



**Karolinska
Institutet**

Early Stage Researcher Project

“Identification of target binding sites using HDX MS and off-targets using Proteome Thermo Profiling”

In

Karolinska Institutet (KI), Sweden

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 **Allostery in Drug Discovery (ALLODD)** under Grant Agreement No. 956314.

The ALLODD project is a collaboration between 13 academic and industrial organizations with 14 ESR/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: KI

Scientist-in-Charge: Dr. Roman Zubarev

Objectives:

A key aspect of the characterization of allosteric sites is their precise localization on the protein target using biophysical methods. In this context, binding-site characterization by differential amide hydrogen/deuterium exchange mass spectrometry (HDX MS) will be used for rapid detection and validation. Although HDX MS has lower spatial resolution (4-8 amino acids) than X-ray crystallography, its speed (\approx 1-2 weeks), low sample consumption (200 nmols) and simplicity (no necessity of protein crystals) makes it an ideal tool for fast binding site confirmation. For each protein, a set of 5 to 10 ligands will be chosen for binding-site characterization. 2) MS methods also provide the key to explore and understand off-target effects (by Proteome Thermo Profiling).



Expected Results:

- 1) Identification and validation of allosteric sites using HDX MS;
- 2) Identification of off-targets using Proteome Thermo Profiling;
- 3) Establishing a target/off-target relationship for allosteric modulators.

Planned Secondement(s):

- **Host1:** UNIVIE, length 3 months, purpose: training in NMR.
- **Host2:** UCB, length: 3 months, purpose: training in allosteric drug design in an industrial setting,
- **Host3:** BRFAA, length: 2 months, purpose: training in comparing HDX experiments with MD simulations.

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.

Benefits

Enrollment in Doctoral degree(s): The ESR will be enrolled in the Ph.D. school at the Karolinska Institutet (KI).

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 by email to roman.zubarev@ki.se indicating Reference: ALLODD_ESR9.

Apply until: 31 January 2022

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