MedicalXpress

Contrary to belief, crucial protein for peripheral nerve repair is manufactured within the axon near the injury site

July 25 2012

Several years ago, Prof. Michael Fainzilber and his group in the Biological Chemistry Department made a surprising discovery: Proteins thought to exist only near the cell nucleus could also be found in the far-off regions of the body's longest cells – peripheral nerve cells that extend processes called axons, reaching up to a meter in length in adult humans.

These proteins, known as importins, have a well-studied role in the vicinity of the nucleus: They shuttle various molecules through the protective nuclear membrane. Fainzilber and his group showed that when a nerve cell is injured somewhere along its length, importins in the long axons hook into a sort of "railcar" mechanism, which then transports the "Help!" message from the injury site all the way to the nucleus.

These findings raised an intriguing question: How did importins get to the axons in the first place? Initial evidence suggested that one critical importin, called importin beta1, is produced locally upon injury near the site where it is needed. The problem was that years of scientific thinking on the subject indicated that proteins do not get manufactured in the axons, as investigations had turned up few of the cellular protein factories known as ribosomes there.

Settling the issue was far from simple: Importins are so crucial that even the smallest embryo could not survive without them. But Rotem Ben-

Tov Perry, a joint research student in Fainzilber's group and that of department colleague Dr. Avraham Yaron, found a way to distinguish the importin beta1 in the cell body from that in the axon: The axonal protein was apparently made from a longer messenger RNA. To see if they could selectively affect just the axonal version of the protein, the groups, together with Prof. Jeff Twiss of Drexel University, Philadelphia, Pennsylvania, took advantage of high precision knock-out technology. Rather than knocking a whole gene out of the system, they managed to remove one little piece of the messenger RNA that carries the encoded instructions for manufacturing importins: just the longer bit that sends the RNA to the axon.

Now they observed plenty of importin beta1 in the cell body, but none in the axons. Mice with the knocked out segment of RNA took much longer to recover from peripheral nerve injury, and the genes that are normally active in response to nerve damage were activated to a lesser degree. All of this suggests that the importin beta1 that normally helps inform the extended nerve cell about injury is, indeed, produced locally in the axon.

Fainzilber: "The data shows conclusively that importin beta1 protein is produced in axons, and Rotem's work has validated the importins' crucial role in nerve repair." The findings, which appeared recently in *Neuron*, may help point the way toward better treatments for nerve damage and aid in finding ways to speed up the repair.

Provided by Weizmann Institute of Science