing the 'wave'

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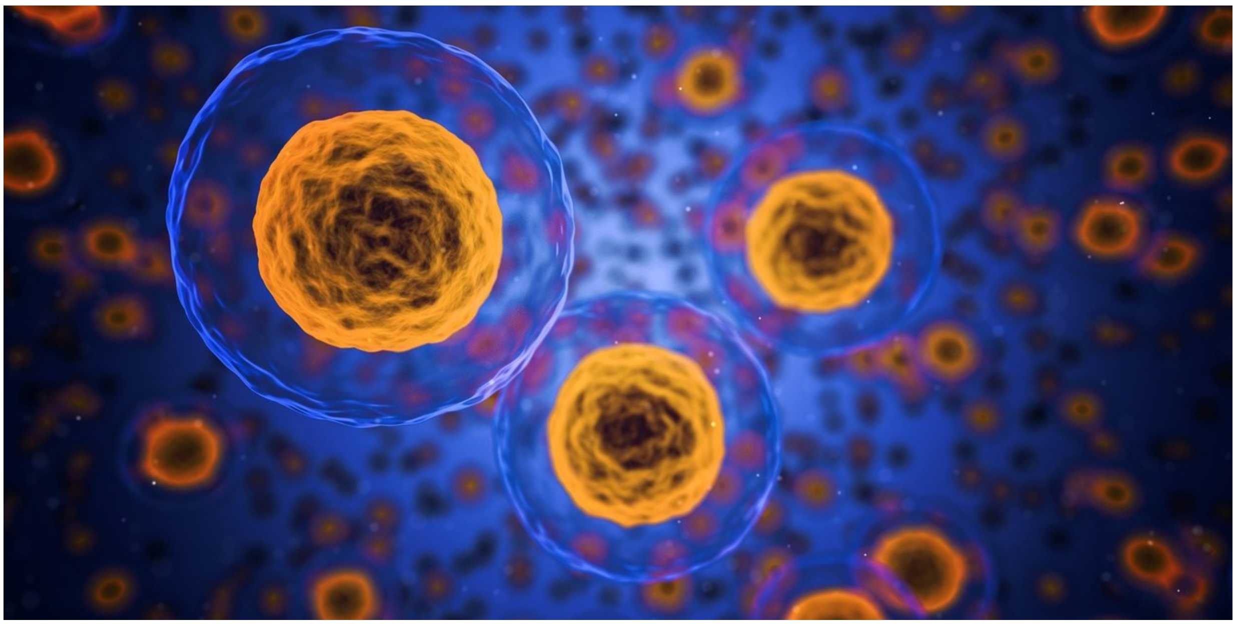

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Cells work around the clock to deliver, maintain, and control every aspect of life. And just as with humans, communication is a key to their success.

Every essential biological process requires some form of communication among cells, not only with their immediate neighbors but also to those significantly farther away. Current understanding is that this information exchange relies on the diffusion of signaling molecules or on cell-to-cell relays.

Publishing in the journal *Developmental Cell*, a research team at Kyoto University's Graduate School of Medicine reports on a novel method of communication relying on 'mechano-chemical' signals to control cell movement. The research group focused on a fundamental pathway—MAPK/ERK, or ERK pathway—and were able to demonstrate how the movement of a single cell could trigger a cascading reaction resulting in the migration of a cell collective.

"Mechanical and biochemical signals in cells fundamentally control everything from homeostasis, development, to diseases," explains Tsuyoshi Hirashima, leader of the study.

"We knew from past experiments how vital the ERK pathway is in cell activity, but the mechanism of how it can propagate in a collection of cells was incomplete."

MAPK/ERK is so fundamental that it exists in all cells, controlling a wide range of actions from growth and development to eventual cell death. The pathway is activated when a receptor protein on the cell surface binds with a signaling molecule, resulting in a cascade of proteins and reactions spreading throughout the cell's interior.

Employing a live imaging technique that can visualize an individual cell's active ERK pathway, the team began observing the effects of cell movement. What they found was unexpected: when a cell began to extend itself, ERK activity increased, causing the cell to contract.

"Cells are tightly connected and packed together, so when one starts contracting from ERK activation, it pulls in its neighbors," elaborates Hirashima. This then caused surrounding cells to extend, activating their ERK, resulting in contractions that lead to a kind of tug-of-war propagating into colony movement.

"Researchers had previously proposed that cells extend when ERK is activated, so our results came as quite a surprise."

The team incorporated these observations into a mathematical model, combining mechano-chemical regulations with quantitative parameters. The output demonstrated consistency with experimental data.

"Our work clearly shows that the ERK-mediated mechano-chemical feedback system generates complicated multicellular patterns," concludes Hirashima.

"This will provide a new basis for understanding many biological processes, including tissue repair and tumor metastasis."

More information: Naoya Hino et al, ERK-Mediated Mechanochemical Waves Direct Collective Cell Polarization, *Developmental Cell* (2020). DOI: 10.1016/j.devcel.2020.05.011

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