Funded PhD project in Integrated Structural & Cell Biology in Grenoble, France

Title of the PhD project:
C1IgMsite: Molecular and structural investigations of the complement C1 complex interactions with IgMs

PhD supervisors:
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Host laboratory:
Institut de Biologie Structurale, CAID group

Project summary:
The complement system, in particular its classical pathway, is the first line of the immune response to eliminate pathogens and altered-self. It is triggered by the binding of the C1 complex to the antigen-bound Immunoglobulins type-M (IgM). Its molecular activation mechanisms have so far challenged detailed characterizations, because of the very complex nature of the molecules and of their interactions. A renewed interest appeared recently and efforts are made thanks to new major discoveries and technical improvements in protein engineering, biophysics and structural biology.
The general project proposes to revisit fundamental and long-lasting questions on the very intricated and not-yet fully elucidated mechanism of the IgM/C1 system. We gather a consortium of three European teams located in Grenoble (IBS, France – the coordinator), in Wien (BOKU, Austria) and in Leiden (LUMC, Netherlands) to exploit the new developments in recombinant IgM and C1 production, in protein/protein interaction biochemistry, biophysics and in high-resolution electron microscopy.
The C1IgMsite PhD project will be focused on:
- developing and optimizing protein engineering protocols to produce recombinant forms of the C1 complex components: C1q and C1r2s2,
- developing C1q mutant libraries,
- performing functional mapping of C1q binding sites to IgM using ELISA, Surface Plasmon Resonance and/or BioLayer Interferometry,
- solving high resolution structures of antigen/IgM/C1 complex by single-particle cryo-electron microscopy and cryo-electron tomography.

Required skills:
Master degree in biochemisty, protein engineering, structural biology, biophysics or immunology

Student role:
The PhD student will be involved in all the experimental processes described above, from protein engineering design and sample production (molecular biology, cellular biology biochemistry, protein expression, sample purification by chromatography and sample quality controls), to experimental design and sample preparations for the applied biophysics methods (SPR, BLI and others) and electron microscopy, as well as data processing, structural resolution and presentation of the results. The student will be involved in writing manuscripts for publication in peer-reviewed journals.

Keywords:
Structural biochemistry, electron microscopy, complement, immunoglobulins, structure-function

Relevant publications of the team:

- Thielens, N. et al. Mol. Immunol. 89, 73–83 (2017). doi: 10.1016/j.molimm.2017.05.025
- Cedzyński, M. et al. Front. Immunol. 10, (2019). doi: 10.3389/fimmu.2019.01869
- Bally, I. et al. Proc. Natl. Acad. Sci. U. S. A. 110, 8650–8655 (2013). doi: 10.1073/pnas.1304894110
- Bally, I. et al. Front. Immunol. 10, (2019). doi: 10.3389/fimmu.2019.00461
- Hennicke, J. et al. Plos One 15, e0229992 (2020). doi: 10.1371/journal.pone.0229992