



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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ESR7: Understanding PDE binding kinetics

Host: VU University Amsterdam, The Netherlands

Academic supervisors: Dr. Chris de Graaf and prof. dr. Iwan de Esch (VU University Amsterdam)

Industrial supervisor: Dr. Wolfgang Jahnke (Novartis Pharma)

Synopsis

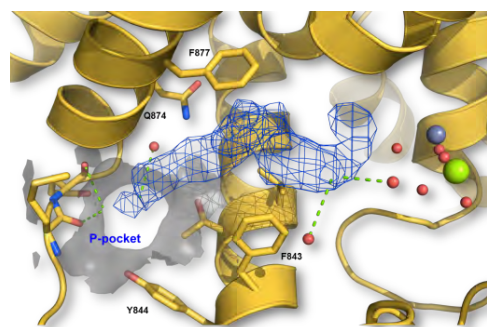
This project will investigate of binding kinetic while growing hit fragments, building on interesting data that has already been generated for *Trypanosoma brucei* Tbr-PDE ligands. The project will combine design, synthesis and molecular dynamics studies to unravel the molecular features of structure-kinetics relationships.

Objectives

1. Use SPR biosensors to measure the differences in binding kinetics of ligands for human hPDE4 and parasite TbrPDE proteins.
2. Perform Random Acceleration Molecular Dynamics (RAMD) studies to determine ligand access and egress mechanisms and factors determining the kinetics of ligand binding to PDEs.
3. Guide fragment hit growing to develop optimised compounds with well-defined kinetic selectivity profiles.

Approach

Trypanosoma brucei (Tbr) is the causative parasite of human African trypanosomiasis (HAT), also known as African sleeping sickness, a disease that has been grossly neglected as it is only a problem in the poorest areas of Africa. Tbr-PDE enzymes are validated drug targets to treat this illness. These Fragnet studies will lead to a better understanding of kinetic binding properties of Tbr-PDE ligands. This molecular understanding can be used to achieve kinetic selectivity and thereby create safe and efficient drugs for this neglected disease.



Qualifications

Applicants must have a background in molecular modelling (including molecular dynamics studies). Experience with organic synthesis or SPR biosensor instruments would be an advantage. The project can be fine-tuned according to the background and interests of the successful candidate.

Key publications

1. Jansen *et al.* J. Med. Chem. **2013**, 56, 2087-2096.
2. Orlling *et al.* Discov Today. **2012**, 55, 8745-8756.



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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