PhD project No. 20, Prof. Schamel

Scientific Area	Immune-related diseases
Two project titles	A) Modified TCRs on human T cells targeting tumor cells B) Chimeric antigen receptors to fight against SARS-CoV-2
Host country	Germany
Supervisor, institution	Prof. Wolfgang Schamel, University of Freiburg, Germany
Co-Supervisor, institution	A) Prof. Gennaro De Libero, University of Basel, Switzerland B) Prof. Daniel Pinschewer, University of Basel, Switzerland
Mentor, institution	A) and B) Dr. Ursula Schulz, CellGenix, Freiburg Germany
Secondment institution	A) and B) University of Basel, Switzerland and Medical Center - University of Freiburg, Germany

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

The Schamel lab is focussed in understanding how the T cell receptor (TCR) works. We have discovered that it undergoes a conformational change when bound to its ligand. Recently, the lab has used the insight into TCR function to engineer novel TCRs and chimeric antigen receptors (CARs) to combat tumours (see publications below). In pre-clinical mouse models and in clinical trials (done by others), the new receptors have shown to be superior to the FDA-approved CARs.

Topic description, including techniques to be used

Project A)

We plan to engineer new TCRs by fusing a single-chain Fv fragment of an anti-tumour antigen antibody to the TCR. This will be expressed on primary human T cells, to reprogramme them to recognize and kill tumour cells. The focus will be to introduce an off-switch into the construct, in order to be able to shut off the T cell response, in case that the side-effects of T cell activation get too strong. This will be done in cell culture and in pre-clinical mouse models.

Techniques: DNA cloning, lentiviral transduction of primary human T cells, flow cytometry, protein biochemistry, killing assay, ELISA, mouse models

Project B)

We plan to engineer new CARs by using a single-chain Fv fragment of an anti-SARS-CoV-2 antibody. This will be expressed on primary human T cells, in order to reprogramme them to recognize virus infected cells. The focus will be to induce a strong and anti-viral immune response of the T cells, to limit viral replication and viral spread. This will be done in cell culture and in pre-clinical mouse models.

Techniques: DNA cloning, lentiviral transduction of primary human T cells, flow cytometry, viral infection and titration, killing assay, ELISA, mouse models

Recommended applicant's training (technical expertise and knowledge)

Techniques: cell culture, DNA cloning, flow cytometry, SDS-PAGE, Western blotting
Knowledge: Tumour immunology, virology, cell biology, signaling

Maximum two relevant publications

Hartl et al., 2020, Nature Immunology: Noncanonical binding of Lck to CD3e promotes TCR signaling and CAR function.

Baeuerle et al., 2019, Nature Communications: Synthetic TRuC receptors engaging the complete T cell receptor for potent anti-tumor response.

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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