Internship project Master 2
Year 2017-2018

Laboratory/Institute: Institut de Biologie Structurale **Director:** Winfried Weissenhorn
Team: EBEV **Head of the team:** Winfried Weissenhorn

Name and status of the scientist in charge of the project: Pauline Macheboeuf **HDR: yes** ☐ **no** X
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Program the Master's degree in Biology:

☐ Neurosciences and Neurobiology ☐ Immunology, Microbiology, Infectious Diseases

X Integrative Structural Biology ☐ Physiology, Epigenetics, Development, Differentiation

Title of the project: Analyse structurale du facteur de restriction viral Viperin

Objectives (up to 3 lines):

The objective of the project is to solve the high resolution structure of the viral restriction factor viper and to study its interaction with the Trifunctional Protéin (TFP) to understand its implication in cytomegalovirus infection.

Abstract (up to 10 lines):

The viral infections lead to the activation of the innate immune system and to the liberation of interferons that stimulate the activation of interferon-stimulated genes namely restriction factors. Viperin is one of these restriction factors that has been proven to restrict several enveloped viruses like influenza virus, hepatitis C virus or HIV-1. Nevertheless, a few studies have revealed that the cytomegalovirus can hijack viperin in order to facilitate its release of the infected cells. Indeed, the cytomegalovirus protein vMIA forces viperin to interact with the Trifunctional Protein (TFP) and inhibit it in order to disrupt the actin cytoskeleton and allow the virus to escape more easily from the infected cells and increase its infection capability.
In order to understand the cytomegalovirus infection mechanism, we propose to solve the high resolution structure of the complex between viperin and TFP and to study this interaction *in vitro* and *in vivo* to get more informations on potential inhibitors against cytomegalovirus infection.

Methods (up to 3 lines):

Expression and purification of viperin and TFP proteins. Biochemical and biophysical characterizations of the complexes. Crystallogenesis. Crystals X-ray diffraction. Structure solving and structure analysis.

Up to 3 relevant publications of the team:

D. Lutje-Hulsik *et al.,* **P. Macheboeuf** *et al.,* **W. Weissenhorn** & L. Rutten (2013). A gp41 MPER-specific llama VHH requires a hydrophobic CDR3 for neutralization but not for antigen recognition. **PLoS Pathogens**, 9 (3) e1003202

A. Hinz *et al.,* **W. Weissenhorn** (2010). Structural basis of HIV-1 tethering to membranes by the Bst2/tetherin ectodomain. **Cell Host & Microbes** 7, 314-232.

P. Macheboeuf *et al.*(2010). Strptococcal M1 protein constructs a pathological host fibrinogen network. **Nature** 472 (7341) 64-8.

Requested domains of expertise (up to 5 keywords):

Molecular biology, Biochemistry, biophysical methods, structural biology, Interest in virology.