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UNIVERSITÀ
DEGLI STUDI
DI URBINO
CARLO BO

Early Stage Researcher Project

“Allosteric modulation of GPCRs at the protein –
membrane interface”

in

University of Urbino, Italy

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 **Allosteric modulation of GPCRs at the protein – membrane interface (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 allosteric modulation of protein function that will be applied to therapeutically relevant systems.

Project Description

Host Organisation: UNIURB

Scientist-in-Charge: Prof. Giovanni Bottegoni

Objectives:

Membrane components have recently been characterized as important regulators of membrane protein activity. Lipids exert these effects by directly and specifically binding to the protein surface rather than simply modifying the bilayer biophysical properties. Here, we aim at: 1) systematically characterizing putative binding hot-spots for membrane components (e.g., cholesterol, PIP2, etc) in GPCRs by specifically adapting to the task at hand a multi-scale protocol which we have previously reported (Ferraro et al., Plos ONE 2016). Then, 2) we will target these putative binding sites in virtual ligand screening campaigns. This goal is particularly innovative as we attempt to find drug-like compounds displaying affinity for pockets evolved to lodge lipids (Fu, Bottegoni, et al. Nat Neuroscience 2011).



Expected Results:

- 1) systematic characterization of binding sites for membrane components (e.g., cholesterol, PIP2, etc.) at the protein–membrane interface in GPCRs.
- 2) Identification of novel PAMs, NAMs, or SAMs by targeting pockets characterized in (1).

Planned Secondement(s):

- **Host1:** Heptares, timing M10, length: 3 months, purpose: biophysical and in vitro characterization of selected hits,
- **Host2:** Merck, timing M20, length 3 months, purpose: training in cell-based and biochemical assays,
- **Host3:** Charite, timing M30, length 3 months, purpose: Training in X-ray crystallography.

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: Previous experience in/knowledge of one or more among:

- 1) medicinal chemistry,
- 2) coarse grained and/or atomistic molecular dynamics simulations,
- 3) virtual ligand screening protocols,
- 4) Python programming is not mandatory but will be considered a plus.

Benefits

Enrollment in Doctoral degree(s): The ESR will have the possibility to join a three-year PhD program at UNIURB starting Autumn 2022, under the supervision of Prof. Bottegoni (UNIURB) and Dr. de Graaf (Heptares).



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: giovanni.bottegoni@uniurb.it

Apply until: 31 January 2022

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