An oxygenase that forms and deoxygenates toxic epoxide.

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Catabolism may give rise to toxic intermediates that compromise cell vitality, such as epoxide formation in the recently elucidated and apparently universal bacterial coenzyme A (CoA)-dependent degradation of phenylacetic acid. This compound is central to the catabolism of a variety of aromatics, such as phenylalanine, lignin-related compounds or environmental contaminants. The key phenylacetyl-CoA monooxygenase (epoxidase) of the pathway, PaaABCE, is also connected to the production of various primary and secondary metabolites, as well as to the virulence of certain pathogens. However, the enzyme complex has so far not been investigated in detail. Here we characterize the bacterial multicomponent monooxygenase PaaABCE that, surprisingly, not only transforms phenylacetyl-CoA into its ring-1,2-epoxide, but also mediates the NADPH-dependent removal of the epoxide oxygen, regenerating phenylacetyl-CoA with formation of water. We provide evidence for a catalytic di-iron centre that is probably the key to the unprecedented deoxygenation of an organic compound by an oxygenase. Presumably, the bifunctionality is vital to avoid toxic intracellular epoxide levels if the subsequent catabolic steps are impeded. Our data suggest that detoxification is assisted by two thioesterases (PaaI and PaaY) forming non-reactive breakdown products. Hence, PaaABCE may harbour an intrinsic escape mechanism from its own toxic product and represents the archetype of a bifunctional oxygenase/deoxygenase. Analogous reactions may possibly be catalysed by other di-iron epoxidases.

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