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**Junior Clinician Scientist**

nTTP-GCT-Cohort 2026

Center for Child and Adolescent Medicine  
Department of Pediatrics I - Hematology,  
Oncology, Gastroenterology, Nephrology,  
Rheumatology  
UNIVERSITY HOSPITAL TUEBINGEN

**Fields of Research:**

- Translational Pediatric Oncology
- Advanced cell therapies
- CAR T cell therapy against solid tumors
- Novel CAR T cell designs

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**Translational Scientist**

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Department of Pediatrics I - Hematology,  
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Rheumatology  
UNIVERSITY HOSPITAL TUEBINGEN

**Fields of Research:**

- Genetic engineering
- Advanced cell therapies
- CAR T cell therapy
- Molecular biology
- Cellular signaling

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## Development of a novel base editing platform for tandem CAR T cell therapy against pediatric neuroblastoma

### Project Description:

Using an innovative cellular gene-therapy approach, we aim to improve CAR T cell efficacy in pediatric neuroblastoma by **combining dual antigen-targeting with a novel CAR T cell base-editing platform enhancing functional persistence by adopting intracellular T cell signaling capacities.**

We will develop an **advanced tandem CAR T cell product** targeting two neuroblastoma associated tumor antigens to overcome antigen loss or downregulation and address tumor heterogeneity. We will employ a **spatial biology approach** to comprehensively analyze clinical neuroblastoma samples and *in vivo*-derived xenograft tissues. This will provide detailed insights into target antigen expression, tumor microenvironment composition, and T cell infiltration and functionality at different disease stages and treatment time points in patients and *in vivo*.

To overcome limited CAR T cell persistence and dysfunction, we will additionally establish a GMP-ready **base editing platform to optimize T cell intrinsic signaling capacities** in the context of neuroblastoma directed tandem CAR T cell therapy. Specifically, we will translate our pre-clinical findings demonstrating that the PI3K $\delta$  E81K point mutation enhances CAR T cell persistence *in vivo*, improves metabolic fitness, and maintains functionality under reduced antigen availability (Bucher et al., *Nat. Cancer*, 2026).

For establishing the **clinical-scale manufacturing**, we will integrate our base-edited tandem CAR construct on the **CliniMACS prodigy platform**, leveraging established GMP-compliant CAR T-cell production workflows. This will yield an adaptable and flexible GMP platform capable of incorporating innovative genetic modifications, including beneficial single point mutations such as PI3K $\delta$  E81K, into next-generation CAR T cell products.

