

AWARD: POSTER AWARD FOR PROJECT ON CRISPR-BASED OPTIMIZATION OF NK CELLS AGAINST MULTIPLE MYELOMA

The work of Tobias Bexte was awarded a "BEST POSTER AWARD" at this year's symposium of the Deutschen-Gesellschaft für Gentherapie e.V. (DG-GT). The IRTG/CRC fellow Tobias Bexte is medical student in his practical year and is on new NK cell therapies in the group of Prof. Dr. Ullrich (TP12) in the "Experimental Immunology" group at the Department of Pediatrics and Adolescent Medicine of the University Hospital Frankfurt.

At the annual meeting 2022 of the DG-GT in Hannover with the topic "Making Gene Therapy A Clinical Reality" Tobias Bexte presented his project of a CRISPR-Cas9 based method for gene modification of primary natural killer cells (NK cells). These genetically optimized NK cells showed improved functionality against various multiple myeloma cell lines and increased functionality against degenerate cells derived from the bone marrow of multiple myeloma patients.

NK cells are part of the body's innate immune defense against foreign and infected cells. They have a variety of activating and inhibitory receptors. These inhibitory receptors, such as the "NKG2A" receptor, can inhibit the natural killer function of NK cells after tumor contact for example in multiple myeloma. Tobias Bexte established a CRISPR-Cas9-based gene editing platform in collaboration with the research group of Prof. Toni Cathomen from the University Medical Center Freiburg for the knockout (KO) of inhibitory receptors. In the research group of Prof. Evelyn Ullrich in Frankfurt he could show a high and successfully disruption of the NKG2A inhibitory receptor in primary NK cells.

This highly specific modified NK cells showed increased functionality against various tumor cell lines. Importantly, the researcher could demonstrate an increased functionality of CRISPR-modified NKG2A KO NK cells against primary bone-marrow derived tumor cells from differently pretreated multiple myeloma patients. These analyses were performed in a close collaboration with Dr. Ivana von Metzler (Department of Hematology and Oncology, University Hospital Frankfurt). These results open new possibilities for innovative and optimized NK immune cell therapies against various cancers.

One advantage of NK cell-based immunotherapy is that they can be obtained from healthy foreign human donors. Furthermore, NK cells therapies showed already promising clinical results without side effects serious side effects like Graft-versus-Host Disease or cytokine release syndrome).

The presented protocol of CRISPR-Cas9 gene editing of primary NK cells provides a robust platform to overcome verity immune checkpoint inhibition - not only for the treatment of multiple myeloma - but also against different other tumor entities. Therefore, Bexte and the team at AG Ullrich are already working on further optimizations, including for NK cell therapies against diseases such as acute lymphoblastic leukemia.

The whole team of IRTG/CRC-1292 around spokesperson Prof. Dr. Hansjörg Schild and co-spokesperson Prof. Dr. Tobias Bopp congratulates Tobias Bexte for this achievement.



Prof. Dr. Hildegard Büning and Cand. med. Tobias Bexte at the award ceremony; annual meeting of the DG-GT 2022 in Hannover. Photo: DG-GT e.V.