PhD project No. 11, Prof. Lillemeier

Scientific Area	Innate and Adaptive Immunity
Two project titles	A) Single molecule microscopy analyses of signaling mechanisms in T cells B) Modulating T cell signaling for improved anti-tumor responses
Host country	Germany
Supervisor, institution	Prof. Dr. Björn Lillemeier, University of Freiburg, Germany
Co-Supervisor, institution	PD Dr. Susana Minguet, University of Freiburg Germany
Mentor, institution	Prof. Dr. Carolyn King, University of Basel, Switzerland
Secondment institution	Universities of Basel, Strasbourg or Vienna

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

During infections, autoimmunity and cancer T cell activity and functions are controlled by an interplay of activating (i.e. T cell receptor; TCR) and inhibitory (i.e. Programmed Cell Death Protein; PD-1) signaling pathways. These pathways are localized at the plasma membrane and have evolved to integrate its unique architecture into their molecular mechanisms. We investigate the spatial and temporal principles of these mechanisms using multidisciplinary approaches. Our ultimate goal is to modulate T cell signaling to identify potential drug targets for future immunotherapies.

Topic description, including techniques to be used

Project A)

We aim to reveal molecular mechanisms that control the dynamics and distribution of T cell signalling molecules at the plasma membrane. Our research plan is to (1) visualize signaling molecules of the TCR and PD-1 pathways at nanometer-resolution, (2) identify protein interactions, post-translational modifications and conformational changes that control their behavior, and (3) perturb their functions using mutant analyses.

Techniques: single molecule microscopy, molecular and cellular biology, biochemistry and biophysics

Project B)

We and others have identified several mutations in Zap70 kinase, a critical TCR signaling molecule, that alter T cell activation (i.e. signalling thresholds and strength). We will test these mutants in mouse models to determine their effects on anti-tumor responses. Our goal is to identify signaling mechanisms that can be targeted with small molecule inhibitors in future immunotherapies.

Techniques: CRISPR/Cas9, primary T cell culture and analyses, animal models for cancer, FACS, molecular biology

Recommended applicant's training (technical expertise and knowledge)

Techniques: Cell culture, molecular biology, biochemistry
Knowledge: T cell biology, signal transduction

Maximum two relevant publications

Katz et al., 2017, Nature Immunology: A cycle of kinase activation and release at the T-cell receptor amplifies and disperses antigenic stimuli.

Y.S. Hu et al., 2016, PNAS: Superresolution imaging reveals nanometer- and micrometer-scale spatial distributions of T-cell receptors in lymph nodes.

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 ☐

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