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Structural and biophysical investigations into vitamin B6 synthase assembling

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Infectious diseases are one of the leading causes of death in the world and the number of antibiotic-resistant infections is increasing, according to the World Health Organization (WHO). *Staphylococcus aureus* methicillin-resistant (MRSA) and VRSA (vancomycin-resistant *S. aureus*) strains are among the global priorities listed by the WHO for research and development (R&D) of new antibiotics. (1) The genome sequencing allowed the identification of pathogen-specific enzymes and pathways, desirable targets for antimicrobial drug discovery. Among these pathways, the vitamin B6 (pyridoxal 5-phosphate) *de novo* synthesis pathway is an interesting example. (2) Pyridoxal 5-phosphate (PLP) is an essential cofactor for various enzymes in all organisms which are involved in the biosynthesis of amino compounds such as amino acids. A multimeric complex of two enzymes, Pdx1 and Pdx2, performs the synthesis. Although this enzymatic pathway has been widely studied, the assembling mechanism of Pdx1 and Pdx2 is unknown. (3) In this project, we propose to investigate the bacterial *S. aureus* PLP synthase complex by biophysical and structural analyses. Dynamic Light Scattering (DLS) and X-ray solution scattering (SAXS) analyses evidenced a salt dependency in SaPdx1 oligomerization. Crystals of SaPdx1 were obtained and X-ray diffraction data were collected at the new Manacá beamline (Sirius, Campinas) with a high-resolution of 2.6 Å and the structure is being refined. Both SaPdx1/SaPdx2 complex, wild type and mutant, were purified and the assembling was confirmed by SEC, DLS, and SDS-PAGE gels. The complex stoichiometries were quantitatively determined, for the first time, by SEC-SAXS analysis. Crystallization trials were carried out for both complexes and two conditions were selected for optimization by conventional methods and by XtalController technology. Two X-ray diffraction datasets were collected at PETRA III, DESY, Germany. One from wild type SaPdx1-2 complex with a resolution of 4 Å and the other from mutant SaPdx1-2 with 3 Å resolution. Both datasets are being processed using the autoPROC package.

Palavras-chave: *Staphylococcus aureus*. Protein crystallography. Dynamic light scattering.

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