

Self-sorting cells disrupt development

October 20 2016, by Christina Hueschen

In a developing embryo, some cells can self-segregate – like oil separating out of water – to help create the tissues and organs of the human body. For example, brain cells separate into clusters that give rise to different regions of the brainstem.

But that sorting also can go awry, which is what Audrey O'Neill, PhD, a postdoctoral scholar in UC San Francisco's Program in Craniofacial Biology in the School of Dentistry, studies.

A video that she captured over a 16-hour period shows purple cells that produce one extra molecule – the protein Ephrin-B1 – that the green cells don't have, but can detect. That small difference changes the way the green cells move. Because the purple and green cells move and push against each other differently, they self-segregate into clusters in a stunning dance.

"This beautiful pattern of segregation unfortunately leads to disease," O'Neill said.

It happens in an X-linked genetic disorder called craniofrontonasal syndrome (CFNS), in which mutations in the Ephrin-B1 gene cause head and face deformities. CFNS most severely affects females who have one normal copy of Ephrin-B1 and one mutant copy. During development, half of their cells produce normal Ephrin-B1 and half do not. Like the purple and green cells in O'Neill's video, the two populations can segregate into abnormal, patchy patterns that disrupt healthy development.



For CFNS patients, having some healthy cells is actually worse than having none. This mixture of healthy and <u>mutant cells</u> is called "mosaicism."

O'Neill, who works in the lab of Jeffrey Bush, PhD, captures these videos to help her decode the molecular steps that link Ephrin-B1 mosaicism to cell sorting. She wants to know what changes inside the green cells to make them move differently, and how Ephrin-B1 triggers that change.

O'Neill said that it's an exciting time to ask these kinds of molecular questions.

"Developmental biology is becoming more focused on disease, and focused on what developmental diseases can teach us about the functions of molecules," she said. "We're not just characterizing the problems created by a genetic mutation; we're asking, 'What does that tell us?'"

More information: Audrey K. O'Neill et al. Unidirectional Eph/ephrin signaling creates a cortical actomyosin differential to drive cell segregation, *The Journal of Cell Biology* (2016). DOI: 10.1083/jcb.201604097

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