Medical Xpress

First evidence that chitosan could repair spinal damage

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Spinal injuries are some of the most debilitating that anyone can suffer. However, Richard Borgens and his team from the Center for Paralysis Research at the Purdue School of Veterinary Medicine can now offer spinal cord damage sufferers some hope. They publish their discovery in the *Journal of Experimental Biology* that chitosan, a sugar, can target and repair damaged spinal cord nerve membranes and restore nerve function.

Richard Borgens and his colleagues from the Center for Paralysis Research at the Purdue School of Veterinary Medicine have a strong record of inventing therapies for treating nerve damage. From Ampyra, which improves walking in multiple sclerosis patients to a spinal cord simulator for spinal injury victims, Borgens has had a hand in developing therapies that directly impact patients and their quality of life.

Another therapy that is currently undergoing testing is the use of polyethylene glycol (PEG) to seal and repair damaged spinal cord nerve cells. By repairing the damaged membranes of nerve cells, Borgens and his team can restore the spinal cord's ability to transmit signals to the brain. However, there is one possible clinical drawback: PEG's breakdown products are potentially toxic. Is there a biodegradable non-toxic compound that is equally effective at targeting and repairing damaged nerve membranes?

Borgens teamed up with physiologist Riyi Shi and chemist Youngnam Cho, who pointed out that some sugars are capable of targeting damaged membranes. Could they find a sugar that restored spinal cord activity as effectively as PEG? Borgens and his team publish their discovery that chitosan can repair damaged nerve cell membranes in The Journal of Experimental Biology on 16 April 2010.

Having initially tested mannose and found that it did not repair spinal cord nerve membranes, Cho decided to test a modified form of chitin, one of the most common sugars that is found in crustacean shells. Converting chitin into chitosan, Cho isolated a segment of guinea pig spinal cord, compressed a section, applied the modified chitin and then added a fluorescent dye that could only enter the cells through damaged membranes. If the chitosan repaired the crushed membranes then the spinal cord tissue would be unstained, but if the chitosan had failed, the spinal cord neurons would be flooded with the fluorescent dye. Viewing a section of the spinal cord under the microscope, Cho was amazed to see that the spinal cord was completely dark. None of the dye had entered the nerve cells. Chitosan had repaired the damaged cell membranes.

Next Cho tested whether a dose of chitosan could prevent large molecules from leaking from damaged spinal cord cells. Testing for the presence of the colossal enzyme lactate dehydrogenase (LDH), Borgens admits he was amazed to see that levels of LDH leakage from chitosan treated spinal cord were lower than from undamaged spinal cords. Not only had the sugar repaired membranes at the compression site but also at other sites where the cell membranes were broken due to handling. And when the duo tested for the presence of harmful reactive oxygen species (ROS), released when ATP generating mitochondria are damaged, they found that ROS levels also fell after applying chitosan to the damaged tissue: chitosan probably repairs mitochondrial membranes as well as the nerve cell membranes.

But could chitosan restore the spinal cord's ability to transmit electrical signals to the brain through a damaged region? Measuring the brain's response to nerve signals generated in a guinea pig's hind leg, the duo saw that the signals were unable to reach the brain through a damaged spinal cord. However, 30·min after injecting chitosan into the rodents, the signals miraculously returned to the animals' brains. Chitosan was able to repair the damaged spinal cord so that it could carry signals from the animal's body to its brain.

Borgens is extremely excited by this discovery that chitosan is able to locate and repair damaged spinal cord tissue and is even more enthusiastic by the prospect that nanoparticles of chitosan could also target delivery of neuroprotective drugs directly to the site of injury 'giving us a dual bang for our buck,' says Borgens.

More information: Cho, Y., Shi, R. and Borgens, R. B. (2010). Chitosan produces potent neuroprotection and physiological recovery following traumatic spinal cord injury. J. Exp. Biol. 213, 1513-1520. http://jeb.biologists.org

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