



The objectives of FragNet are to (a) train a cohort of ESRs across FBLD methods and (b) develop individual skills in research into either new methods in FBLD or to apply FBLD to interrogate biological systems.

We are looking for highly motivated and talented students with a MSc degree who are interested in an ambitious multidisciplinary project on Fragment-Based Lead Discovery (FBLD).

At this moment we have 15 vacancies



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ESR4: Development of FBLD techniques for Intrinsically Disordered Proteins

Host: Vernalis Research, UK (PhD enrolment at University of York)

Industrial supervisor: Dr Ben Davis (Vernalis Research)

Academic supervisor: Prof. dr. Rod Hubbard (University of York)

Synopsis

FBLD technologies are continuously being improved to capture new opportunities. ESR4 will explore Intrinsically Disordered Proteins (IDPs) and Intrinsically Disordered Regions (IDRs). The significance of these proteins has recently become apparent. This project will begin to evaluate the possibility of using FBLD to develop small molecule ligands that bind to IDPs and IDRs, and modulate their folding and function.

Objectives

1. Evaluate literature studies of ligands binding to intrinsically disordered proteins (IDPs).
2. Identify suitable IDP test system(s) with tractable expression, purification, stability and behaviour in aqueous solution.
3. Evaluate and develop fragment based screening (FBS) methods to identify fragments which bind to the IDP.
4. Validate and evolve initial fragments to show enhanced potency and characterise response of IDP to these ligands.

Approach

A number of IDP-ligand interactions have been identified in the literature, and assessment of these will provide both a key initial dataset and a valuable training in the biophysical techniques and approaches used to study protein-ligand interactions. Evaluation of the suitability of one or more IDPs for FBLD approaches will also provide a robust dataset, since any outcome will be of interest. Once the experimental methodology has been tested on the literature IDP systems, they will be applied against one or more tractable IDP or IDR systems, identified either from the literature or through collaborations (for example, with research groups at the University of York who are investigating the structural biology of disease-related IDPs).

The experimental methodology will then be extended to screen low affinity fragments for binding to this tractable IDP system, and to characterise the structural and kinetic basis for observed fragment: IDP interactions. Fragments which are determined as validated ligands for the IDP will then be explored through well-described FBLD evolution strategies, such as near neighbour analysis and template morphing, in order to enhance the affinity of the ligand: IDP interaction and if possible to characterise the response of the IDP to ligand binding

**Qualifications:**

An MSc degree in Chemistry, Biochemistry, Biophysics or Molecular Life Sciences is required. Expertise in protein expression and/or protein biophysics is required, along with a keen interest in the protein folding and molecular interactions. The ability to work independently as part of a small team is essential, along with strong communication and interpersonal skills. Previous experience of NMR would be an advantage.

Key publications:

1. Tompa *et al.* 2015 *Curr. Opin. Struct. Biol.* 35, 49–59.
2. Follis *et al.* 2008 *Chem. Biol.* 15, 1149–55.
3. Krishnan *et al.* 2014 *Nat. Chem. Biol.* 10, 558–66.



FragNet offers:

- Generously funded positions (duration 36 months) for 15 Early stage researchers (ESRs)
- High profile research projects in an Innovative European Training Network Program
- Excellent facilities for research and education
- Research training in both academic and industrial settings
- Training in state-of-the-art scientific and transferable skills
- Intensive contacts with international collaborators & secondments in other research laboratories

FragNet is looking for candidates that:

- are highly motivated and talented
- are able to work in a multidisciplinary team
- are keen on intra-European mobility to perform PhD research abroad
- have good communication skills

Selection criteria of the candidate:

- fulfil the eligibility criteria (ESR, international mobility) for Marie Skłodowska-Curie Innovative Training Networks (Horizon 2020)
- have a MSc degree in Life Sciences or obtain a MSc degree by September 2016
- have completed a research internship with relevant expertise
- have obtained high grades during his/her studies
- be fluent in English

Application procedure:

1. Send your application mentioning the **ESR number** in the subject line to hrm@fragnet.eu.
2. **Deadline for applications: 31 January 2016.**
3. Please send all the necessary information as **one pdf file** to hrm@fragnet.eu.
 - Detailed **CV** (include information on your BSc and MSc studies, languages, achievements, expertise)
 - **Motivation letter**, addressed to the FragNet selection committee, explaining your motivation why you apply with us. You have to indicate which FragNet ESR project(s) you are interested in (please motivate your selection and indicate which has your preference).
 - Provide contact details of at least 2 references (names, addresses, emails).
 - **Reference letter** from one of the enlisted references
 - Copies of your key educational certificates
 - **Transcript of Records** (i.e. documents enlisting your performance as BSc and MSc student over time by listing the course units or modules taken, credits gained and the grades awarded). If you have not completed your MSc degree yet include all grades obtained so far.
4. You may apply to more than one ESR position. If you do, submit a separate and dedicated application file for each position.
5. If applicable provide a language certificate Application is OPEN 3. The applications will be assessed by the FragNet selection committee, in which all group leaders are represented. Candidates are in particular evaluated on creativity, originality, intellectual capacity and quality of CV and motivation letter. The selection committee also takes into account interdisciplinary and gender balance.
6. Potential (Skype) interviews will be arranged with the group leaders associated with the ESR projects.
7. The ultimate starting date for the ESR projects is: **1st September 2016**, as the complete Fragnet ESR cohort will participate in the first Fragnet workshop that will be organized in York, UK in September 2016.

For other FragNet related questions please contact: info@fragnet.eu

Eligibility criteria

Eligibility criteria of Marie Curie Initial Training Networks apply. Only applicants who comply to the following conditions will be considered:

Conditions of experience (ESR)

Candidates must be, at the time of recruitment by the host organisation, in the first four years (full-time equivalent) of their research careers and have not yet been awarded a doctoral degree. This is measured from the date when they obtained the MSc degree which would formally entitle them to embark on a doctorate.

Conditions of international mobility

Eligible candidates may be of any nationality but must not, at the time of recruitment have resided or carried out their main activity (work, studies, etc.) in the country of their host organisation for more than 12 months in the 3 last years immediately prior to the reference date.



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