Contribution ID : **13** Type : **not specified**

X-Ray Crystallography of Betaine Aldehyde Dehydrogenases: A Tool for the Study of their Catalytic Mechanism

Thursday, 5 May 2011 13:15 (0:30)

Abstract content

Aldehyde dehydrogenases (ALDHs) are a group of ubiquos and ancient enzymes that catalyze the oxidation of a broad variety aldehydes to their corresponding carboxylic acids with the concomitant reduction of NAD(P)+ to NAD(P)H. Their catalytic mechanism involves three chemical steps: (1) the nucleophilic attack of the catalytic cysteine on the aldehyde substrate resulting in formation of the hemithioacetal intermediate; (2) the transfer of the hydride from the hemithioacetal to NAD(P)+, resulting in formation of the thioester intermediate; and (3) the nucleophilic attack of a water molecule on the thioester intermediate, leading to the release of the acid product. The ALDH enzymes can be dimers, tetramers o hexamers with approximately 490-500 residues per subunit. Currently, 36 different ALDH crystal structures, in their apo forms or in complex with different ligands, are available in the Protein Data Bank. Crystallographic data, included those obtained by our research group on the betaine aldehyde dehydrogenases from Pseudomonas aeruginosa and Spinacea oleracea, contributed to the knowledge of specific details at atomic level about each of the catalytic steps and of the catalytic residues involved, but there is still a considerable amount of open questions about the mechanism of catalysis of these enzymes. All ALDH crystals determined to date exhibit big cell dimensions and a large number of residues per asymmetric unit (2000-6000), with space groups C2, P212121, P1, or P3221. The use of a source of high intensity X-ray radiation has been of great help in increasing the resolution of the diffracted crystals, and the access to CCD detectors let us work with the cell dimensions of the crystals. Financially supported by CONACYT (grants 59654 and 101986) and UNAM (PAPIIT grant IN204708).

Summary

Primary author(s) : Dr. GONZÁLEZ-SEGURA, Lilian (Departamento de Bioquímica, Facultad de Química, Universidad Nacional Autónoma de México)

Co-author(s) : Mr. DÍAZ-SÁNCHEZ, Ángel G. (Departamento de Bioquímica, Facultad de Química, Universidad Nacional Autónoma de México); Dr. RUDIÑO-PIÑERA, Enrique (Departamento de Medicina Molecular y Bioprocesos, Instituto de Biotecnología, Universidad Nacional Autónoma de México); Prof. MUÑOZ-CLARES, Rosario A. (Departamento de Bioquímica, Facultad de Química, Universidad Nacional Autónoma de México)

Presenter(s) : Dr. GONZÁLEZ-SEGURA, Lilian (Departamento de Bioquímica, Facultad de Química, Universidad Nacional Autónoma de México)