Graz University of Technology

Institut für Biochemie

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PhD thesis in Protein Biochemistry

Topic - Red light activated phosphatases

The Institute of Biochemistry at the Graz University of Technology is looking for a highly motivated PhD candidate with a genuine interest in understanding molecular mechanisms of biochemical processes. More specifically, the research group around Andreas Winkler is planning to recruit a PhD for 3.5 years, working in a recently funded FWF-project on PPM red light-regulated phosphatases (10.55776/PAT6932824).

As a PhD student you will be part of a motivated team embedded in an established local research consortium combining a range of integrative structural biology approaches to address current challenges in the fields of protein signaling and allosteric regulation of enzyme activity. Understanding principles of sensor-effector modularity and how nature adapts them for diverse requirements, is key to improve success rates of artificial designs for the generation of novel optogenetic tools. In this project, the focus will be set on combining biochemistry and various tools of structural biology (crystallography and hydrogen-deuterium exchange coupled to mass spectrometry) including collaborations in cryo-EM (Elmar Behrmann, University of Cologne) to address the structure-function relationship in red-light photoreceptors [1] coupled to phosphatases to complement recent efforts that focused on a different enzymatic output [2, 3, 4, 5]. Eventually, appreciation of molecular details of sensor-effector modularity will be helpful for a more rational approach to the design of artificial light regulated functionalities.

The project provides in-depth, interdisciplinary training in biomedical and biotechnological research in an international and stimulating environment. The thesis project follows an integrative approach and combines structural biology, enzymology, computational protein design and biophysics to decipher molecular mechanisms of catalysis and development of biomedical tools, employing a wide range of cutting-edge techniques.

Applicants must hold (or be close to obtaining) an undergraduate degree equivalent to a Master in any discipline of natural or life sciences. The ability to work in a team, initiative, flexibility as well as good organizational and learning skills are required. The selection procedure, all training activities and communications will be in English. Thus, excellent written and spoken English skills are required. Successful applicants will get employed for up to four years (initial contract for one year with the option of prolongation upon successful performance) with a contract that includes social benefits.

Interested applicants should include a motivation letter, CV, one-page summary of their research experience and contact details of two potential referees in their online applications via the TU Graz job portal until April 30th 2025. Prospective starting dates throughout summer 2025 can be discussed upon acceptance.

[1] Hughes and Winkler (**2024**) New insight into phytochromes: connecting structure to function. *Annual review of plant biology,* **75** (1), 153-183.

[2] Gourinchas, *et. al*. (**2017**) Long-range allosteric signaling in red light–regulated diguanylyl cyclases. *Science Advances*, **3**, e1602498.

[3] Gourinchas G, Heintz U, Winkler A (**2018**) Asymmetric activation mechanism of a homodimeric red light regulated photoreceptor. *eLife* 7, e34815.

[4] Böhm C, Todorović N, Balasso M, Gourinchas G, Winkler A (**2023**) The PHY domain dimer interface of bacteriophytochromes mediates cross-talk between photosensory modules and output domains. *Journal of Molecular Biology*, 433 (15), 167092.

[5] Tran QH, Eder OM, Winkler A (**2024**) Dynamics-driven allosteric stimulation of diguanylate cyclase activity in a red light-regulated phytochrome. *Journal of Biological Chemistry*, 300 (5), 107217.