PhD project No. 23, Prof. Jeker

Scientific Area	Immune-related diseases
Two project titles	A) Understanding microRNA biology to improve T cell therapy B) Exploiting microRNAs for CAR T design
Host country	Switzerland
Supervisor, institution	Prof. Lukas Jeker, University of Basel, Switzerland
Co-Supervisor, institution	A) Prof. T. Cathomen, University of Freiburg, Germany B) Prof. T. Cathomen, University of Freiburg, Germany
Mentor, institution	A) and B) to be determined later
Secondment institution	A) and B) University of Basel, Switzerland and University of Freiburg, Germany

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

The Jekerlab has studied microRNAs in cell types that affect immune regulation. Our current focus is on microRNAs that regulate T cell differentiation and function. We have demonstrated that the miR-17-92 cluster is important for multiple T cell types. More recently we have shown that miR-17-92 is a key regulator of CD4+ T cell activation. We have identified genes that are directly and indirectly regulated by the miR-17-92 cluster. We aim to deepen our mechanistic understanding and leverage this knowledge to improve T cell therapies. This goes in line with our research program on genome engineered cellular therapies.

Topic description, including techniques to be used

Project A)

We plan to characterize the function of the identified miR-17-92 target genes. To this end we use genome engineering in murine T cells and we generate mouse models with new genetic modifications. We will study how alteration (deletion/modification) of miR-17-92 target genes affects T cell biology. We will study the genome engineered T cells in vitro and in mouse models in vivo.

Techniques: Molecular biology, CRISPR/Cas9, gene targeting, mouse models, flow cytometry, transcriptome analysis, cell culture

Project B)

We plan to use genome engineering of microRNA target genes to improve T cell therapies including chimeric antigen receptor (CAR) T cells. In addition, we plan to exploit microRNAs for T cell therapies. We will generate mouse models and will validate our findings in human T cells.

Techniques: Molecular biology, CRISPR/Cas9, gene targeting, mouse models, flow cytometry, transcriptome analysis, cell culture, mouse and primary human T cells

Recommended applicant's training (technical expertise and knowledge)

Techniques: molecular biology, cell culture, flow cytometry

Knowledge: cell biology, T cell biology, gene regulation including posttranscriptional gene regulation

Maximum two relevant publications

Kornete et al., 2018, Journal of Immunology: Highly Efficient and Versatile Plasmid-based Gene Editing in Primary T Cells

Doelz et al., 2020, bioRxiv.org : The non-coding RNA miR-17-92 is a central mediator of T cell activation

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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