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MECHANOTRANSDUCTION

Catching the X-waves

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> force alone could drive collective cellular invasion in cancer

Movement of monolayers of epithelial cells is associated with metastasis. It has been argued that chemical stimuli and chemical gradients alone cannot explain this form of cellular migration, and some evidence has implicated a role for mechanotransduction — the perception and reaction to a mechanical force. A paper published in *Nature Physics* has experimentally and mathematically modelled epithelial cell migration and has identified mechanically generated waves that are important for cellular motility.

The authors took advantage of soft lithography techniques to produce a polydimethylsiloxane membrane with a rectangular opening that was placed on top of a polyacrylamide gel coated with collagen I. Madin-Darby Canine Kidney cells were grown to near confluence in the rectangular opening, and then the membrane was removed allowing the cells room to expand. Traction-force microscopy and monolayer-stress microscopy were used to analyse the cellular responses. The cells at the edges of the monolayer were the first to respond and migrate, followed by cells further from the edge. Similar patterns of traction forces were noted: cells at the outer edges had large traction forces, whereas those at the centre did not.

Cells in a monolayer also exert forces on their neighbours as they are attached to them through cell–cell junctions. Analyses of the stress within the monolayer showed that force transmission from cell to cell, like the migration patterns, was generated at the leading edge and then progressively propagated towards the centre. The authors also noted more complex spatiotemporal fluctuations in force traction, monolayer stress and cell motility. To examine these variables more closely, they averaged them over the observable monolayer length, reducing the dimensionality of the system to one spatial dimension and one temporal dimension. This revealed the presence of clear wave-like crests for strain rate, which the authors called X-waves, owing to the pattern that they produced on a kymograph — a graphical representation of spatial position over time.

So are chemical stimuli involved in generating these waves? To answer this question the authors built a mathematical model. X-waves could be generated in this model using two assumptions: that a cell acquires a motile phenotype only when an adjacent cell creates space or pulls on the shared inter-cellular junction; and that the cell contains a strain threshold that, once exceeded, results in the cytoskeleton first reinforcing the strain and then breaking down (fluidizing). These findings indicate that although chemical stimuli and/or gene expression could be involved in epithelial monolayer migration these are not necessary for the generation of X-waves. They also imply that force alone could drive collective cellular invasion in cancer.

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ORIGINAL RESEARCH PAPER Serra-Picamal, X. *et al.* Mechanical waves during tissue expansion. *Nature Physics* 8 Jul 2012 (doi:10.1038/NPHYS2355)