PhD project No. 18, Prof. De Libero

Scientific Area	Innate and adaptive immunity
Two project titles	A) The physiology of MR1T cells and their role in autoimmune diseases B) MR1T cells in cell therapy of tumors
Host country	Switzerland
Supervisor, institution	Prof. Gennaro De Libero, University of Basel, Switzerland
Co-Supervisor, institution	A and B) Prof. Wolfgang Schamel, University of Freiburg, Germany
Mentor, institution	A) and B) Dr. José Carballido, Novartis, Basel, Switzerland
Secondment institution	A and B) University of Freiburg, Germany

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

The De Libero lab investigates T cells that recognize non-peptidic self-antigens presented by the MR1 antigen-presenting molecule. We have discovered and called this novel T cell population MR1T cells and are studying their role in human diseases. We also found that they recognize metabolites that preferentially accumulate in tumor cells, thereby we also exploit the potential use of MR1T cells in the therapy of solid tumors.

Topic description, including techniques to be used

Project A)

We plan to isolate MR1T cells from patients with autoimmune and allergic diseases, characterize their phenotypes, functions, TCR repertoire, antigen specificities, and expansion. These studies will be performed using peripheral blood of patients, which will be used to establish MR1T cell clones. The most relevant clones will be then further investigated. We also will use MR1 tetramers loaded with appropriate antigens to examine MR1T cells *ex vivo*, to sort them and perform transcriptomics and TCR gene sequence determination as single cells.

Techniques: multidimensional flow cytometry, cell culture, DNA cloning, bioinformatic analysis.

Project B)

We plan to establish MR1T cell clones specific for solid tumors, test their capacity to cross-react with different tumors and identify tumor-specific antigens presented by MR1. The TCR genes of selected MR1T cell clones will be transferred in recipient killer cell. Engineering TCR genes will be made to increase the efficacy of T cell response and tumor cell killing. T cells expressing engineered MR1T TCRs will be used in mouse models of human tumors.

Techniques: cell culture, DNA cloning, lentiviral transduction of primary human T cells, killing assay, ELISA, mouse models.

Recommended applicant's training (technical expertise and knowledge)

Techniques: cell culture, DNA cloning, flow cytometry, mouse handling
Knowledge: T cell immunology, cell biology, tumour immunology

One or two relevant publication(s)

M. Lepore et al., 2017, Elife 6, Functionally diverse human T cells recognize non-microbial antigens presented by MR1.
A. Vacchini et al., 2020, Frontiers in Immunology: MR1-Restricted T Cells Are Unprecedented Cancer Fighters.

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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