Scientists get one step closer to finding how to repair damaged nerve cells

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A team of researchers at the IRCM led by Frédéric Charron, PhD, in collaboration with bioengineers at McGill University, uncovered a new kind of synergy in the development of the nervous system, which explains an important mechanism required for neural circuits to form properly. Their breakthrough, published today in the scientific journal *PLoS Biology*, could eventually help develop tools to repair nerve cells following injuries to the nervous system (such as the brain and spinal cord).

Researchers in Dr. Charron's laboratory study neurons, the nerve cells that make up the central nervous system, as well as their long extensions known as axons. During development, axons must follow specific paths in the nervous system in order to properly form neural circuits and allow neurons to communicate with one another. IRCM researchers are studying a process called axon guidance to better understand how axons manage to follow the correct paths.

"To reach their target, growing axons rely on molecules known as guidance cues, which instruct them on which direction to take by repelling or attracting them to their destination," explains Dr. Charron, Director of the Molecular Biology of Neural Development research unit at the IRCM.

Over the past few decades, the scientific community has struggled to understand why more than one guidance cue would be necessary for axons to reach the proper target. In this paper, IRCM scientists uncovered how axons use information from multiple guidance cues to make their pathfinding decisions. To do so, they studied the relative change in concentration of guidance cues in the neuron's environment, which is referred to as the steepness of the gradient.

"We found that the steepness of the gradient is a critical factor for axon guidance; the steeper the gradient, the better the axons respond to guidance cues," says Tyler F.W. Sloan, PhD student in Dr. Charron's laboratory and first author of the study. "In addition, we showed that the gradient of one guidance cue may not be steep enough to orient axons. In those instances, we revealed that a combination of guidance cues can behave in synergy with one another to help the axon interpret the gradient's direction."

In collaboration with the Program in Neuroengineering at McGill University, Dr. Charron's team developed an innovative technique to recreate the concentration gradients of guidance cues in vitro, that is to say they can study the developing axons outside their biological context.

"This new method provides us with several benefits when compared to previous techniques, and allows us to simulate more realistic conditions encountered in developing embryos, conduct longer-term experiments to observe the entire process of axon guidance, and obtain extremely useful quantitative data," adds Sloan. "It combines knowledge from the field of microfluidics, which uses fluids at a microscopic scale to miniaturize biological experiments, with the cellular, biological and molecular studies we conduct in laboratories."

"This is true multidisciplinary work, and an excellent example of what the Program in Neuroengineering aims to accomplish in situations where neurobiologists like myself have a specific question they want to address, but the current tools aren't adapted to answer their question," mentions Dr. Charron. "Thus, thanks to this unique program, we teamed up with McGill's bioengineers and microfluidic and mathematical modelling experts to create the device required for our study."

"This scientific breakthrough could bring us closer to repairing damaged nerve cells following injuries to the central nervous system," states Dr. Charron. "A better understanding of the mechanisms involved in axon guidance will offer new possibilities for developing techniques to treat lesions resulting from spinal cord injuries, and possibly even neurodegenerative diseases."

Injuries to the central nervous system affect thousands of Canadians every year and can lead to lifelong disabilities. Most often caused by an accident, stroke or disease, these injuries are currently very difficult to repair. Research is therefore required for the development of new tools to repair damage to the central nervous system.

More information: *PLoS Biology*, journals.plos.org/plosbiology/ … journal.pbio.1002119

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