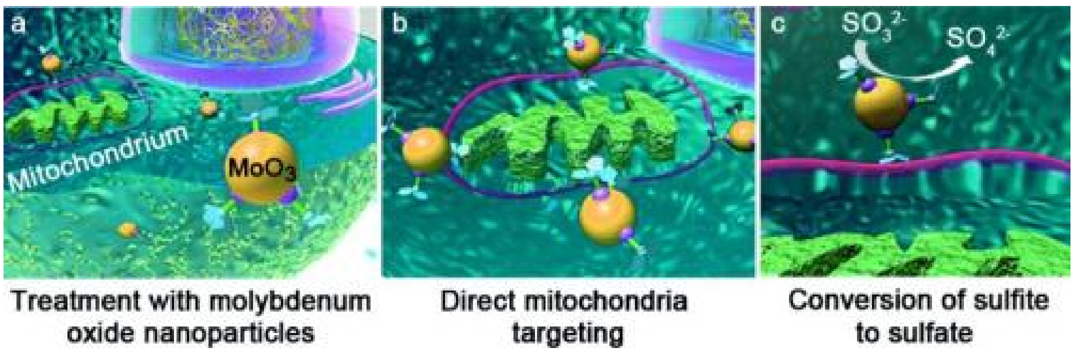
PHYS ORG

Artificial enzyme mimics the natural detoxification mechanism in liver cells

June 30 2014



Mode of action of molybdenum oxide nanoparticles: (a) treatment of sulfite oxidase deficient liver cells; (b) mitochondria are directly targeted, nanoparticles accumulate in proximity to the membrane; (c) sulfite is oxidized to cellular innocuous sulfate.

Scientists at Johannes Gutenberg University Mainz in Germany have discovered that molybdenum trioxide nanoparticles oxidize sulfite to sulfate in liver cells in analogy to the enzyme sulfite oxidase. The functionalized Molybdenum trioxide nanoparticles can cross the cellular membrane and accumulate at the mitochondria, where they can recover the activity of sulfite oxidase.

Sulfite oxidase is a molybdenum containing enzyme located in the mitochondria of liver and kidney cells, which catalyzes the oxidation of sulfite to sulfate during the protein and lipid metabolism and therefore plays an important role in cellular detoxification processes. A lack of functional sulfite oxidase is a rare but fatal genetic disease causing neurological disorders, mental retardation, physical deformities as well as degradation of the brain, which finally leads to premature death. Various dietary or drug treatments for a sulfite oxidase deficiency have been tried with moderate success.

It was the fact that molybdenum oxide is incorporated in the enzymes active site that provided the inspiration for the approach now taken by the team of scientists working under the lead of Professor Wolfgang Tremel of the JGU Institute of Inorganic Chemistry and Analytical Chemistry as well as Dr. Dennis Strand and Professor Susanne Strand of the Department of Internal Medicine of the Mainz University Medical Center. The researchers hope that this study may lay the basis for a therapeutic application of molybdenum trioxide nanoparticles and therefore new possibilities to treat sulfite oxidase deficiency.

Lowered sulfite oxidase levels can cause health problems even for otherwise healthy persons. In addition, sulfites are used as preservatives in food, e.g., in red wine, grape juice, or pickles in a jar. People having low levels of the sulfite oxidase react with symptoms like fatigue, asthma, drop in blood sugar, or headache.

With their study the Mainz scientists enter scientifically uncharted territory, because so far there are just a few studies of enzymatically active nanoparticles. "It is indeed astonishing, that simple inorganic nanoparticles can mimic an enzymatic activity," said Ruben Ragg, first author of this study. In a previous work Professor Wolfgang Tremel and his team had shown that vanadium oxide nanowires contain an enzymatically induced antifouling activity that efficiently prevents ships from being infested by marine microorganisms. "It is a long-standing goal of chemistry to synthesize artificial enzymes that imitate the essential and general principles of natural enzymes," added Tremel. There is growing evidence that nanoparticles can act as enzyme mimics.

Some nanomaterials were reported to exhibit enzyme-like activities, but the hallmark of enzyme chemistry would be to catalyze transformations in cells in the presence of other competing reactions. This is difficult to achieve, as it requires compatibility with other cellular reactions operating under similar conditions and rates. Therefore, artificial enzymes are not only useful for an understanding of the reaction mechanism of native enzymes but also for future applications as therapeutic agents.

At the same time, the use of molybdenum nanoparticles would have several benefits. "Molybdenum oxide particles are considerably cheaper and also more stable than genetically produced enzymes," added Dr. Filipe Natalio, cooperation partner from Martin Luther University of Halle-Wittenberg. Natalio is designing new materials that can mimic complex structures found in nature by bringing together a wide range expertise from material sciences to biology and chemistry. The next steps of the project will be to test if the enzyme activity of the nanoparticles can be retained in living organisms.

The research teams were supported by an interdisciplinary grant from the JGU Center for Natural Sciences and Medicine (NMFZ) and the Max Planck Graduate Center (MPGC).

More information: Ruben Ragg, et al. Molybdenum Trioxide Nanoparticles with Intrinsic Sulfite Oxidase Activity *ACS Nano* 2014, 8 (5), pp. 5182, 4 April 2014. DOI: 10.1021/nn501235j

Provided by Universitaet Mainz

natural-detoxification.html