Project abstract

Name of DKFZ research division/group:	***Junior Research Group for Pediatric Immuno-Oncology (D270)***
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Group homepage: Please visit our website for further information on our research and recent publications.	***https://www.dkfz.de/en/pediatric-immuno-oncology***

PROJECT PROPOSAL

Our Junior Research Group uses advanced genetic engineering and high-throughput CRISPR screens to improve cellular therapies of cancer. Treatment with CAR (chimeric antigen receptor) T cells has revolutionized the therapy of hematologic malignancies. However, they have not been successful in most solid tumors yet. Our group uses a variety of different techniques to study the interaction of CAR T cells with tumor cells and other immune cells with the aim to build better CAR T cell therapies. The methods performed in our group include molecular biology (PCR, cloning, transformation), CRISPR editing (CRISPR KO, CRISPR knockin(1), CRISPRa (2)), lenti- and retroviral approaches, AAV-based engineering, flow cytometry, cell sorting, cell culture, next generation sequencing and CRISPR screens including computational analysis, functional assays (e.g., proliferation, cytokine release, cytotoxicity) and xenograft and immunocompetent mouse models.

Example projects include:

- Development of new CAR T cells for brain tumor treatment
- Understanding the interactions of CAR T cells with tumor cells
- Building CAR T cells that can better infiltrate solid tumors
- Establishing advanced engineering strategies (e.g., base editing) for improved CAR design
- Understanding resistance mechanisms in malignant cells
- Reprogramming therapeutic T cells for improved fitness and reduced exhaustion

All our projects are located in the field of immunotherapy, genetic engineering and CRISPR screens and we are happy to discuss the candidate's interests, prior experience and envisioned future research directions.

(1) Blaeschke, F., (…) T. L. Roth and A. Marson (2023). "Modular pooled discovery of synthetic knockin sequences to program durable cell therapies." Cell **186**(19): 4216-4234 e4233.

(2) Schmidt, R., Z. Steinhart, (…) F. Blaeschke, (…) and A. Marson (2022). "CRISPR activation and interference screens decode stimulation responses in primary human T cells." Science **375**(6580): eabj4008.