# SCIENCESPRINGDAY

FACULDADE DE CIÊNCIAS E TECNOLOGIA
UNIVERSIDADE NOVA DE LISBOA

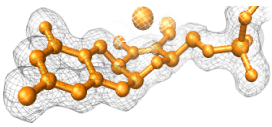
## Chemistry Department

## Mammalian Aldehyde Oxidases, Structure & Function

Macromolecular Crystallography Group

*http://xtal.dq.fct.unl.pt/*

xtal
Crystallography Group @ REQUIMTE



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rede de química e tecnologia

MARIO NEGRI
ISTITUTO DI RICERCHE FARMACOLOGICHE


## Catarina Coelho

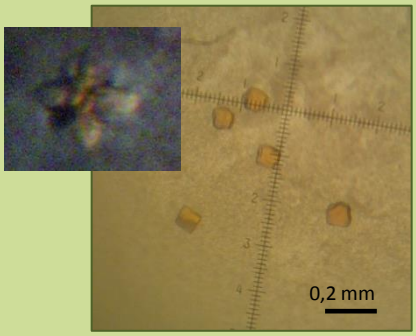
**Postdoctoral Researcher since 2012**

Supervisor: Prof. Maria João Romão


PhD in Structural Biology, 2011 (FCT, UNL); Degree in Biochemistry, 2005 (FCUL, UL); Published 7 ISI papers in international reviewed Journals; Graduate student researcher at Mario Negri Institute (Milan) and at Potsdam University; CAP as a Trainer.

## Objectives

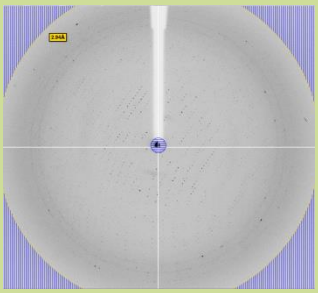
My main research area are structural and biochemical studies of proteins with high relevance in human health, namely human aldehyde oxidase and mouse isoforms (AOXs). The importance of this family of enzymes has been increasing in recent years due to its implicance in clinical trials studies. AOX plays a fundamental role in the metabolism of drugs and xenobiotics. It has been considered the major liver cytosolic drug-metabolizing enzyme given its broad substrate specificity, substituting Cyt-P450 as the central drug-metabolizing system in humans.




Protein Crystals

## Methodology

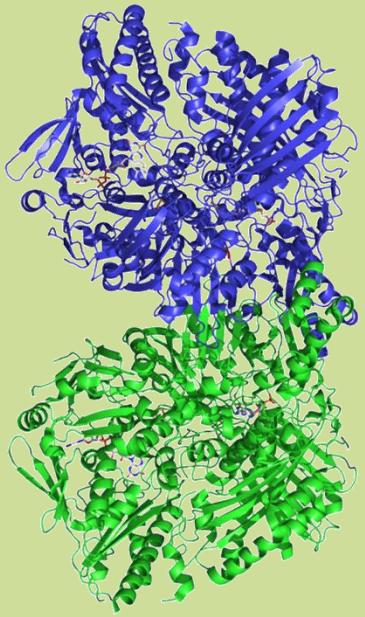
To study the crystal structure of AOXs we need to obtain suitable protein crystals, usually trought the aplication of vapou-difusion techniques. Once the protein has crystallized we use X-Ray diffraction (in house or in a synchrothron radiation source) to obtain a diffraction pattern that will allow us, trought the use of computacional methods, to calculate an electron density map where the crystallographyc model is constructed. Several validation and parametrization parameters are then applied before submitting the final structure to the Protein Data Bank database (http://www.rcsb.org). In parallel, spectroscopic, enzimatic and mechanistic studies will be performed using different substrates, inhibitors and important pharmacological compounds known to be metabolized by the enzyme.



Diffraction Pattern

## Expected Results

The structural and biochemical characterization of human aldehyde oxidase protein and mouse isoforms, will be a valuable tool for protein-drug interaction studies. Comparison between the crystal structures will enable revealing crucial features responsible for AOX enzymatic mechanism, and its rather broad substrate specificity. Combining structural evidences with additional biochemical and spectroscopic information will help to elucidate the true physiological role of aldehyde oxidases in mammals.



Crystal Structure of mouse Aldehyde Oxidase Homologue 3 (mAOX3, PDB ID: 3ZYV)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