PhD project No. 4, Prof. Mueller

Scientific Areas	Haematopoiesis and immune cell differentiation
Project title	A) B cell differentiation by stroma and macrophages in autoimmunity B) B cell survival and transformation by stroma in lymphoma
Host country	France
Supervisor, institution	Christopher G. Mueller, University of Strasbourg, France
Co-Supervisor, institution	Reinhard Voll, Medical Center - University of Freiburg, Germany
Mentor, institution	Transgène, Illkirch-Graffenstaden, France
Secondment institutions	Medical Center - University of Freiburg, Germany; University of Basel, Switzerland (Dr. Marta Trüb)

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

The general topic of the lab is the immune microenvironment with applications to infectious diseases, immunopathology and cancer. We have recently discovered a novel crosstalk between lymph node mesenchymal cells and lymphatic endothelial cells regulating the niche for sinusoidal macrophages. We would now explore the stroma – immune crosstalk in human diseases.

Topic description, including techniques to be used

Project A): B cell differentiation by stroma and macrophages in autoimmunity

Mesenchymal stromal cells regulate immunity by providing recruitment and differentiation cues to immune cells in lymphoid organs, autoimmune tissues and tumors. We will test the premise that the continuous crosstalk between mesenchymal and immune cells has a long-term impact on mesenchymal stroma function. Different types of resting or activated B cells will be co-cultured with mesenchymal cells in the presence and absence of macrophages and the resulting stroma cell imprinting will be characterized on a molecular and functional level. The in vivo equivalent will be assessed by comparing the molecular profiles with that of normal and pathological stroma from lymphoid organs and tissue from autoimmune patients. This opens the avenue to a novel approach of B cell-mediated immunopathology by targeting stromal cells.

Techniques: Human cell isolation and culture, flow cytometry, bioinformatics, multiplexed immunofluorescence

Project B): B cell survival and transformation by stroma in lymphoma

While the lymphoid stroma - immune cell crosstalk in the secondary lymphoid organs is increasingly understood in the context of development, homeostasis and infection, the role that stroma plays for lymphoma development remains so-far unclear. By culturing mesenchymal stromal subsets with normal or lymphoma B cells from human biopsies, the consequences on B cell activation, differentiation and malignant transformation will be assessed. Key candidate gene products involved in a supportive crosstalk will be identified by molecular profiling and functionally tested in inhibition studies. This would lead to novel therapeutic developments against B cell lymphomas.

Techniques: Human cell isolation and culture, flow cytometry, bioinformatics, gene silencing and/or gene deletion by CRISPR/Cas9.

Recommended applicant's training (technical expertise and knowledge)

Techniques: Flow cytometry (+FlowJo software), bioinformatics, primary cell cultures
Knowledge: Good background in immunology, a plus: B cell biology, autoimmunity or lymphoma

Maximum two relevant publications

Camara et al., 2019, Immunity 50: Lymph Node Mesenchymal and Endothelial Stromal Cells Cooperate via the RANK-RANKL Cytokine Axis to Shape the Sinusoidal Macrophage Niche.

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 involve 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 involve animals, such as mice.	YES ☐ / NO ☒

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