PhD student position

Therapeutic targeting of T-follicular cells in graft-versus-host disease

1.1.2023 — 31.12.2025

A PhD position is available in the group of PD Dr. Friederike Berberich-Siebelt at the Institute for Pathology, Julius-Maximilians-University of Würzburg, Germany. The successful candidate will be part of the research consortium 'Modulation of graft-versus-host and graft-versus-leukemia immune responses after allogenic stem cell transplantation' supported by the German Research Foundation / CRC 221. Furthermore, enrollment in the Graduate School of Life Sciences (GSLS) will ensure structured doctoral research training in a highly interdisciplinary research environment.

Chronic (c) GvHD is immunologically distinct from acute (a) GvHD and its clinical presentation and symptoms are heterogeneous. Still, aGvHD predisposes for cGvHD. In cGvHD patients, isotype-switched antibodies are frequent as in various autoimmune diseases. Preclinical cGvHD models point towards disturbed germinal center (GC) formation containing GC-B cells and T-follicular helper (T_{FH}) cells, but reduced T-follicular regulatory (T_{FR}) cells.

Interestingly, T_{FH} and T_{FR} cells both express high levels of activated NFATc1 (alias NFAT2), a member of the transcription factor family NFAT.[1,2] This raises the question how the standard GvHD therapy, which includes calcineurin (NFAT) inhibitors affects these different immune cell populations and compartments. Previously, we revealed that signaling of NFAT in T cells is crucial for aGvHD.[3,4] Now we ask whether it is equally important for cGvHD. For this, T cells and / or Treg cells from NFAT-deficient mice can be transplanted in cGvHD models.

To explore the relevance of T_{FH} cells in cGvHD in general, molecular control and function can be addressed according to our previous scRNA-seq analysis of

human T_{FH} cells. Besides flow cytometric and immunohistological analyses of T_{FH} subsets from cGvHD patients, basic mechanisms can be evaluated in murine models of cGvHD by interference of CRISPR/Cas9-edited signaling pathways in T_{FH} and T_{FR} cells.[3]

Therefore, we are looking for a highly motivated and enthusiastic student with a good training in immunology as well as a solid background in molecular biology. Candidates with profound experience in pre-clinical mouse models will be considered first, whereas a minimum in mouse handling abilities is a pre-condition for the position.

Applications to path230@mail.uni-wuerzburg.de must contain a CV including records, a short motivation letter and the names of two references. Application deadline is September 15th, 2022.

1. Koenig A, Vaeth M, Xiao Y, et al. NFATc1/alphaA and Blimp-1 Support the Follicular and Effector Phenotype of Tregs. *Front Immunol*. 2021;12:791100.
2. Vaeth M, Muller G, Stauss D, et al. Follicular regulatory T cells control humoral autoimmunity via NFAT2-regulated CXCR5 expression. *J Exp Med*. 2014;211(3):545-561.
3. Majumder S, Jugovic I, Saul D, et al. Rapid and Efficient Gene Editing for Direct Transplantation of Naive Murine Cas9(+) T Cells. *Front Immunol*. 2021;12:683631.
4. Vaeth M, Bauerlein CA, Pusch T, et al. Selective NFAT targeting in T cells ameliorates GvHD while maintaining antitumor activity. *Proc Natl Acad Sci U S A*. 2015;112(4):1125-1130.