How clutch molecules enable neuron migration

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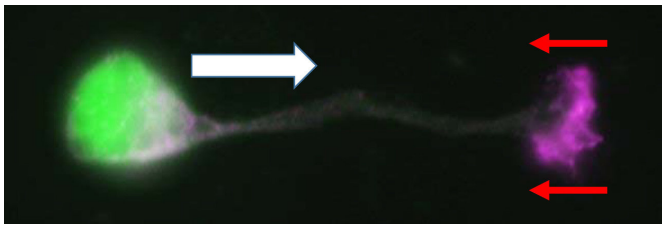

At the tip of the neuronal leading process, shootin 1b (red) couples F-actin retrograde flow (force) with cell adhesion, thereby pushing off the surrounding surface (red arrows) for migration (white arrow). Credit: Naoyuki Inagaki

The brain can discriminate over 1 trillion odors. Once entering the nose, odor-related molecules activate olfactory neurons. Neuron signals first accumulate at the olfactory bulb before being passed on to activate the appropriate brain region. Unlike other parts of the brain, the olfactory bulb receives a continuous supply of new neurons, even into adulthood. To reach the olfactory bulb, these neurons migrate from elsewhere. A new study seen in *Cell Reports* by researchers at the Nara Institute of Science and Technology (NAIST) reports that shootin 1b is critical for neuron migration to the olfactory bulb.

"Neuron migration is essential for proper brain development and adaptation, and abnormalities are associated with brain malformation, mental retardation and psychiatric diseases like schizophrenia," says NAIST Professor Naoyuki Inagaki, who led the study. The migration depends on neurons changing their morphology by extending their leading edge and retracting their lagging edge. This process involves a combination of intracellular molecules that generate force and those that bind to the cell's surrounding surfaces.

Inagaki has made a career of studying the molecules responsible for changing cell morphology and, in particular, has been studying clutch molecules. "Think of it like running. Your legs create force to move, but if they do not push off the ground, you do not move. Clutch molecules are what transmit the force to the external environment," he says.

His lab has previously shown that the clutch molecule shootin 1a is crucial for neurons to extend axons that connect with other neurons. In the new study, it shows that without a shootin isoform, shootin 1b, neurons cannot migrate effectively to the olfactory bulb in mice.

Experiments found that shootin 1b accumulated in the leading process of the neurons. Mutation experiments that removed shootin 1b resulted in leading processes that would undergo less extension, and the cells would not move effectively, leaving an undeveloped olfactory bulb.

"The leading process uses F-actin retrograde flow to generate force," explains Dr. Takunori Minegishi, first author of the study. F-actin retrograde flow is used by many cells to move. The flow comes from two molecules, actin and myosin, interacting with one another.

Force microscopy of living cells found that shootin 1b bound to actin and to L1-CAM, an adhesion molecule that binds cells to their surroundings. Thus, shootin 1b coupled the F-actin retrograde flow with cell adhesion.

"Cells are amazing mechanical machines that convert outside stimuli to movement. Discovering shootin 1b brings new understanding to how neurons migrate to form a functional brain," says Inagaki.

More information: Takunori Minegishi et al, Shootin1b Mediates a Mechanical Clutch to Produce Force for Neuronal Migration, *Cell Reports*

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