PhD project No. 26, Prof. Breitling

Scientific Area	Immune-related diseases
Two project titles	Determining binding epitopes for autoantibodies in A) lupus or B) in Sjögren's syndrome
Host country	Germany
Supervisor, institution	Prof. Frank Breitling, Karlsruhe Institute of Technology, Germany
Co-Supervisor, institution	A) and B) Prof. Reinhard Voll, Medical Center - University of Freiburg, Germany
Mentor, institution	A) and B) Dr. Volker Stadler, PEPperPRINT GmbH, Heidelberg
Secondment institution	A) and B) Karlsruhe Institute of Technology, Germany and Medical Center - University of Freiburg, Germany

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

The Breitling lab builds machines and develops techniques to synthesize very high-density peptide arrays that are commercialized by PEPperPRINT. Our nano3D printer (Löffler et al., Nat. Comm) allows us to synthesize >40.000 peptides per glass slide in array format and with added posttranslational modifications. We have shown that these arrays allow us to identify antibody specificities patrolling in a patient's blood, and, in addition, for each of these antibody specificities the exact peptide sequence they bind to. These sequences are used to query databases, e.g. to ask the question if a virus-specific antibody may also binds to a human protein. Such a – hypothetical – regulatory antibody might have the task to protect important human proteins from our immune system, and a virus or tumour cell might exploit that trait. We want to find out if such antibodies exist and characterize them.

Topic description, including techniques to be used

Proteins are modified when they encounter an enzyme, e.g. a kinase. We think that such posttranslational modified proteins are used to inform the organism about important events, e.g. massive cell destruction, where hitherto confined enzymes are released to suddenly modify protein targets they normally wouldn't meet. In *rheumatoid arthritis* (RA) such modified proteins are targeted by autoantibodies that report these modifications to the immune system. Although some targeted proteins are known, modified autoantigens and exact epitopes may be partially unknown in autoimmune diseases; likely due to autoantibodies targeting posttranslationally modified peptides.

Techniques: Our peptide arrays allow us for the first time to synthesize tens of thousands posttranslationally modified peptides in an affordable way to find out if they are targeted by autoantibodies. Literature will help us to identify known antigenic proteins for a given disease, and, eventually known posttranslational modifications. These proteins are then synthesized in the array format as overlapping peptides. Alternatively, very large numbers of random peptides will help us to find out if autoantibodies give more signals with a given modification #1 compared to modification #2.

Project A) Using sera from patients with systemic lupus erythematosus

Project B) Using sera from patients with Sjörgen's syndrome

Recommended applicant's training (technical expertise and knowledge)

Techniques & Knowledge: interest / education in either bioengineering, chemical biology or biochemistry, immunology, auto immune diseases, in order to do chemical synthesis, run an experimental robot from a customer's perspective, and do database queries

Relevant publications

Löffler et al., 2016, Nat. Comm.: nano3D printer:
Mattes et al., 2019, Adv. Mat.: Review solid material based synthesis

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.