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Simon Bradbrook/NPG

CELL MIGRATION

EMT promotes contact inhibition of locomotion

> "cells seem to acquire the ability to undergo CIL during developmental EMT"

Collision between cells can cause them to move away from each other, a process that is known as contact inhibition of locomotion (CIL). Scarpa *et al.* shed new light on the molecular mechanisms behind this phenomenon, showing that neural crest cells must switch from expressing epithelial cadherin (E-cadherin) to expressing neural cadherin (N-cadherin) during epithelial–mesenchymal transition (EMT) for CIL to occur.

Neural crest cells from *Xenopus laevis* undergo CIL, and the authors asked whether their ability to do so is intrinsic or is acquired during development. They looked at cell populations before (premigratory neural crest (Premig-NC) cells) and after (migratory neural crest (Mig-NC) cells) EMT had taken place and observed that 80% of collisions between cultured Mig-NC cells showed CIL compared with only 40% of such collisions in Premig-NC cells. Furthermore, cell mixing in cultures was higher for Premig-NC cells, most of which formed stable contacts on collision and thus could not disperse, whereas Mig-NC cells underwent dispersion, which requires EMT. Thus, cells seem to acquire the ability to undergo CIL during developmental EMT.

Importantly, the authors noticed that colliding Premig-NC and Mig-NC cells formed junctions with similar dynamics. However, junctions disassembled more quickly in Mig-NC cells, reducing the duration of cell–cell contact. Cells are known to 'switch' the type of cadherin (an adhesion junction component) that they express during neural crest EMT, and the authors found that Premig-NC cells predominantly express E-cadherin and Mig-NC cells predominantly express N-cadherin. Thus, 'cadherin switching' might be necessary for CIL.

Indeed, experiments showed that E-cadherin suppresses CIL. CIL is required for *in vivo* migration, and overexpressing E-cadherin reduced neural crest migration in *X. laevis* and zebrafish embryos. Also, *in vitro*, E-cadherin overexpression in Mig-NC cells reduced CIL, increased cell mixing and promoted the formation of RAC1-positive protrusions near cell–cell contacts; such protrusions normally form near the cell free edge during CIL. Conversely, inhibiting E-cadherin in Premig-NC cells reduced cell intermixing and changed the position of protrusions from cell–cell contacts to the cell free edge where they might support CIL.

How does E-cadherin suppress CIL? RAC1 activity was shown to increase at the cell free edge during CIL to form new protrusions and, importantly, this promoted junction disassembly. By contrast, the authors found that E-cadherin interacts with the adhesion junction component p120 catenin to promote RAC1 activity (and presumably protrusions) at cell–cell junctions, preventing junction disassembly and CIL. Finally, using traction force microscopy, the authors showed that overexpressing E-cadherin in Mig-NC cells disrupts the distribution of cellular forces that pull junctions apart in wild-type Mig-NC cells undergoing CIL.

Thus, this study shows why switching from E-cadherin to N-cadherin expression during developmental EMT is crucial for CIL of neural crest cells and thus developmental migration.

Katharine H. Wrighton

ORIGINAL RESEARCH PAPER Scarpa, E. *et al.* Cadherin switch during EMT in neural crest cells leads to contact inhibition of locomotion via repolarization of forces. *Dev. Cell* http://dx.doi.org/10.1016/j.devcel.2015.06.012 (2015)
FURTHER READING Lamouille, S., Xu, J. & Derynck, R. Molecular mechanisms of epithelial–mesenchymal transition. *Nat. Rev. Mol. Cell Biol.* **15**, 178–196 (2014)