

**M1-Molecular and Cellular Biology (MCB)
Internship Proposal Form
Chemistry-Biology Department**

(Deadline Wednesday 20th October 2016)

Laboratory Address and Affiliation

Institut de Biologie Structurale,
IRPAS group (Immune response to pathogens and altered self)
UMR 5075 CNRS-CEA-Université Joseph Fourier
CAMPUS EPN, 71, avenue des Martyrs, Grenoble

Laboratory/Team Research area (Keyword)

Innate immune proteins/ complement proteases/ host-pathogen interaction

Summary of the Proposed Internship Project (10 lines)

Title: Structural and functional impacts of patient mutations found in C1r/s proteases

DESCRIPTION:

Rare mutations in the C1r and C1s proteases have been recently identified in patients. Whereas these two highly controlled proteases are known as innate immune triggers, these mutations are unexpectedly associated to periodontitis, leading for example to premature loss of teeth. These dominant heterozygote missense or in-frame insertion/deletion mutations thus likely correspond to a gain of a new function for these proteases. To better understand the molecular mechanisms involved in these new pathophysiological conditions, we need to investigate how the mutations impact the structural integrity of the proteins and their function.

One interesting aim will be to test *in vitro* new potential targets of these proteases. Another one will be to reproduce *in vitro* some natural mutations and check their impact on structural integrity, as compared to the wild type. Finally, we will consider any opportunity to observe consequences of the mutations at the cellular level. This work is performed in collaboration with an Austrian medical research team and will be supported by an international ANR research grant.

Methodologies and/or Techniques to be used

Biochemistry, eukaryotic recombinant protein production, site-directed mutagenesis, X-ray crystallography, small angle X-ray scattering, thermal shift assay, microscopy

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Additional information

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