Boundary stops molecule right where it needs to be

May 24 2012

A molecule responsible for the proper formation of a key portion of the nervous system finds its way to the proper place not because it is actively recruited, but instead because it can't go anywhere else.

Researchers at Baylor College of Medicine have identified a distal axonal cytoskeleton as the boundary that makes sure AnkyrinG clusters where it needs to so it can perform properly.

The findings appear in the current edition of *Cell*.

"It has been known that AnkyrinG is needed for the axon initial segment to form. Without the axon initial segment there would be no output of information within the nervous system," said Dr. Matthew Rasband, associate professor of neuroscience at BCM. "Every known protein found at the axon initial segment depends on AnkyrinG, so if it is eliminated then the axon initial segment doesn't form and the neuron doesn't fire."

To answer the question of how AnkyrinG gets to where it needs to be for proper function, Rasband, along with first author Dr. Mauricio Galiano, postdoctoral associate in neuroscience at BCM, and colleagues, began by analyzing how the axon initial segment forms. They found that AnkyrinG always appeared in exactly the same spot during development.

"It would start to enter into the axon and then it was almost as if it hit a wall and couldn't go any further," Rasband said. "We would see it stop

very close to the cell body and then it would backfill. This showed us that there was some type of boundary or barrier marking that area."

To further study the properties of the boundary they began to look at ways they could disrupt or move it to test the effects of AnkyrinG clustering in different areas.

In cell cultures mouse models they were able to move the boundary to different distances along the axon. Doing this allowed researchers to change the length of the axon initial segment. If the boundary was farther away from the cell body than the length of the segment was longer. If it was closer to the cell body, then the length was shorter.

When researchers removed the boundary all together, AnkyrinG would not cluster in the appropriate area and the axon initial segment would not form.

"We had anticipated there was a kind of molecule that recruited AnkyrinG but instead we found a barrier that excludes it," Rasband said. "These results have important implications because they imply a similar exclusion mechanism might be in play or functioning not only at the axon initial segment, but all of the places where AnkyrinG is found."

Rasband said within many disorders like autism or epilepsy proteins that AnkyrinG is responsible for forming are disrupted. So understanding how this molecule functions properly could one day play a role in finding treatment targets for diseases.

Provided by Baylor College of Medicine