Scientists create leader cells with light

Research led by the Institute for Bioengineering of Catalonia (IBEC) has studied the migratory movement of groups of cells using light control. The results show that there is no leader cell that directs the collective movement, as previously thought, but that all cells participate in the process. These findings are relevant to the design of treatments to stop tumour invasion or accelerate wound healing, physiological processes closely linked to cell migration.

In processes such as embryonic development, wound healing or cancer invasion, cells are known to move in groups in a coordinated way. Leading these groups of cells are so-called leader cells, which are highly mobile and seem to direct the migration of the whole group, just as groups of animals often organise themselves according to the instructions of a leader.

A study led by the Institute for Bioengineering of Catalonia (IBEC) has attempted to generate leader cells in the laboratory using optogenetic control, in order to test whether there really are cells that direct this collective movement and cells that follow them, and how information is transmitted from one to the other in order to move in a coordinated way.

The research team used genetically modified cells that were able to follow the movement of blue light. Where the cell is illuminated by the light beam, the protein Rac1 is activated, causing a protrusion known as a lamellipodium, which facilitates cell movement.

In the model developed by the research team, cells are placed on a substrate consisting of a gel with a stiffness similar to that of body tissue, containing a linear pattern, so that groups of different numbers of cells are formed in a row following the pattern. These 'trains' of cells are then illuminated with the blue light beam to study their collective movement.

'We have created a kind of train with different carriages, which are the cells. What we observed is that the illuminatedcells are not able to pull a minimum number of followers, so they don't lead the movement. So, we don't have a train, but each carriage has its own engine and controls its speed and acceleration, each individual cell is an active player in the collective movement,' says Leone Rossetti, a former IBEC researcher and first author of the paper.

These experiments show that there is no leader cell that directs the collective behaviour, but that cells that were thought to be followers also participate in the movement.

'These results are relevant when designing treatments to stop tumour invasion or accelerate wound healing. We will have to act on the whole set of cells involved in the movement, and not just on the single cell that we thought was leading the movement of the rest,' explains Xavier Trepat, ICREA Research Professor at IBEC and leader of the study.

The relationship between cell forces and speeds is one of the most fundamental and unsolved problems in cell migration. However, the physical rules that describe the movement of bodies in the macroscopic world cannot be directly usedat the cellular level, so it is necessary to create new models that allow us to describe movement at the microscopic level. In collaboration with Ricard Alert from the Max Planck Institute for the

Physics of Complex Systems Physics in Dresden, the researchers have developed a mathematical model that determines how the spatial distribution of the forces generated by cells translates into their migration speed.

Xavier Trepat, who led the research, is also a professor at the University of Barcelona (UB) and a member of the Centre for Biomedical Research Network in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN). This study is part of Leone Rossetti's postdoctoral work, funded by a Marie Skłodowska-Curie grant.

Referenced article:

Leone Rossetti, Steffen Grosser, Juan Francisco Abenza, Léo Valon, Pere Roca- Cusachs, Ricard Alert and Xavier Trepat. **Optogenetic generation of leader cells reveals a force-velocity relation for collective cell migration.** *Nature Physics* (2024). DOI: https://doi.org/10.1038/s41567-024-02600-2