PhD project No. 6, Dr. Flacher

Scientific Area	Hematopoiesis and immune cell differentiation
Two project titles	A) Immune defense of the human olfactory mucosa against viral infections B) Autophagy for nonpeptidic antigen presentation by skin DCs
Host country	France
Supervisor, institution	Dr. Vincent Flacher, University of Strasbourg, France
Co-Supervisor, institution	A) Prof. Hartmut Hengel, University of Freiburg, Germany B) Prof. Gennaro de Libero, University of Basel, Switzerland
Mentor, institution	A) Dr. Julien Maruotti, Phenocell, Grasse, France B) Dr. Frédéric Gros, INSERM UMR - S1109, Strasbourg, France
Secondment institution	A) University of Freiburg, Germany B) University of Basel, Switzerland

Short description of the supervisor's lab with introduction to the topic

My team is interested in the regulation of the immune system by their organ-specific microenvironment. We focus on the function of DCs and macrophages of peripheral tissues, i.e. the skin, in human and mouse models. My current projects include 3D models of neuro-immune crosstalk and the metabolic regulation of DC/Mph maintenance.

Topic description, including techniques to be used

Project A) The nasal mucosa, including the olfactory epithelium, represents a primary infection site for respiratory viruses. Damages to olfactory neurons, caused by the virus or the antiviral response, may lead to anosmia. Olfactory neurons could also represent a portal for viral invasion of the central nervous system. However, there is only limited knowledge on the immune network protecting them from viral infections. Immune cells, neurons and neuronal stem cells will be isolated from human nasal mucosa, aiming at the construction of 2D and 3D models of viral infections, i.e. by SARS-CoV2.
Techniques: Primary human cell isolation, immunohistochemistry (including tissue clearing, confocal and light-sheet microscopy), RT-qPCR, flow cytometry and cell sorting, stem cell culture and differentiation, 3D tissue reconstruction, viral infections

Project B) We recently found that, in the absence of autophagy, skin DCs undergo a dramatic shift in their metabolic pathways, due to impaired lipid catabolism. Non-polymorphic MHC class I-related molecule MR1 presents nonpeptidic metabolites as self-antigens to MR1-restricted T (MR1T) cells. Autophagy is involved in the presentation of classical MHC-I and MHC-II antigens, yet little is known about its role in the production of nonpeptidic antigens by DCs. We will study the metabolome of autophagy-deficient DCs and the generation, maintenance and antigen repertoire of MR1T cells.
Techniques: Mouse models, primary cell isolation and culture, immunohistochemistry, flow cytometry and cell sorting, RT-qPCR, metabolomics

Recommended applicant's training (technical expertise and knowledge)

Techniques: Cell culture, flow cytometry, immunofluorescence microscopy, RT-qPCR
Knowledge: Cutaneous/mucosal immunology, CRE/lox mouse models, neurobiology, virology

Maximum two relevant publications

Muller Q, […] Flacher V, Berthod F., 2018, Acta Biomater: Development of an innervated tissue-engineered skin with human sensory neurons and Schwann cells differentiated from iPS cells.
Voisin B, […] Flacher V, Mueller CG , 2019, BioRxiv: The hair cycle underlies regulation of Langerhans cell renewal.

The EURIdoc programme has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement number 101034170.

Ethics description

1. Humans	
This research involves human participants.	YES ☐ / NO ☒
This research involves physical interventions on the study participants.	YES ☐ / NO ☒
2. Human Cells /Tissues	
This research involves human cells or tissues, such as blood.	YES ☒ / NO ☐
3. Personal Data	
This research involves personal data collection and/or processing.	YES ☐ / NO ☒
This research involves further processing of previously collected personal data (secondary use).	YES ☐ / NO ☒
4. Animals	
This research involves animals, such as mice.	YES ☒ / NO ☐

The EURIdoc programme has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement number 101034170.