In Vivo Generation of Chimeric Antigen Receptor T cells with T cell-retargeted Adeno-Associated Virus Vectors

Lead Applicant:
Prof. Dr. rer. nat. Hildegard Büning
Institute of Experimental Hematology
Hannover Medical School

Co-Lead and Project Partner:
Prof. Dr. med. Michael Hudecek
Chair in Cellular Immunotherapy, Department of Internal Medicine II
University Clinic Würzburg

CARtrAAVic aims to further revolutionize CAR-T therapy by developing an innovative in vivo approach to generate CAR-T cells directly in the patient's body. The project aims for efficient in vivo delivery of CAR genes through T cell-tropic AAV vectors, eliminating the need for complex ex vivo procedures such as cell isolation, activation and expansion of cells in a GMP facility. By administering T cell-tropic AAV vectors intravenously, CARtrAAVic is designed to stimulate T cells in situ to fight tumors and enable a more physiological response with low toxicity. CARtrAAVic also aims to address key clinical challenges of conventional CAR-T therapies such as cytokine release syndrome and duration of response. In addition, the in vivo concept of the platform is prone to reduce production costs and manufacturing time and will thereby improve the availability of CAR-T therapies. The planned innovative dual AAV vector system also increases safety by minimizing the risks of off-target integrations. The project is strategically planned to provide preclinical proof of concept and prepare for clinical development. Key milestones include optimization of the AAV vector dose, and demonstration of safety and efficacy in preclinical models. Ultimately, CARtrAAVic aims to bring a scalable, chemotherapy-free, next-generation CAR-T therapy platform with broad therapeutic potential, rapid and broad availability and a sustainable cost structure into clinical application.