

PhD project No. 3, Prof. Voll

Scientific Areas	Hematopoiesis and immune cell differentiation
Project title	A) Stroma – plasma cell interaction as driver of autoimmune disease B) Mesenchymal cell specialization and B lymphocyte differentiation
Host country	Germany
Supervisor, institution	Reinhard E. Voll, Medical Center - University of Freiburg, Germany
Co-Supervisor, institution	Christopher G. Mueller, University of Strasbourg, France
Mentor, institution	To be determined later, possibly Lionex, Braunschweig, Germany
Secondment institution	University of Strasbourg, France; University of Basel, Switzerland (Dr. Marta Trüb)
Short description of the supervisor's lab with introduction to the topic	
<p>We are investigating the pathogenesis of autoimmune diseases, systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), in humans as well as mouse models in order to identify new targets for treatment. One focus is the role of plasma cells as drivers of pathogenesis due to the production of pathogenic antibodies. The crosstalk of mesenchymal cells and lymphocytes, namely plasma cells residing in inflamed organs is poorly understood, but may be critical for pathogenesis.</p>	
Topic description, including techniques to be used	
<p>Project A) Stroma – plasma cell interaction as driver of autoimmune disease Stroma may be a hitherto underexplored cause for prevailing and treatment-refractory autoimmune diseases. Using mouse models of autoimmunity as well as human cells from biopsies, we will address a novel concept of lymphoid stroma – immune cell crosstalk. The recruitment, activation, and differentiation of B cells into plasma cells will be studied in secondary lymphoid organs and tertiary lymphoid structures found in inflamed kidneys of NZBxNZW F1 mice as well as in cell cultures. The stromal cell and immune cell compartment will be studied by multi-parameter flow cytometry as well as single cell RNA-sequencing <i>ex vivo</i> and <i>in vitro</i>. <u>Techniques:</u> Human and mouse cell isolation and cell culture, mouse experimentation, multicolor spectral flow cytometry, bioinformatics, multiplexed immunofluorescence.</p> <p>Project B) Mesenchymal cell specialization and B lymphocyte differentiation Macrophages, mesenchymal and endothelial stromal cells can form a functional unit that may play an important role for differentiation and survival of B cells. We will study the role of these accessory cells for B cell differentiation and survival in the bone marrow and in secondary and tertiary lymphoid tissue using wild-type and autoimmune mouse models. Human cell co-culture systems will be established using cells from human bone-marrow biopsies. The capacity of the multi-partner cell cultures to accelerate B cell differentiation into plasma cells and to maintain plasma cell survival will be assessed <i>in vivo</i> and <i>in vitro</i>. By using single cell RNA sequencing and modulation of gene expression the molecular players involved in the crosstalk will be defined. <u>Techniques:</u> Human cell isolation and culture, mouse experimentation, multicolor spectral flow cytometry, bioinformatics, multiplexed immunofluorescence, single cell RNA sequencing.</p>	
Recommended applicant's training (technical expertise and knowledge)	
<p>Techniques: flow cytometry, primary cell cultures, mouse experimentation Knowledge: Immunology, B cell and/or mesenchymal cell biology and autoimmunity</p>	
Maximum two relevant publications	
<p>Sehnert B, Mietz J, Rzepka R, Buchholz S, Voll RE, 2021, Int J Mol Sci.: Neuraminidase inhibitor zanamivir ameliorates collagen-induced arthritis. Neubert K, Meister S, Moser K, Weisel F, Voll RE, 2008, Nat Med.: The proteasome inhibitor bortezomib depletes plasma cells and protects mice with lupus-like disease from nephritis.</p>	

Ethics description

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