SCIENCESPRINGDAY

FCT FACULDADE DE CIÊNCIAS E TECNOLOGIA UNIVERSIDADE NOVA DE LISBOA

Chemistry Department

Drug Design, Mo-enzymes & X-rays

Macromolecular Crystallography Group

xtal Crystallography Group @ REQUIMTE — http://xtal.dq.fct.unl.pt/

requimte rede de química e tecnologia

alfama

Universität Potsdam

US University of Sussex

Teresa Santos Silva

Auxiliary Researcher from 2009

2007-2009 - Post-doc in protein crystallography (FCT)

2002-2006 - PhD in protein crystallography (FCT)

1996-2001 - Degree on Applied Chemistry - Organic Chemistry (FCT)

Objectives

1. X-ray Crystallography applied to DRUG DESIGN

CO releasing molecules (CORMs) are metal based complexes with anti-inflammatory, anti-apoptotic and anti-proliferative effects.
The aim of this project is to understand the interaction between serum proteins and CORMs at the molecular level.

2. Structural characterization of Molybdenum enzymes and chaperones

Mo containing enzymes are widely spread in nature and conduct crucial processes as purines catabolism or xenobiotics oxidation.
The reaction mechanism, together with cofactor insertion are key steps that need critical analysis and are the main objectives of this work.

Methodology

1.
Protein – CORM interaction is assessed by several techniques as ICP, FTIR, MS and X-ray crystal diffraction.
Proteins as human Transferrin, human Albumin, bovine Hemoglobin and hen egg white Lysozyme have been sucssefully crystallized. Data collected at the synchrotron show medium (3Å) to atomic resolution (1.2Å).

2.
Two aldehyde oxidoreductases, AOR and PaoABC, have been crystallized and the structures solved at atomic resolution.
PaoABC is a novel Mo enzyme
AOR in the presence of several inhibitors and substrates has been crystallized and details of liagnds in the active site are/have been analyzed.

Expected Results

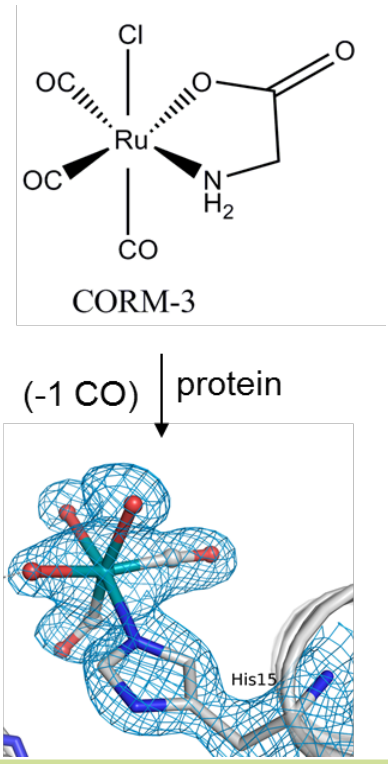
1.
Details into metal binding could be achieved with this approach, showing a covalent bond between the protein (lysozyme) and the experimental CORM used. The structure of Transferrin and another Ru CORM has been obtained and is currently under refinement.
References:

Santos-Silva, et al, JACS, **2011** and Curr Med Chem, **2011**; Santos et al, JIB, **2012**; Seixas et al, Dalton T, **2012**.

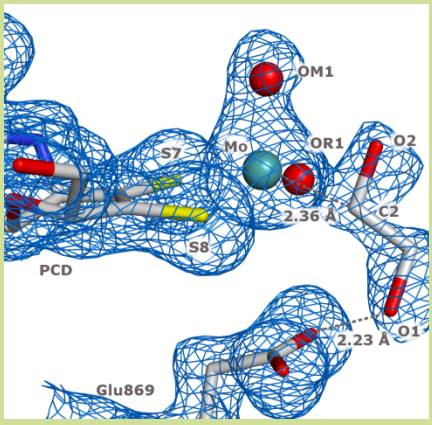
2.
Reaction mechanism of the two Mo-enzymes is going to be revised due to unexpected features found in the Molybdenum active site. Furthermore, structural charaterization of the interaction between enzyme PaoABC and chaperone PaoD is going to be adressed.
References:

Santos-Silva, et al, JACS, **2009**; Correia et al, in prep, Cardoso et al, in prep.

1- X-ray structure of CORM-3 bound to Lysozyme



2- X-ray structure of inhibited Aldehyde Oxidase



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