

Scientists reveal nerve cells' navigation system

May 9 2011

Johns Hopkins scientists have discovered how two closely related proteins guide projections from nerve cells with exquisite accuracy, alternately attracting and repelling these axons as they navigate the most miniscule and frenetic niches of the nervous system to make remarkably precise connections.

The discovery, reported April 28 in the journal *Neuron*, reveals that proteins belonging to the "semaphorin" family of guidance cues are crucial for getting neuronal projections exactly where they need to be not only across long distances, but also in the short-range wiring of tiny areas fraught with complex circuitry, such as the central [nervous system](#) of the fruit fly.

Because signaling that affects the growth and steering of neuronal processes is critical for repairing and regenerating damaged or diseased nerve cells, this research suggests that a more refined understanding of how semaphorin proteins work could contribute to treatment strategies, according to Alex Kolodkin, Ph.D., a professor in the neuroscience department at Johns Hopkins and a Howard Hughes Medical Institute investigator.

Using embryonic flies, some native (normal) and others genetically altered to lack a member of the semaphorin gene family or the receptor that binds to the semaphorin and signals within the responding neuron, the team labeled particular classes of neurons and then observed them at high resolution using various microscopy strategies to compare their

axon projections.

In the native developing flies, the team saw how certain related semaphorins, proteins that [nerve cells](#) secrete into the intracellular space, work through binding their plexin receptor. First, a semaphorin-plexin pair attracts a certain class of extending neurons in the embryonic fly central nervous system assemble a specific set of target projections. Then, a related semaphorin that binds to that same plexin receptor repels these same neurons so as to position them correctly with in the central nervous system. Finally, the attractive semaphorin/plexin interaction assures the establishment of precise connections between these central nervous system axons and sensory neurons that convey messages about the external environment by extending their [axons](#) into the CNS from the periphery and contacting the assembled CNS pathways. Flies lacking this semaphorin/plexin signaling showed defects in these connections, which the researchers were able to reverse when these cues and receptors were re-introduced into flies lacking them.

To investigate whether the absence of semaphorin in flies had behavioral consequences, the team collaborated with investigators at Janelia Farm laboratories of the Howard Hughes Medical Institute and used specialized computer software to follow the movements of hundreds of fly larvae crawling on a small dish. The plate was perched on a large speaker that vibrated with pulses of sound, letting the team compare the movements of normal larvae to mutants missing semaphorin.

The "tracking" software measures differences in normal foraging behavior (mostly crawling straight and occasionally making turns) when a sound is activated. The larvae with intact semaphorin/plexin responded to sound stimulation by stopping, contracting and turning their heads from side to side. The semaphorin mutants failed to respond to the same stimuli. The researchers repeated the experiment using mutant larvae missing the protein to which semaphorin binds – its plexin receptor—and

these larvae also showed no reaction to sound-vibration.

"The fly larvae sensory neurons, located on the larval body wall, send axon projections that do not make contact with their appropriate targets in the central nervous system when semaphorin/plexin signaling is absent," Kolodkin says. "This tells us that semaphorin cues guide not only neuronal processes assembly in the central nervous system, but also incoming projections from sensory neurons to the CNS targets."

The Kolodkin lab's experiments in the invertebrate fruit fly [central nervous system](#) mirror related findings in the mouse reported Feb. 10, 2011 in *Nature*. Then, they showed that a different semaphorin cue is important for certain neurons to make precise connections within the developing inner plexiform layer of the retina, an elaborately laminated club-sandwich-like structure that must be precisely wired for accurate visual perception in mammals.

To demonstrate that semaphorins are necessary for neuronal projections from distinct classes of neurons to make their way to correct layers in this retinal "sandwich," the scientists examined the retinas of 3-, 7- and 10-day-old mice that were genetically modified to lack either a member of the semaphorin gene family or its appropriate plexin receptor. These mutants showed severe connectivity defects in one specific inner plexiform layer, revealing faulty neuronal targeting.

"In two distinct neural systems in flies and mammals, the same family of molecular guidance cues – semaphorins and their receptors – mediate targeting events that require exquisite short-range precision to generate complex neuronal connectivity," says Kolodkin who, as a postdoctoral fellow in the mid-1990s, first discovered the large family of semaphorin guidance cues working with the grasshopper nervous system.

"This work begins to tell us how, in a very small but highly ordered

region of the nervous system, select target innervation and specific synaptic contacts between different classes of neurons can be established in the context of evolving circuit complexity" Kolodkin says.

More information: www.cell.com/neuron/

Provided by Johns Hopkins Medical Institutions

Citation: Scientists reveal nerve cells' navigation system (2011, May 9) retrieved 27 April 2024 from <https://medicalxpress.com/news/2011-05-scientists-reveal-nerve-cells.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.