



Postdoctoral Fellowship

Center of Infection and Immunity of Lille

Chemical Protein Synthesis Group

An 18-month postdoctoral fellow position is open to join the CPS group at the *Institut Pasteur de Lille* (Chemical Protein Synthesis Group, CIIL UMR CNRS 9017). The successful applicant will work at the interface of chemistry and biology to produce amino acid analogues and assess their reactivity within the frame of the ANR-PRCI program “MISTER” (Metabolic Incorporation of latent fast-reacting thioESTERs). The position starting date is ideally set for October-November 2023.

Context and Project outline

In recent years, the production of genetically engineered elastomeric protein biopolymers has been the subject of intense research with promising applications in biomedical or materials science. Despite significant advances, versatile and efficient approaches are still needed to further improve and diversify the properties of the targeted materials. The final goal of the MISTER project is to develop a fully integrated approach, spanning from chemistry to synthetic biology, that will enable the selective functionalization of proteins with activatable and extremely fast-reacting thioester derivatives.

We recently disclosed the reactivity of an oxalyl thioester-containing lysine derivative and discussed its potential as a fast and chemoselective crosslinking functionality for peptides and proteins.^{1, 2} The objective of the postdoc project is to achieve the genetically encoded incorporation of such a synthetic amino acid or any analogue that would enable the aforementioned chemistry within recombinant proteins.

Associated to the Chemical Protein Synthesis Group, the recruited applicant will perform the synthesis of non-canonical amino acids, will document mechanistic aspects of their reactivity in native chemical ligation-related reactions^{3, 4} (stopped flow reaction rate-based determination, kinetic modeling) and evaluate their stability in the peptide and protein context. He/she will work in tight collaboration with the synthetic biology group headed by Dr Birgit Wiltschi (Univ. Vienna, Austria) to achieve their genetically encoded incorporation.

Keywords

Organic synthesis, non-canonical amino acids, native chemical ligation

Starting Date

As soon as possible (no later than Nov 2023)



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Candidate Profile

Dedicated and highly motivated, candidates should have completed a PhD in organic chemistry or in the field of biomolecules and show a strong interest for projects at the interface of chemistry and biology.

Candidates will have an experience in synthetic chemistry or peptide chemistry as well as a strong knowledge of purification (HPLC) and characterization techniques (NMR, mass spectrometry). An additional expertise in solid phase synthesis is highly desirable.

Project advisors

Dr Vangelis Agouridas and Dr Oleg Melnyk (CBF – CIIL, Institut Pasteur de Lille)

Applications including a CV, a motivation letter, and a summary of research work should be sent by email to : vangelis.agouridas@ibl.cnrs.fr / oleg.melnyk@ibl.cnrs.fr

1. Snella, B.; Grain, B.; Vicogne, J.; Capet, F.; Wiltschi, B.; Melnyk, O.; Agouridas, V., Fast Protein Modification in the Nanomolar Concentration Range Using an Oxalyl Amide as Latent Thioester. *Angew. Chem. Int. Ed.* **2022**, *61*, e202204992.
2. Grain, B.; Desmet, R.; Snella, B.; Melnyk, O.; Agouridas, V., Incorporation of a Highly Reactive Oxalyl Thioester-Based Interacting Handle into Proteins. *Org. Lett.* **2023**, *25*, 5117-5122.
3. Agouridas, V.; Ollivier, N.; Vicogne, J.; Diemer, V.; Melnyk, O., Redox-Controlled Chemical Protein Synthesis: Sundry Shades of Latency. *Acc. Chem. Res.* **2022**, *55*, 2685-2697.
4. Agouridas, V.; El Mahdi, O.; Diemer, V.; Cargoet, M.; Monbaliu, J. M.; Melnyk, O., Native Chemical Ligation and Extended Methods: Mechanisms, Catalysis, Scope, and Limitations. *Chem. Rev.* **2019**, *119*, 7328-7443.