Scientists synthesize nanoparticle-antioxidants to treat strokes and spinal cord injuries

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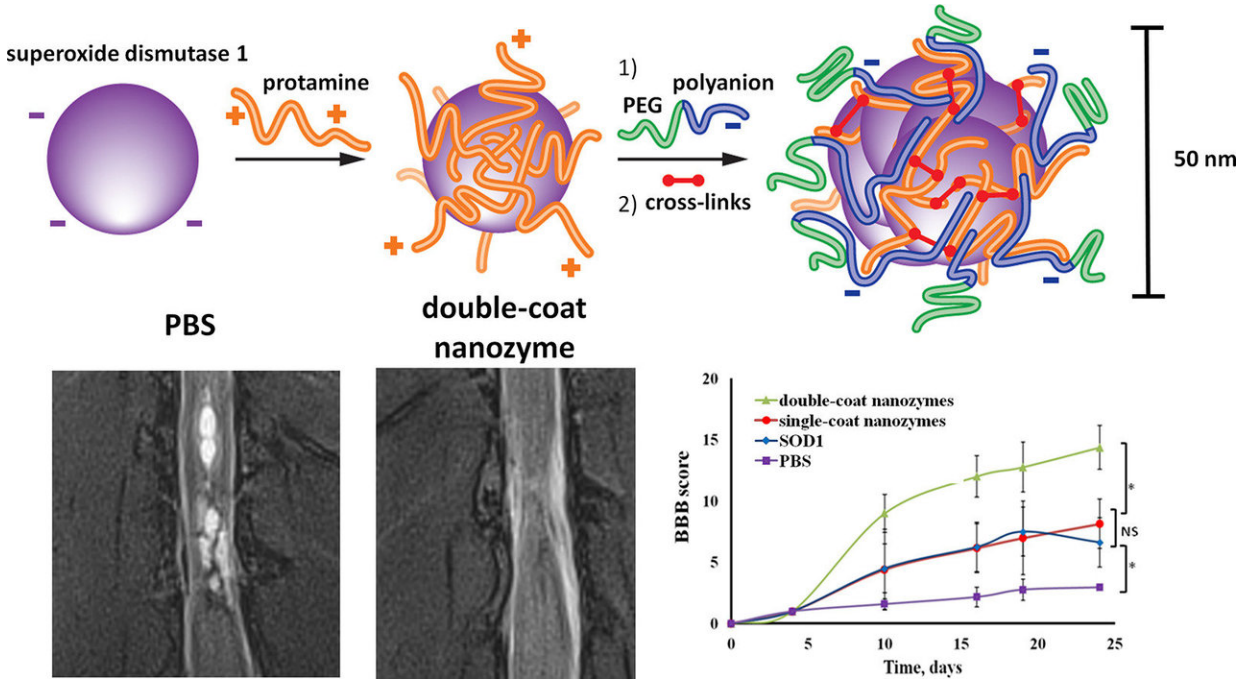

An international science team has developed an innovative therapeutic complex based on multi-layer polymer nano-structures of superoxide dismutase (SOD). The new substance can be used to effectively rehabilitate patients after acute spinal injuries, strokes, and heart attacks. Credit: NUST MISIS

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dismutase (SOD). The new substance can be used to effectively rehabilitate patients after acute spinal injuries, strokes, and heart attacks.

One of the most devastating forms of trauma to the human body is a spinal cord injury, a serious clinical problem around the globe. In addition to the direct damage to nerve fibers, subsequent problems like the overproduction of free radicals and inflammation also pose serious risk.

Spinal cord injuries, strokes and cardiac arrest are caused by impacts, ruptured blood vessels and tissue necrosis. When blood arteries contract or become clogged inside an organ's adjacent tissues, this leads to hypoxia, a pathological process linked with oxygen shortages. This factor blocks the final link of the respiratory chain at the cellular level and creates an excessive number of so-called free radicals or active forms of oxygen. They, in turn, destroy cellular membranes and initiate a sequence of reactions that damage and destroy body cells and tissues. These complications damage the spinal cord still further and kill neurons, making the clinical picture even more complicated.

An international team of scientists from Russia and the United States, organized by Maxim Abakumov, the head of the NUST MISIS Biomedical Nanomaterials Laboratory, has identified a solution to the problem of the pathological formation of free radicals in cases of spinal injuries or strokes. An innovative therapeutic complex based on synthesized nanoparticle antioxidants will help to create an effective rehabilitation system. The research results were recently published in the *Journal of Controlled Release*.

A special ferment/antioxidant called superoxide dismutase (SOD1) acts as an effective agent that naturally absorbs free radicals. If delivered quickly enough to a damaged organ, it can mitigate the stressful oxidization process caused by an excessive number of free radicals, and

hence stop the process of tissue destruction. However, it is unstable in the bloodstream during intravenous injections, disintegrating quickly and failing to neutralize free radicals on time.

"In order to create a stable therapeutic complex based on the SOD1 substance, we developed catalytically active forms of superoxide dismutase, or nanozymes. For example, we obtained the SOD1 poly-ion complex for the first time in history. This complex features additional poly (amino acid) block co-polymers and PEG/poly-glutamine acid acting as a surface cover," said Maxim Abakumov, project co-author, Head of NUST MISIS' Biomedical Nanomaterials Laboratory.

This made it possible to develop a porous polymer capsule measuring between 40-50 nanometers. It acts as a reusable trap that not only absorbs but also neutralizes free radicals. "We developed nanozymes with high fermentative activity levels that can preserve and protect SOD1 compounds in physiological conditions. This increases the circulation time of active SOD1 compounds inside the bloodstream, as compared to free SOD1 molecules. The substance's half-life increased from six to 60 minutes," Abakumov said.

A research team headed by the University of North Carolina Professor Alexander Kabanov obtained encouraging laboratory results during experimental tests. A single intravenous nanozyme injection containing 5,000 equivalent SOD1 units per one kilogram of body weight sped up the restoration of kinetic functions in rats with moderate spinal cord injuries. Swelling/edema was reduced, the spinal cord contracted, and post-traumatic cysts formed.

The successful test of the SOD1 ferment's nanozymes on rodents proves that it can effectively eliminate free radicals, reduce swelling and edema levels, and more quickly rehabilitate patients after spinal cord injuries, strokes or cardiac arrest. Team members are set to launch pre-clinical

tests in the near future.

More information: N.V. Nukolova et al, Multilayer polyion complex nanoformulations of superoxide dismutase 1 for acute spinal cord injury, *Journal of Controlled Release* (2017). DOI: 10.1016/j.jconrel.2017.11.044

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