



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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ESR2: Novel 3D fragments

Host: University of York, UK

Academic supervisor : Prof. dr. Peter O'Brien and Prof. dr. Rod Hubbard (University of York)

Industrial Supervisor: Dr. Ben Davis (Vernalis Research)

Synopsis

The applicant will join a team working on the design, synthesis and assessment of novel 3D fragments. The focus of the project is on chemical synthesis with opportunities to explore aspects of cheminformatics (for analysing compounds), molecular modelling (how the compounds bind to proteins) and experimental fragment screening.

Objectives

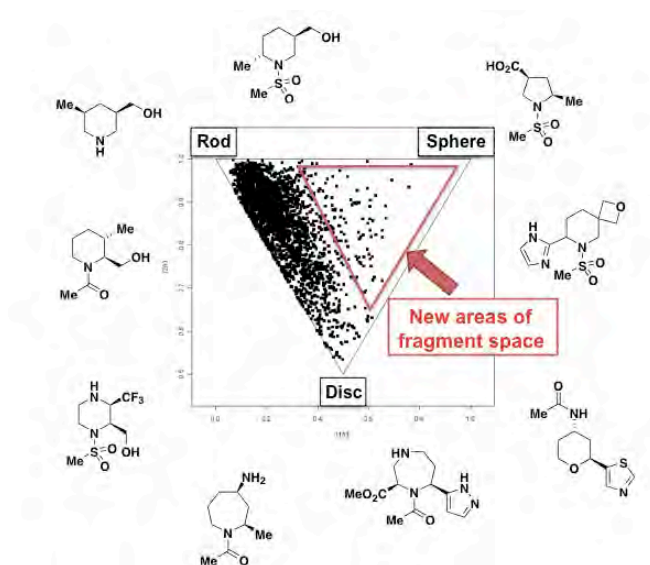
1. Design of 3-D fragment library.
2. Synthesis of selected fragments.

Approach

Most of the compounds in fragment libraries[1, 2] are commercially available small molecules which have been selected by medicinal chemists based on their experience on ease of synthesis and what they have seen before in existing drugs. This means that many fragments are flat heterocycles. This has worked well for many proteins that bind to and recognise metabolites such as ATP, but may not be ideal for other proteins, such as those that bind carbohydrates. There are also analyses which suggest that more 3D compounds have better properties as drugs[3]. One of the major issues with such compounds is they contain multiple stereo-centres which makes synthesis to improve the compounds more challenging. Some of the synthetic chemistry developed at York provides a way to achieve this. This project builds on recent work in the O'Brien laboratory (aided by cheminformatics analysis by the Hubbard group) to design and synthesise novel 3D lead-like compounds[4]. The compounds will be designed based on common features of drug molecules and some of our 3-D fragments are shown below. Principal moments of inertia (PMI) plots, which are a representation of 3-D space, will be used to evaluate the designed compounds and selection criteria will be developed to identify compounds. Selected compounds will then be synthesised.

Qualifications

The skills required are an interest and aptitude for compound synthesis; the amount of time spent outside of the synthetic laboratory (on modelling or experimental screening) will depend on the interests of the successful applicant.



Key publications

1. Doak *et al.* <http://dx.doi.org/10.1071/CH13280>, **2013**.
2. Baurin *et al.* *J Chem Inf Comput Sci*, **2004**, 44, 2157-66.
3. Lovering *et al.* *J Med Chem*, **2009**, 52, 6752-6.
4. Luthy *et al.* *Bioorg Med Chem*, **2015**, 23, 2680-94.



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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