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Early Stage Researcher Project

“Biophysical characterization of allosteric interactions using NMR spectroscopy”

in

University of Vienna

You want to participate in a training programme in and beyond the fields of physical chemistry of biological systems, theoretical and computational chemistry, biological chemistry, biochemistry, targeted drug delivery/discovery and medicinal chemistry?

14 Early Stage Researcher (ESR) positions are available within the EU-funded Marie Skłodowska Curie Innovative Training Network on **Allo**stery in **D**rug **D**iscovery (**ALLODD**) under Grant Agreement *No. 956314*.

The ALLODD project is a collaboration between 13 academic and industrial organizations with 14 PhD students in total. The aim of ALLODD is to train a new generation of scientists to exploit the concept of allostery in drug design, putting together a whole array of technologies to identify and characterize allosteric modulators of protein function that will be applied to therapeutically relevant systems.

Project Description

Host Organisation: UNIVIE (www.univie.ac.at)

Scientist-in-Charge: Dr. Christoph Rademacher

Most drugs on the market are designed to bind directly to primary active sites (also known as orthosteric sites) of their biological targets. Allosteric modulators offer important advantages over orthosteric ones: they can be more selective because allosteric sites are less conserved, they can change protein levels or localization within the cell, change subtle aspects of protein function (e.g. form or conformation of the quaternary structure) and are unique in their ability to provide enzymatic activation. Furthermore, allosteric drugs can be used synergistically with orthosteric ligands, an approach that has been successfully used to prevent emergence of resistance in cancer therapy. Allostery may also be the key to drug proteins that have been considered undruggable due to the absence of a known active site, such as KRAS. The Rademacher lab investigates the identification and development allosteric drugs using C-type lectin receptors as targets applying biophysical methods such as NMR and SPR. Involvement in drug discovery teaching is optional.

**Objectives:**

- 1) Identification and characterization of potential allosteric sites and allosteric modulators from biophysical screening.
- 2) Application of ligand-based NMR methods (STD, waterLOGSY, ¹⁹F NMR, CPMG-filtering) for screening and druggability assessment of target proteins.
- 3) Binding site identification and validation using protein NMR methods (HSQC, TROSY) using either ¹⁵N labeled protein or incorporation of fluorinated amino acids (W/Y/F) into larger receptor complexes.
- 4) Identification of allosteric signal transmission pathways in proteins using CHESPA and related methods as well as incorporation site specific labels (¹⁹F-labeled amino acids e.g.W/Y/F).

Expected Results:

- 1) Druggability assessment and allosteric site identification from fragment-based screening using ligand-based NMR.
- 2) Verification and characterization of allosteric sites using protein NMR techniques.

Planned Secondement(s):

- **Host1:** UB, timing M10, length: 2 months, purpose: training in computer-aided drug design,
- **Host2:** Merck, timing: M18, length: 3 months, purpose: training in cell-based assays,
- **Host3:** KI, timing M30: length: 3 months, purpose: training in HDX experiments

Eligibility Criteria

There are **strict eligibility requirements** to apply for participation in a Marie Skłodowska Curie Innovative Training Network:

- Applicants for the ESR/PhD positions should be in the first 4 years (full-time equivalent) of their research careers and not yet have been awarded a doctorate.
- Applicants must not have resided or carried out their main activity (work, studies, etc.) in the host country for more than 12 months in the 3 years immediately before the recruitment date. In addition, local regulations of the host countries may apply.

Specific Requirements/Qualifications:

- 1) MSc degree, excellent knowledge in Biochemistry and Structural Biology.



2) Very good knowledge of written and spoken English.

Desirable but not Required Skills: Knowledge in NMR spectroscopy as well as the expression and purification of lectins from E. coli inclusion bodies.

Application documents: Letter of motivation – academic curriculum vitae (incl. publication list) – contact details of people who could provide a letter of reference.

Benefits

Enrolment in Doctoral degree(s): No.

We are offering a competitive, interdisciplinary environment with a track record of intense mutual collaboration. In addition to the individual training-through-research, our program includes further elements such as workshops, summer schools, internships and secondments to the partners' laboratories.

The successful candidate:

- will be funded for 36 months with a competitive salary in accordance with the MSCA regulation for Early Stage Researchers, including living allowance, mobility allowance and a family allowance (if married).
- will have to perform the secondments defined in his/her personalized career development programme.

To be a part of ALLODD:

Apply to and contact for further information: Applicants should apply either through the [portal](#) of the university or by email to jobcenter@univie.ac.at and use Reference number: 12284

Apply until: 31 January 2022

Starting date: The earliest starting date will be **1 November 2021**. The latest will be **1 September 2022**.