Crystal structures of Uricase complexed with its real substrate and product

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Uricase is a copper-containing enzyme that catalyzes the conversion of uric acid to allantoin during the breakdown of purines in some mammalian species, as well as in amphibians and most fishes. Uricase from small organisms, however, does not require any metal ion or cofactor for its catalytic activity. Since humans do not produce uricase, this enzyme may be useful as a drug to prevent uric acid accumulation.

To clarify the reaction mechanism, three X-ray structures of uricase from a prokaryote *Arthrobacter globiformis*, and of complexes with its substrate uric acid and with a product allantoin have been solved at 2.0, 1.9 and 1.9 Å resolutions, respectively. In every structure, the two subunits are associated to form a ring-shaped dimer, and the two dimers are stacked on each other to complete a cylinder-like tetramer with a long tunnel at the center. The site of uric acid and allantoin binding to the protein are the same, located at interface between two subunits of the ring.

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