

# Identification of a key molecular pathway required for brain neural circuit formation

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The research group of Dr. Frédéric Charron, a researcher at the Institut de recherches cliniques de Montréal (IRCM), has made a discovery which could help treat spinal cord injuries and neurodegenerative diseases. This new finding has been published in the current issue of the prestigious scientific journal *Neuron*. Patricia T. Yam, Sébastien D. Langlois and Steves Morin, all at the IRCM, are listed as co-authors.

The brain is composed of billions of interconnected [neurons](#). To correctly form neuronal circuits, the developing axons (a long extension of a neuron) require attractive and repulsive [molecules](#) to lead them to their appropriate targets. One such molecule is Sonic Hedgehog (Shh). Five years ago, as a postdoctoral fellow in the laboratory of Dr. Marc Tessier-Lavigne at Stanford University, Frédéric Charron discovered that Shh acted as an axonal attractant for brain and spinal cord neurons. "How exactly Shh elicited this effect has remained unknown so far," pointed out Dr. Charron. "The molecular pathway my team discovered provides part of an answer."

Their recent work showed that Shh exerts its attractive effect through a group of molecules called Src family kinases (SFKs) that, until now, were not known to be linked to Shh function. Remarkably, these novel Shh effector molecules are absolutely required for the ability of Shh to guide axons. Connecting axons with an appropriate set of targets is very complex. Inappropriate wiring or damage to these neuronal connections leads to severe abnormalities of the nervous system. "Knowing the effectors of axon guidance molecules such as Shh", adds Dr. Charron,

"helps us to understand the molecular mechanisms by which axons reach their target. It paves the way to new therapies to treat spinal cord injuries, neurodevelopmental disorders, and neurodegenerative diseases."

This new discovery was made possible through the invention of a novel technique to control and observe the behavior of axons in response to guidance molecules. A patent application for this technique has been filed recently. This invention is expected to speed up the discovery of drugs that control axon pathfinding.

"Dr. Charron is one of the country's leading newly arrived neuroscientists. This research has important long-term implications for the repair of spinal cord injury: if we knew all of the molecules required to guide axons correctly during spinal cord healing, we would probably know how to heal spinal cord injuries," says Dr. Rod McInnes, Scientific Director of the Canadian Institutes of Health Research Institute of Genetics. "This is beautiful research that adds another major brick to our building a complete understanding of how the [spinal cord](#) is made, and how injury of it can be treated."

More information:

[www.cell.com/neuron/abstract/S0896-6273\(09\)00247-5](http://www.cell.com/neuron/abstract/S0896-6273(09)00247-5)

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