

Master Structural & Functional Biochemistry

INTERNSHIP PROJECT 2021-2022

Membrane-lipid therapy: Identification and characterization of new anti-HIV compounds

Contact: fabrice.dumas@univ-tlse3.fr

Supervisor: Fabrice Dumas (fabrice.dumas@univ-tlse3.fr) project in collaboration with Bernard Lagane (Infinity, Purpan)

Institute: Institut de Pharmacologie et de Biologie Structurale (IPBS) –CNRS UMR5089

Team: “Phagocyte Architecture and Dynamics (Drs. Verollet and Poincloux).

The Human Immunodeficiency Virus (HIV) is the etiological agent of Acquired Immunodeficiency Syndrome (AIDS). To date, it is estimated that approximately 35 million people are infected with HIV worldwide and more than 2 million additional people are infected each year. Since the beginning of the epidemic, approximately 78 million people have been infected with HIV and 39 million people have died of AIDS-related illnesses (UNAIDS Statistics 2013). Despite a very significant improvement in the life span of infected people, the antiretroviral treatments currently used still do not allow the complete elimination of the virus from the body. Indeed, the virus is able to evolve rapidly and becomes resistant to most current antiretroviral therapies.

MLT (Membrane Lipid Therapy) uses membrane perturbators in the treatment of certain diseases. Most of these molecules are derivatives of natural fatty acids that can modify the structure and organization of cell membranes and alter cell-signaling pathways (1). In our laboratory, we have 16 molecules that we will test for their potential anti-HIV efficacy. Preliminary results on 5 of these molecules have allowed us to identify 2 molecules capable of blocking the infection of T-cells in a very efficient way.

The objective of the internship is to:

- test the anti-HIV efficacy of the 11 as yet unstudied compounds (cytotoxicity, infection, dose effect, kinetics)
- validate the results obtained on T-cells and extend the study to macrophage and cell-to-cell transfer mechanisms
- decipher the mechanism of action of molecules with good efficacy and which are drug candidates

In light of our new findings, we speculate that these molecules could also prove effective against other enveloped viruses like SARS-CoV-2 and we will seek to provide proof-of-principle for the use of new therapeutics against SARS-CoV-2 entry.

Techniques used during the internship: cell culture, flow cytometry, viral infection tests, immunofluorescence staining, microscopy.

- (1) Escribá P. V., et al. Membrane lipid therapy: Modulation of the cell membrane composition and structure as a molecular base for drug discovery and new disease treatment. *Progress in Lipid Research* 59 (2015), pp. 38–53.