A Postdoc position is available in the group of PD Dr. Friederike Berberich-Siebelt at the Institute for Pathology, Julius-Maximilians-University of Würzburg, Germany, funded by the German Cancer Aid (DKH).

T cells gain more and more attention as therapeutic T-cell products to be infused into patients, foremost cancer patients. Either they are transferred contained in allogeneic stem cell transplants (allo-HSCT) or modified with some kind of tumor-specific T-cell receptor (TCR).

Sophisticated manipulations of those T cells are based on new insights into T-cell biology as well as revolutionizing techniques like CRISPR/Cas9. We have developed protocols to gene-edit highly efficiently primary murine and human T cells – pre-stimulated, but also directly – by CRISPR/Cas9 without virus transduction. Here, we want to explore if the deletion of one NFAT family member in human CD8+ T cells and human CD8+ CAR-T cells preserves their function, while avoiding false or chronic activation.
NFAT directly transmits TCR engagement and therefore antigen recognition. This holds essentially true for chimeric antigen receptor (CAR) signaling. It leads to T-cell activation with effector functions including cytokine secretion and directed cytotoxicity. Chronic TCR stimulation, however, enforces an extreme high and unbalanced level in activated nuclear NFAT, which is prone to commence the transactivation of an aberrant expression profile.

In our mouse models for allo-HSCT, ablation of one NFAT member - or even just an NFATc1 isoform - in all co-transplanted CD3⁺ T cells protects against acute graft-versus-host disease (GvHD), but maintains the graft-versus-leukemia (GvL) effect.²³ Accordingly, a precise understanding of NFAT signal transduction in human CD8⁺ T as well as CAR-T cells could lead to measures to fine-tune T-cell responses for the benefit of cancer patients. This would give us a remedy against GvHD, cytokine release syndrome (CRS) and / or differentiation into dysfunctional "exhausted" T<sub>EX</sub> cells, while the GvL effect and specific tumor eliminations were retained.

Therefore, we are looking for a highly motivated and enthusiastic candidate with a strong background in T-cell immunology. Candidates with profound experience in CAR-T cells, in tumor or GvHD/ GvL models are especially encouraged to apply. In general, mouse-handling abilities are a pre-condition for the position.

Applications to path230@mail.uni-wuerzburg.de must contain a CV including records and publication list, a short motivation letter and the names of two references. Application is open until the position is filled.