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Scientists discover brain cell development process implicated in mental retardation

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Scientists at Rutgers, The State University of New Jersey, have discovered a biological process in brain cell development that may help explain some causes of mental retardation. This understanding may one day help other researchers develop therapies that can reduce specific forms of retardation.

In a paper published in *The Journal of Neuroscience*, Rutgers cell biologists Hongxin Chen and Bonnie Firestein show that proteins of the Rho family, when excessively present in developing brain cells known as neurons, inhibit another protein that promotes healthy neuron development. Firestein earlier demonstrated how this protein, called cypin, promotes healthy branching patterns in the tree-like structures at the end of neurons that receive signals. Inadequate branching in these structures, called dendrites, has been observed in conditions such as Alzheimer's disease, autism and some types of mental retardation.

"Imbalances of Rho proteins have been known to affect dendrite branching, and therefore have been implicated in causing mental retardation," said Firestein, associate professor of cell biology and neuroscience. "How this happens, however, has not been clear. Now we're seeing that Rho proteins signal other proteins downstream. In our case, we discovered that a type of Rho protein called RhoA is inhibiting cypin production when it is overactive or present in excess. The resulting lack of cypin is detrimental to healthy branching development in dendrites."

Firestein and Chen, a postdoctoral research fellow, believe that this finding offers a new potential target for future drug therapies aimed at promoting healthier dendrite branching. “Scientists could try to block Rho activity, but since Rho is present in lots of different types of cells, reducing Rho activity could have widespread side effects,” said Firestein. “Looking for a protein that Rho is signaling to could result in a more targeted treatment.”

Cypin is restricted to a few regions in the brain, most notably the hippocampus, which controls learning and memory. Faulty dendrite branching there is likely to cause retardation. Therefore, a therapy that focuses specifically on development of hippocampal neurons might be more effective and less harmful to other organs and tissues.

Firestein first identified and isolated cypin in 1999, and has recently focused on how it works in the hippocampus. Cypin assembles protein molecules called tubulin into microtubules, which form the long chain molecules that are structural basis, or the “skeleton,” of a dendrite. An effective assembly process is needed to form the branching patterns needed for proper functioning.

Source: Rutgers, the State University of New Jersey