Project abstract

Name of DKFZ research division/group:	***Translational Pediatric Sarcoma Research (B410)***
Contact person:	***Prof. Thomas Grünewald, MD, PhD***
Group homepage: Please visit our website for further information on our research and recent publications.	***https://www.kitz-heidelberg.de/en/research/research-groups/sarcoma/transl-ped-sarcoma-research***

PROJECT PROPOSAL

Our division investigates the molecular mechanisms that drive the initiation, progression, and therapy resistance of pediatric sarcomas. We aim to decipher how oncogenic alterations, especially fusion transcription factors and cooperating genetic variants, reshape cellular programs and tumor ecosystems to promote malignant transformation and metastatic progression. By integrating mechanistic discovery with translational research, we seek to develop improved diagnostic tools and innovative therapeutic strategies for young sarcoma patients.

Our core research areas include:

- Molecular mechanisms of pediatric sarcoma initiation and progression
- Oncogenic fusion transcription factors and transcriptional network rewiring
- Genetic predisposition and interaction between germline variants and somatic mutations
- Mechanisms of metastasis, tumor evolution, and therapy resistance
- Multi-omics characterization of pediatric sarcomas and biomarker discovery
- Identification and preclinical validation of novel therapeutic targets and treatment strategies
- Development of precision oncology approaches for sarcoma patients

To address these questions, we combine multi-omics profiling (genomics, transcriptomics, epigenomics, metabolomics, and proteomics), single-cell and spatial technologies, functional genomics approaches such as CRISPR-based perturbation screens, advanced imaging and proteomics, and systems biology analyses. These approaches are complemented by *in vitro* and *in vivo* disease models, including genetically engineered models and

patient-derived cell lines and xenografts, as well as access to well-annotated clinical samples and cohorts through our close integration with clinical partners and clinical cooperation units based at DKFZ.

Our division is embedded in a highly collaborative translational research environment at the German Cancer Research Center and the Hopp Children's Cancer Center Heidelberg (KiTZ), enabling close interaction between basic scientists, clinician scientists, and pediatric oncology programs. This setting provides unique opportunities to translate molecular discoveries into clinically relevant applications aimed at improving diagnosis, risk stratification, and treatment for children and young adults with sarcoma.

We particularly welcome motivated clinician scientists interested in bridging laboratory research with clinically relevant questions in pediatric oncology. Potential projects can be tailored according to the candidate's scientific interests, clinical background, and long-term career goals, with the overarching aim of translating mechanistic insights into tangible benefits for young cancer patients.