

Position Offer:

Doctoral position: Investigating the mechanism of biotin synthase

A doctoral position is available to work on the structural and functional study of a new class of biotin synthase. The position is shared between the Metalloproteins Unit (MU) at the Institut de Biologie Structurale (IBS; <https://www.ibs.fr/research/research-groups/metalloproteins-group/>) and the Biocatalysis team at the Laboratoire de Chimie et Biologie des Métaux (LCBM; <https://www.cbm-lab.fr/en/Pages/BioCat/Presentation.aspx>) both located in Grenoble – France.

Biotin synthase is the enzyme responsible for the final step in biotin biosynthesis. This enzyme is a member of the radical *S*-adenosyl-L-methionine (SAM) protein superfamily and uses radical chemistry to catalyze the two-step insertion of a sulfur atom into the thiolane ring. We recently identified a new type of biotin synthase that does not sacrifice its auxiliary FeS cluster to provide the sulfur atom. In this project, we aim at studying this new enzyme, combining structural and biochemical studies with spectroscopic analyses and theoretical calculations to unravel the mechanism of this enzyme along two main axes. The first one corresponds to the search for the sulfur provider and to the structural and functional characterization of its transfer between the two partners. The second axis corresponds to the tracking and characterization of biotin synthase reaction intermediates. This project is therefore at the interface between biochemistry, bioinorganic chemistry and structural biology. The candidate will focus on these two aspects and will be in charge of the protein production, functional analyses, including the search for the physiological partner, as well as the different structural characterizations using X-ray crystallography and cryo-electron microscopy. They will also participate, through collaboration to the spectroscopic characterization of the intermediates already settled in Grenoble. The candidate will share their time at the Institut de biologie Structural, which is fully equipped with state-of-the-art gloveboxes to work under anaerobic conditions “*from gene to structure*”. They will also work at the Laboratoire de Chimie et Biologie des Métaux notably to perform all the *in vitro* functional analyses and sample preparation for spectroscopic studies. The candidate will benefit from a highly stimulating environment to afford a future career either in academia or in R&D.

The candidate should hold a *Master* degree in structural biology, biochemistry, chemical biology or equivalent and some previous wet-lab experimental experience. They should have good knowledge in protein expression and purification. A strong background in chemistry and enzyme mechanisms would be an advantage.

We are looking for a highly enthusiastic and open-minded candidate with good communication skills who likes to work in a multidisciplinary team.

This corresponds to a 3-year contract. Starting date: October 2024

To apply, please provide a detailed resume, transcripts of records, a cover letter and two reference letters to Yvain Nicolet and Sandrine Ollagnier-de-Choudens. You can contact them for further information: (yvain.nicolet@ibs.fr (+33 4 57 42 86 03); sandrine.ollagnier@cea.fr (+33 4 38 78 91 22)).