

Tryptophan metabolism in immuno-oncology of liver cancer



NICOLAS BAUDIN
INTERNSHIPS IN FRANCE INITIATIVE

Name of the hosting institution in France	University of Bordeaux
Name of the host laboratory / research team	INSERM U1035 (Biotherapies of Genetic, Inflammatory diseases and Cancer), miRCaDe team.
Address	146 rue Léo Saignat, 33076 Bordeaux cedex, France
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Name of the supervisor	Aksam Merched
Function	Professor and team leader
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Internship offer

Topic of the internship (title) Tryptophan metabolism in immuno-oncology of liver cancer

Proposed dates of the internship* **Start** 2020-12-14 **End** 2021-06-11

* The supervisors have indicated the dates proposed are flexible and are able to be postponed subject to COVID-19 border closures.

Scientific and academic objectives of the internship (detailed description of the internship content, work expected from the intern and expected outcomes):

Context Tryptophan (Trp) is an essential amino acid, critical not only for protein synthesis, but also for the generation of several bioactive compounds, such as the kynurenines and serotonin. Trp is mainly metabolized along the kynurenine pathway to yield nicotinamide and NAD⁺. The rate-limiting step in this pathway is catalyzed by tryptophan dioxygenase (TDO) in the liver cells or indoleamine dioxygenase (IDO) in the immune cells. Due to the close relationship between kynurenin metabolism and inflammatory responses, kynurenins emerge as important actors in cancer processes and analogues of Trp metabolites are being tested in clinical trials for the treatment of cancer. Goals The aim of this project is to study the involvement of the Trp pathway in liver cancer by:

-assessing the effect of Trp metabolites on the proliferation of liver cancer cell lines and on macrophage polarization.
-studying the consequences of modulating the expression of IDO and TDO on oncogenesis and immunosuppression The overall goal of this project is to bring novel therapeutic approaches acting in both metabolism and immunosuppression of cancer cells, which will minimize resistance to ongoing immunotherapeutic approaches and reduce the toxic side effects commonly encountered with chemotherapy. Methods Functional assays include cell proliferation, apoptosis, cytotoxicity (MTS, ApoTox, etc.). Modulation of gene expression will be performed by CRISPR/Cas9 and lentiviral transduction. Coculture system will be utilized to induce macrophage polarization, which will be characterized by FACS, qPCR and functional immune assays. The candidate will receive extensive training in cell culture, and all the above-mentioned functional assays and molecular biology tools, in a physiological context dealing with immunology, metabolism and oncology. She/he will enjoy interacting with different members of our international team.

Expected profile of applicant

Level of study	Master, Postgraduate
Discipline	Cell and molecular biology, biochemistry, immunology, genetics
Required qualities, knowledge and skills	Motivated, very well organized, good level of knowledge in biochemistry, immunology, and molecular biology