UFR de Chimie et de Biologie
UNIVERSITÉ Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2021-2022

Laboratory/Institute: Institute for Advanced Biosciences **Director:** Prof. Pierre Hainaut
Team: Structural Biology of Novel Drug Targets in Human Diseases
Head of the team: Andrés Palencia
Webpage: https://noveltargets-palencia.com
Name and status of the scientist in charge of the project: **HDR: yes ☒ no ☐**
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Program(s) of the Master's degree in Biology:

☒ Immunology, Microbiology, Infectious Diseases ☒ Structural Biology of Pathogens
☐ Physiology, Epigenetics, Differentiation, Cancer ☐ Neurosciences and Neurobiology

Title of the project:

Characterization of an Aminoacyl-tRNA Synthetase as a Novel Antibacterial Drug Target

Objectives (up to 3 lines):

Expression, purification and structural studies of bacterial aminoacyl-tRNA synthetases as novel antibacterial drug targets and applications for the development of antibiotics with reduced risk of emergence of drug resistance.

Abstract (up to 10 lines):

Pathogenic Gram-negative bacteria represent a worldwide public health concern, not only because of the frequency of infections but also because of the phenomena of drug resistance. Today, it is estimated that about seventy percent of infections in intensive care units are caused by Gram-negative bacteria. This highlights the desperate need of new classes of drugs, ideally directed to novel targets, which will allow to develop the next generation of antibiotics. Here we will investigate the potential of novel boron compounds to treat infections caused by bacterial pathogens, specifically the top 1 priority in the list by WHO. You will use a highly multidisciplinary approach by combining our expertise in structural biology and biophysical approaches focused on drug discovery with molecular microbiology to provide insights ranging from the atom scale to the *in cellulo* level. We believe that the synergy arising from this interdisciplinary research, involving highly complementary teams, both in academia and pharmaceutical companies provides the optimal environment to successfully develop this project to accelerate the discovery of novel antibiotics.

Methods (up to 3 lines):

Protein expression and purification, biophysical methods for measuring protein-small molecule interactions, Protein-RNA interactions; macromolecular crystallography, cryo-electron microscopy, RNA in vitro transcription, RNA production.

Up to 3 relevant publications of the team:

- Lukarska, M. & Palencia, A. Aminoacyl-tRNA synthetases as drug targets. *The Enzymes,Elsevier.* 48:321-350 (2020).
- Chopra, S.†, Palencia, A.†, Virus, C., Tripathy, A., …Cusack, S.. Plant tumour biocontrol agent employs a tRNA-dependent mechanism to inhibit leucyl-tRNA synthetase. *Nature comm* 4, 1417 (2013).
- Palencia, A., Crepin, T., Vu, et al. Structural dynamics of the aminoacylation and proofreading functional cycle of bacterial leucyl-tRNA synthetase. *Nature structural & molecular biology* 19, 677-84 (2012).

Requested domains of expertise (up to 5 keywords):

Protein Expression and Purification, Structural Biology, Infectious Diseases, Antibiotics