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Host laboratory:

LCBM, BioCat team

<https://www.cbm-lab.fr/en>

Title of the M2 research internship:

Ergothioneine: biosynthesis and role in iron sulfur cluster stability in relation with oxidative stress

Project summary:

Ergothioneine (EGT) is a fascinating small-molecular antioxidant. Only fungi and bacteria are able to produce it, eukaryotes adsorb it through the diets. There is a growing interest in EGT for its potential health benefits and its role in aging and dementia in human where a specific ETT eukaryotic cell transporter exists, but also in mycobacterium virulence.

The literature suggests that the primary role of EGT may be more specific than antioxidant, playing a cofactor role in some enzymes. Indeed the unique chemical functions building EGT: the trimethyl ammonium coupled to a carboxylate and the thione-imidazol group suggest a role for specific interactions. EGT may chelate $\text{Cu}^{+2+}/\text{Zn}^{2+}/\text{Co}^{2+}$, but, surprisingly, the interaction with $\text{Fe}^{2+}/\text{3+}$ ions has never been described, despite its predictability. It will be crucial to study it in the context of the oxidative stress and air sensitive iron-sulfur cluster.

Our project aims to provide new knowledge: 1) on the Mycobacterium biosynthesis of EGT including two iron-containing metalloenzymes and to test EGT derivatives, to pave the way for pharmaceutical developments; 2) to study the effect of EGT on air sensitive iron-sulfur cluster containing proteins.

The master 2 internship will be dedicated to participate to the production of these two EGT biosynthesis enzymes from Mycobacterium smegmatis as previously described and to test EGT derivatives, in collaboration with the Tetrahedron company, on their activity, in a prospective antibacterial strategy. Furthermore, the effect of EGT on stability of iron/iron-sulfur clusters containing metalloproteins will be tested. This work will involve several scientists of the BioCat group. This is a topic that starts in 2022 which have been already support by the "plan de relance" for two years on a confidential particular side of the project in collaboration with the Innoverda start-up. An ANR letter and an IRGA project have been submitted too.

Keywords:

mycobacterium, ergothioneine, iron sulfur cluster

Relevant publications of the team:

Mathieu S, Cisse C, Vitale S, Ahmadova A, Degardin M, Perard J, Colas P, Miras R, Boturyn D, Coves J, Crouzy S, Michaud-Soret I* (2016), ACS chem.biol., 11, 2519.

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