Public Abstract

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Title:Study of PvcA and PvcB, Two Enzymes Involved in Making Isonitrile-Containing Natural Products in Bacterial Pathogens

Isonitriles are organic molecules that contain a nitrogen-carbon triple bond moiety. They are widely used in organic synthesis, such as the multi-component reactions to synthesize peptides. But effective synthesis of isonitriles with different modifications is limited. Regarding this, researchers are eager to investigate new methods to synthesize isonitriles, and also to look for novel compounds.

Interestingly, a variety of isonitriles are widely distributed in biological systems. Many of them exhibit a strong antibiotic, fungicidal or antimalarial effect. The abundance of the natural isonitriles, their diverse structures and potential bioactivities may provide important implications in organic synthesis and pharmaceutical development.Thus, it is important to unravel the knowledge underlying their biosynthesis.

PvcA and PvcB are two biocatalysts involved in making isonitrile metabolites. PvcA is proposed to convert the amino group of tyrosine into the isonitrile group. PvcB operates downstream of PvcA and catalyzes an oxidation on the PvcA product. Catalytic activities of these two proteins and the possible mechanisms underlying their activities were investigated in this study. Our data demonstrated PvcB to be an oxygenase and to be responsible for the chemical diversity of the isonitrile products in different organisms. The different activities exhibited by the PvcB homologous proteins might be partially due to the structural differences of these enzymes. The PvcA protein was demonstrated to convert tyrosine into tyrosine isonitrile. Our results showed the presence of the precursor of the isonitrile carbon in the crude cell lysates and suggested it as a phosphorylated metabolite. But the identity of this compound remains unknown.

By studying the reactions catalyzed by the PvcA and PvcB proteins in one pathway, we will have a good knowledge of the synthesis of isonitriles in other species. This will allow researcher to obtain large quantities of this class of bioactive molecules, which will further facilitate their functional studies and enlarge their implications in both chemistry and biochemistry.