A Pocketful of Uranium: Construction of a Selective Uranium-Binding Protein

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(PhysOrg.com) -- The use of uranium as a nuclear fuel and in weapons increases the risk that people may come into contact with it, and the storage of radioactive uranium waste poses an additional environmental risk. However, radioactivity is not the only problem related to contact with uranium; the toxicity of this metal is generally more dangerous to human health.

Researchers are still looking for simple, effective methods for the sensitive detection and effective treatment of uranium poisoning. Researchers led by Chuan He at the University of Chicago and Argonne National Laboratory (USA) have now developed a protein that binds to uranium selectively and tightly. As reported in the journal *Angewandte Chemie*, it is based on a bacterial nickel-binding protein.

In oxygen-containing, aqueous environments, uranium normally exists in the form of the uranyl cation (UO_2^{2+}), a linear molecule made of one uranium atom and two terminal oxygen atoms. The uranyl ion also likes to form coordination complexes. It prefers to surround itself with up to six ligands arranged in a plane around the ion's "equator". The research team thus chose to develop a protein that offers the uranyl ion a binding cavity in which it is surrounded by the protein's side-groups in the manner it prefers.

As a template, the scientists used the protein NikR (nickel-responsive repressor) from E. coli, a regulator that reacts to nickel ions. When NikR is loaded with nickel ions, it binds to a special DNA sequence. This

represses transcription of the neighboring genes, which code for proteins involved in nickel uptake. If no nickel is present in the bacteria, NikR does not bind to the DNA.

The nickel ion is located in a binding cavity in which it is surrounded by a square-planar arrangement of binding groups. By using several mutation steps, the researchers generated a new protein that can bind uranium instead of nickel. Only three amino acids had to be changed. In the specially designed cavity, the uranyl group has six binding partners that surround it equatorially. In addition, there are spaces for the two terminal oxygen atoms of uranyl.

This NikR mutant only binds to DNA in the presence of uranyl, not in the presence of nickel or other metal ions. This confirms its selectivity for uranyl and may make it useful for the detection of uranyl and nuclear waste bioremediation. It also represents the first step towards developing potential protein- or peptide-based agents for treatment of uranium poisoning.

More information: Chuan He, University of Chicago, Engineering A Uranyl-Specific Binding Protein from NikR, *Angewandte Chemie International Edition*, doi: 10.1002/anie.200805262

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