Grenoble Alliance for Integrated Structural & Cell Biology

GRAL MASTER 2 RESEARCH SCHOLARSHIP - Program 2017 - 2018

INTERNSHIP PROPOSAL

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Research project title: Towards engineering C1q functional facets using site-directed mutagenesis

5 Keywords to describe the project: defence collagen, recombinant C1q, ligand recognition, receptor binding, site-directed mutagenesis

Description of the project (aims, experimental techniques, recommended background):
The defence collagen C1q is a soluble oligomeric protein able to sense both microbial and altered-self danger signals and to trigger immune effector mechanisms, including opsonization of the target for phagocytosis enhancement and induction of an appropriate adaptive response. During the past years C1q appeared as a key protein involved at several steps of apoptotic cells clearance (efferocytosis), which likely accounts for its crucial role in maintenance of tissue homeostasis and protection against autoimmunity.
We have recently successfully produced C1q, a complex molecule assembled from 18 polypeptide chains encoded by 3 genes, in a recombinant functional form. The aim of the internship will be to map by site directed mutagenesis C1q residues involved in the recognition of phagocyte receptors and targets (such as bacterial and viral proteins), as well as to produce truncated fragments suitable for future structural studies of C1q-complexes.
The project mainly involves molecular biology, expression and purification of recombinant proteins in mammalian cells, and analysis of protein-protein and/or protein-cell interactions (SPR, FACS). The applicant should have a background and interest in molecular biology, protein biochemistry and structural biology.

Relevant publications of the team:

1. Moreau C., Bally I., Chouquet A., Bottazzi B., Ghebrehiwet B., Gaboriaud C. and Thielens N. (2016) Structural and functional characterization of a single-chain form of the recognition domain of complement protein C1q. *Frontiers Immunol* 7, 79.
2. Bally I., Ancelet S., Moriscot C., Gonnet F., Mantovani A., Daniel R., Schoehn G., Arlaud G.J. and Thielens N.M. (2013) Expression of recombinant human C1q allows identification of the C1r/C1s binding sites. *Proc. Nat. Acad. Sci. USA* 110, 8650-8655.
3. Terrasse R., Tacnet-Delorme P., Moriscot C., Pérard J., Schoehn G., Vernet T., Thielens N.M., Di Guilmi A.M. and Frachet P. (2012). Human and pneumococcal cell surface GAPDH proteins are both ligands of human C1q. *J. Biol. Chem.* 287, 42620-42633.