SCIENCESPRINGDAY

FACULDADE DE CIÊNCIAS E TECNOLOGIA
UNIVERSIDADE NOVA DE LISBOA

Department of Chemistry

Exploring the human metabolism of gases

Luisa B. Maia

(PI)

Research fellow at REQUIMTE

Ph.D. in Pharmaceutical and Clinical Biochemistry

Lic. in Biochemistry

Biological Chemistry @ FCT/UNL
(http://sites.fct.unl.pt/biologicalchemistryatfctunl/)

requimte
rede de química e tecnologia

in collaboration with

Faculdade de Ciências
Universidade de Lisboa

Objectives

The gaseous molecules *conquered* the human signalling pathways: from the common (O_2, CO_2) to the *bizarre* gases (**CO**, H_2S, SO_2), not forgetting the *famous* nitric oxide, **NO**, Nobel Prize awarded.

Over the last years, these gases are being recognised as important human signalling molecules that control vascular tone, host defence, neuromodulation, apoptosis and energy metabolism. Nevertheless, the enzymes that control the gases homeostasis are still poorly explored. Our aim is to study the participation of human xanthine oxidase (XO) and aldehyde oxidase (AO) in novel pathways of formation and consumption of signalling gases.

Methodology

Protein purification (bovine and rat liver enzymes as models of human enzymes)
Enzyme kinetics (polarographic techniques and UV-visible spectroscopy)
Mechanistic studies (UV-visible, EPR, NMR, mass spectroscopies)
In silico studies (theoretical and computational calculations, to support and "add" atomic details to the reaction mechanisms to be proposed)

Tissue cultures (cell lines of hepatocytes and endothelia)
Fluorescence methodologies (probes to follow the gases formation/consumption)
Models of oxidative stress

Expected Results

The project is focused in answer two questions, raised at two different levels:
Molecular Level - How do the enzymes carry out the reactions (the molecular mechanism)**?**
Tissue Level - How the reactions take place in side a living cell**?**
At the "Molecular Level", the enzymes are being kinetically and mechanistically characterised for different reactions involving the formation and consumption of the signalling gases, *e.g.* for the NO formation from nitrite reduction, $NO_2^- \rightarrow {}^\bullet NO$
The "Tissue Level" studies are focused on the evaluation of the *in vivo* significance of the novel reactions, under normoxia and hypoxia.
The work envisaged will contribute to a better characterisation of the XO- and AO-dependent pathways, with emphasis on structural and mechanistic aspects, and to predict how relevant these novel pathways would be *in vivo*.

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