Research profile for applicants

Name of DKFZ research division/group:	***Section of Translational Cancer Epigenomics, Division of Translational Medical Oncology (B340)***
Contact person:	***Priv.-Doz. Dr. Daniel Lipka, email: d.lipka@dkfz.de***
Group homepage: *Visit this website for further information on current research and recent publications.*	www.translational-cancer-epigenomics.de/ https://pubmed.ncbi.nlm.nih.gov/?term=lipka+db&sort=date&size=200
Eligibility:	• ***DKFZ Postdoctoral Fellowships*** • ***Dr. Rurainski Fellowship at DKFZ***

RESEARCH PROFILE AND PROJECT TOPICS

In our group, we combine basic and translational research to discover and implement novel diagnostic and therapeutic approaches to malignant diseases. The main focus is on the analysis of epigenomic alterations occurring in pre-malignant and malignant cells as compared to their normal counterparts in order to understand how aberrant epigenetic programming impacts on tumor initiation and progression.

In a current project, we are investigating the molecular defects elicited by oncogenic *IDH1* mutations. IDH1/2-mutations are found in several malignancies and result in the production of the oncometabolite D-2-hydroxyglutarate (D2HG). D2HG was shown to alter epigenetic regulation and support tumorigenesis. Yet, recent evidence suggests that mutant IDH1 may have D2HG-independent oncogenic effects leading to massive abberations at the chromatin level. Within the proposed project we will assess in close collaboration with the groups of Efrat Shema and Guy Ron the molecular mechanisms underlying the observed chromatin defects in pre-malignant cell states. By applying cutting-edge technologies (EpiCyTOF, metabolomics, ACT-, ATAC-, RNA-seq, nanopore sequencing, CRISPRi and CRISPRa) to established Idh1-R132H *in vitro* and *in vivo* models, we will comprehensively assess the D2HG-independent mechanisms by which expression of mutant IDH1 affects the dynamic remodelling of the histone code during normal hematopoietic differentiation. These analyses will have a substantial impact on our understanding of the molecular mechanisms underlying the oncogenic function of mutant IDH1. Ultimately, these results might lead to the development of novel treatment options beyond inhibition of the mutant enzyme for patients with IDH1-mutant malignancies.

The successful candidate should have excellent communication skills and should demonstrate commitment toward highly interdisciplinary research. This work will benefit from already established experimental models and analysis pipelines but will also involve the development of novel methods. Project-related experience in hematology research, animal work and/or computational biology would be ideal but are not a prerequisite.

We provide excellent working conditions in a dynamic international group of scientists together with national and international collaboration partners in the field of single-cell epigenomics (Dr. Shema [Rehovot, Israel], bioinformatics (Prof. Lutsik [Leuven, Belgium], Prof. Ron [Jerusalem, Israel]), and clinical hematology (Prof. Germing [Düsseldorf], Prof. Platzbecker [Leipzig]).