

PhD position - Synthetic protein chemistry applied to TIP60 coregulator of gene transcription.

A 3-year doctoral thesis work financed by the ANR (Project C-TIP60 - Structure and function of the human TIP60/p400 co-activator) will be supervised by Prof. Vladimir Torbeev and carried out at the CNRS research unit UMR7242 “Biotechnology and Cellular Signalling”. Three other teams will be taking part in the project: A. Ben Shem (P. Schultz’s team at IGBMC, coordinator), A. Hamiche (IGBMC) in Strasbourg and J.-P. Concordet (U1154/UMR7196 Museum National d’Histoire Naturelle) in Paris, possessing expertise in biochemistry, structural biology, epigenetics and cellular engineering. The doctoral student will be responsible for the semi-synthesis of histones and activation domains of transcriptional coactivators possessing mimics of post-translational modifications, reacting functionalities and conformationally modified amino acids, following by reconstitution of nucleosomes into transcription-active complexes. Protein semi-synthesis is a methodology for protein engineering that combines recombinant protein expression and chemical synthesis of polypeptides. The recombinant and chemically synthesized protein fragments will be conjugated by native chemical ligation as well as enzymatically-catalyzed ligations. Cryo-EM will be used to solve their structures and relevant biological functions will be studied.

Publications related to the project:

Bauer V, Schmidtgal B, Gógl G, et al. Conformational editing of intrinsically disordered protein by α -methylation. *Chem Sci*. 2021;12(3):1080-1089. doi:10.1039/d0sc04482b

Fréchar A, Faux C, Hexnerova R, et al. The structure of the NuA4-Tip60 complex reveals the mechanism and importance of long-range chromatin modification. *Nat Struct Mol Biol*. 2023;30(9):1337-1345. doi:10.1038/s41594-023-01056-x

Bachelart T, Kumar S, Jouin A, Yousef M, Kieffer B, Torbeev V. Design, Synthesis and Catalytic Activity of Protein Containing Thiotyrosine as an Active Site Residue. *Chembiochem*, 2024;e202400148. doi:10.1002/cbic.202400148

Qualifications – How to apply

We are searching for a highly motivated candidate, skilled in organic synthesis and eager to practice biological-related experiments. Previous experience in peptide synthesis will be a strong advantage. The candidate will integrate into the team of Biosystems Chemistry at UMR 7242 and will be enrolled in the ED222 Doctoral School in Chemistry. **The anticipated starting date: October 2024 – January 2025.** To apply, please send a letter containing a statement of interest, CV and the names of two mentors for recommendation letters via CNRS job application portal:

<https://emploi.cnrs.fr/Offres/Doctorant/UMR7242-VLATOR-006/Default.aspx>

For more information, please, consult the web-page of the team: <https://torbeevlab.com>. If any questions, contact by email: torbeev@unistra.fr.