Study of the nervous system could have implications for regenerative medicine and cancer

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Cody Smith works with a student in his lab. Credit: University of Notre Dame

In order for the central nervous system to communicate to the rest of the body, the brain and spinal cord house nerves that send and receive signals via neurons or nerve cells. This communication can take place only because structures known as synapses allow this process to happen.

When nerve cells come close enough together to form a synapse, they allow synaptic vesicles to release a chemical substance that transfers the communication signal to the next cell. However, a new study from the University of Notre Dame has shown that these synaptic vesicles are used much earlier, before synapses occur, and that they are also used in the formation of the spinal cord during early development.

"Our research team at Notre Dame wanted to explore what role synaptic vesicles, which are a well-understood piece of the nervous system communication puzzle, could have in early development, if any," said Cody Smith, the Elizabeth and Michael Gallagher Assistant Professor of Biological Sciences and author of the study. "What Evan Nichols, the lead author, found is that long before the central nervous system is complete and neuronal communication is taking place, synaptic vesicles are helping nerve fibers enter the spinal cord and aiding proper development."

The study was published in *Current Biology*, with support from the Freimann Life Science Center. Nichols, a 2019 alumnus, completed the study in the Smith Lab as an undergraduate student at Notre Dame and is now a graduate student at Stanford University.

"Evan has been the lead author on a few of the papers my lab has published," said Smith. "It's been great watching him be so engaged with the research process, and I look forward to seeing more great work from him. I hope this encourages more students to consider how research—and potentially being an author on a paper—could be a part of their undergraduate experience, too."

Funded by the Alfred P. Sloan Foundation, the research showed that enzymes called MMPs are also important for forming spinal cord nerves, and therefore the development of the nervous system. The nervous system is made up of the central nervous system and the peripheral

nervous system, which are connected by the dorsal root ganglion. When Smith and his research team inhibited MMP enzyme activity, dorsal root ganglion nerve fibers were stalled and unable to enter the spinal cord.

Smith says understanding which elements are key to normal or healthy formation of the spinal cord, like MMP enzymes, could help researchers pinpoint how to best target different diseases.

"Learning what takes place throughout early development allows us to see how neurons throughout the body form, and potentially identify how that process could be mimicked for regenerative medicine purposes, like spinal cord injuries," said Smith, affiliated member of Center for Stem Cells and Regenerative Medicine at Notre Dame.

Additionally, MMP enzymes have been found in studies related to cancer metastasis, or the spread of cancer to other parts of the body. Since MMPs were found to serve an important role for the invasion of the spinal cord by the dorsal root ganglion, Smith states that there could be a link between the molecules used at nerve invasion during development and those used when metastatic cancer cells invade new body tissue.

The paper was also featured as a highlight in *Nature Reviews Neuroscience*.

More information: Evan L. Nichols et al. Synaptic-like Vesicles Facilitate Pioneer Axon Invasion, *Current Biology* (2019). DOI: 10.1016/j.cub.2019.06.078

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