PhD project No. 27, Prof. Thimme

Scientific Area	Immune-related diseases
Two project titles	A) Disease-specific heterogeneity of exhausted T cells B) Impact of co-infection on T cell exhaustion
Host country	Germany
Supervisor, institution	Prof. Robert Thimme and Dr. Maike Hofmann, Medical Center - University of Freiburg, Germany
Co-Supervisor, institution	A) and B) Prof. Daniel Pinschewer, University of Basel, Switzerland
Mentor, institution	A) and B) Dr. Souphalone Luangsay, Basel, Switzerland
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 Thimme/Hofmann lab is focused in understanding the failure of the T cell response in chronic viral hepatitis and liver cancer. We have contributed to the current knowledge that T cell failure in chronic viral hepatitis mediated by Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infection is due to viral escape and T cell exhaustion. By analyzing patient samples, we have discovered that exhausted virus-specific CD8+ T cells consist of heterogeneous subsets with different transcriptional, phenotypical and functional characteristics in chronic viral hepatitis. Recently, the lab has used cutting-edge single-cell RNAseq technology to show that HCV-specific CD8+ T cells retain a chronic scar after cure of HCV infection (see publications below) with implications for immunity to re-infection and consequently future treatment regimens.

Topic description, including techniques to be used

Project A)

We plan to assess differences and commonalities in exhausted CD8+ T cells detectable in healthy donors, patients chronically infected with HBV, HCV, HIV and patients suffering from liver cancer (caused by different etiologies) and melanoma on a single cell level. This approach aims at defining rheostats of CD8+ T cell exhaustion and subsequently the functional capacity of CD8+ T cells with the potential to guide future therapeutic regimens.

Techniques: flow cytometry, mass cytometry, histology, imaging mass cytometry, cell culture, RNAseq

Project B)

We plan to investigate the impact of co-infection on exhausted CD8+ T cells since this is common in patients with chronic viral infections and cancer and frequently affects disease progression. In particular, we will analyse HBV- and HCV-specific and liver cancer-associated CD8+ T cell exhaustion in the context of co-infections with HDV, HIV and CMV. Heterogeneity, functional capacities and molecular signatures will be assessed.

Techniques: flow cytometry, mass cytometry, cell culture, co-culture models, viral infection/transduction, ELISA, RNAseq

Recommended applicant's training (technical expertise and knowledge)

Techniques: flow cytometry, cell culture, PCR/RT-PCR, histology

Knowledge: translational immunology, immunity to infection, tumor immunology, virology

Maximum two relevant publications

Hensel et al., 2021, Nature Immunology: Memory-like HCV-specific CD8+ T cell retain a chronic scar after cure of HCV infection.

Alfei et al., 2019, Nature: TOX reinforces the phenotype and longevity of exhausted T cells in chronic viral infection.

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 ☒
Does your research involve further processing of previously collected personal data (secondary use).	YES ☐ / NO ☒
4. Animals	
This research involves involve animals, such as mice.	YES ☐ / NO ☒

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