Poster Presentation

MS29.P24

Crystallographic and kinetic study on riboflavin synthase from Brucella abortus

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Riboflavin synthase (RS) catalyzes the last step of riboflavin biosynthesis in microorganisms and plants, which corresponds to the dismutation of two molecules of 6,7-dimethyl-8-ribityllumazine to yield one molecule of riboflavin and one molecule of 5-amino-6-ribitylamino-2,4(1H,3H)-pyrimidinedione [1]. Due to the absence of this enzyme in animals and the fact that most pathogenic bacteria show a strict dependence on riboflavin biosynthesis, RS has been proposed as a potential target for antimicrobial drug development. Eubacterial, fungal and plant RSs assemble as homotrimers lacking C3-symmetry [2]. Every monomer can bind two substrate molecules, yet there is only one active site for the whole enzyme, which is located at the interface between two neighboring chains. This work reports the crystallographic structure of RS from the pathogenic bacterium Brucella abortus (the etiological agent of the disease brucellosis) in its apo form, in complex with riboflavin, and in complex with two different product analogues, being the first time in which an intact RS trimer is solved with bound ligands. These crystal models support the hypothesis for an enhanced flexibility in the particle and also highlight the role of the ligands in assembling the unique active site. Kinetic and binding studies were also performed to complement these findings. The structural and biochemical information generated may be useful for the rational design of novel RS inhibitors with antimicrobial activity.

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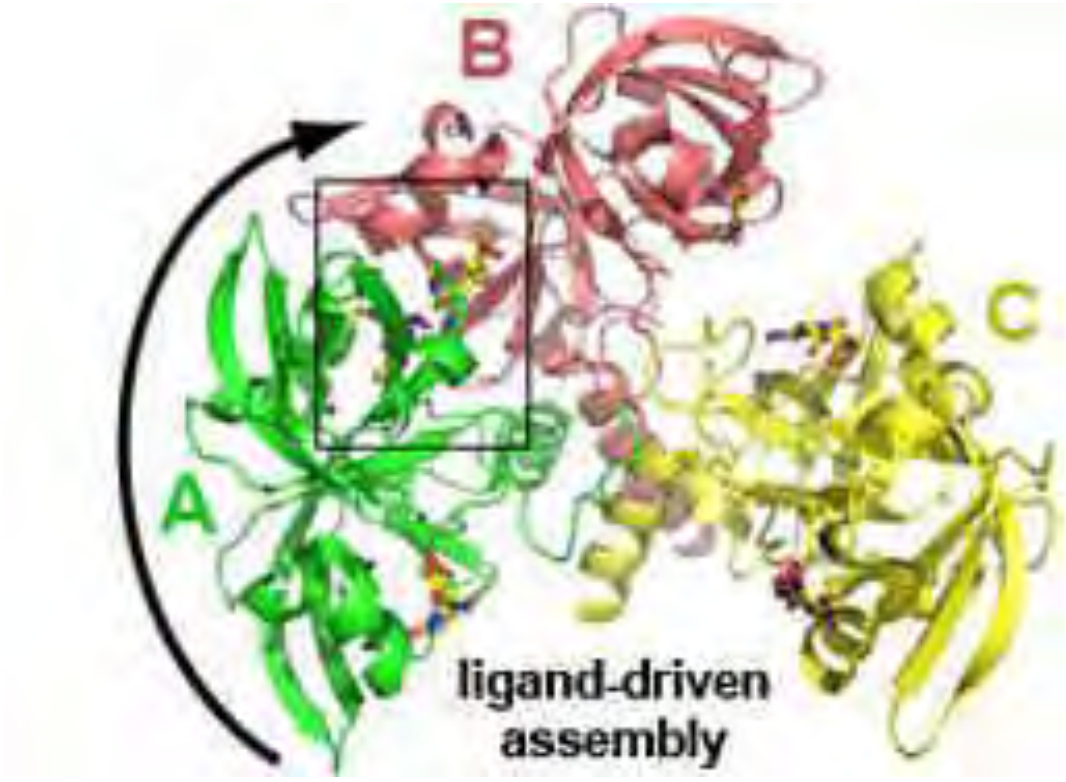

Keywords: Riboflavin biosynthesis, Enzyme-ligand complex, Inhibition by substrate and product