Role of adaptor protein CD2AP in neuron sprouting discovered

April 20 2016

Benjamin Harrison, Ph.D., Jeffrey Petruska, Ph.D. and Kristofer Rau, Ph.D., co-authors of the publication Credit: University of Louisville

University of Louisville researchers have discovered that a protein previously known for its role in kidney function also plays a significant

role in the nervous system. In an article featured in the April 13 issue of the *Journal of Neuroscience*, they show that the adaptor protein CD2AP is a key player in a type of neural growth known as collateral sprouting.

In the first research to be published on this protein's role in the nervous system, Benjamin Harrison, Ph.D., a postdoctoral fellow in the Department of Anatomical Sciences and Neurobiology and lead author of the article, and his colleagues show that CD2AP, an adaptor protein, orchestrates a complex arrangement of other proteins that controls the branching of nerve axons, the tendrils reaching out from the nerve cell to connect to other nerve cells, skin and organs. This nerve growth occurs in uninjured nerve cells as they extend their reach and create new connections.

"CD2AP brings in all the correct players, forms a multi-protein complex and coordinates that multi-protein complex to achieve growth of the neurons," Harrison said. "There are a whole bunch of proteins that it could bring together, but it only brings together the correct proteins to create the correct response. In this case, it changes the structure of the axons through sprouting and elongation."

This axon sprouting may be helpful, but too much of it can be harmful. In normal adult cells, this growth creates new connections and can lead to improved functionality after an injury or stroke. However, if the axons sprout uncontrollably, the result can be exacerbated epilepsy, blood pressure spikes or neuropathic pain. The researchers hope this new understanding of the nerve growth process will lead to therapies that can improve healing and recovery of function following nerve damage while minimizing excessive growth.

"Through targeting this molecule, we could help the body's natural healing process to coordinate the appropriate growth," Harrison said.

The research team, based in the lab of Jeffrey Petruska, Ph.D., associate professor in the Department of Anatomical Sciences and Neurobiology and the Department of Neurological Surgery and the article's corresponding author, identified CD2AP as a player in the neurological system via a screen to detect genes associated with neuron growth. Their research examined how CD2AP interacts with various molecules in controlling the neural sprouting process, particularly its relationship with nerve growth factor (NGF).

"People have been studying nerve growth factor and the responses it induces for a while, but this protein (CD2AP) forms a nice link between NGF and the response in the cell," Harrison said.

Previous research also has associated CD2AP with genetic changes among individuals with Alzheimer's disease and it may be helpful in understanding the mechanisms involved in Parkinson's Disease, Huntington's Disease and spinal cord injuries.

Petruska says this work relates closely to other research being conducted at UofL's Kentucky Spinal Cord Injury Research Center (KSCIRC). He says that understanding these molecular processes could one day be used to amplify the activity-based therapies such as locomotor training now being done with spinal cord injury patients by UofL faculty at Frazier Rehab Center, a part of KentuckyOne Health. Locomotor training helps spinal cord injury patients achieve functional recovery through standing and stepping activity.

"We are starting to discover that there are different modes of nerve growth and different sets of genes that control different kinds of growth," Petruska said. "This is particularly important as it relates to locomotor training. When you train, you enhance the growth factor environment of the injured spinal cord, and those growth factors are involved in the axon plasticity. This mode that we study is dependent on

the growth factors."

Harrison plans to pursue research aimed at developing a drug to provide appropriate nerve growth for spinal cord injury patients.

"My dream," Harrison said, "is to one day do a clinical trial with a drug that targets this protein and can enhance the ability of the patients to respond to the activity-based rehabilitation (locomotor training) that they are doing at Frazier Rehab Center."

More information: B. J. Harrison et al, The Adaptor Protein CD2AP Is a Coordinator of Neurotrophin Signaling-Mediated Axon Arbor Plasticity, *Journal of Neuroscience* (2016). DOI: 10.1523/JNEUROSCI.2423-15.2016

Provided by University of Louisville