Research profile for applicants

Name of DKFZ research division/group:	***Chromatin Networks (B066)***
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Group homepage: *Visit this website for further information on current research and recent publications.*	***https://www.dkfz.de/en/chromatin-networks/ Please visit our website for further information on our research and recent publications that are available at https://malone.bioquant.uni-heidelberg.de/publications/publications.html***

RESEARCH PROFILE AND PROJECT TOPICS

The Division of Chromatin Networks is an interdisciplinary group that studies the dynamic organization of the (epi)genome with the deregulation of gene expression programs and functional cell states in cancer. A special focus is on understanding the regulation of genome functions within their spatial context from the molecular scale of chromatin domains to cellular signaling between cells in a tissue. By applying quantitative fluorescence microscopy-based methods, the dynamic structure of chromatin subcompartments involved in activation or silencing of transcription and telomere maintenance is dissected. This information is combined with functional molecular profiles from single cell sequencing of isolated cells/nuclei in suspension (transcriptome, open chromatin, surface proteins, T/B cell receptors) as well as spatially resolved transcriptomics and antibody-based proteomics. Mechanisms inferred from the integrative data analysis inherent to all projects of the division are then tested in representative cell line models by perturbations of chromatin networks, for example by light-induced epigenetic editing of cis-regulatory elements. This approach is applied to blood cancers as well as solid tumors to resolve tumor heterogeneity and associated therapy resistance as well as telomere maintenance mechanisms that provide tumor cells with an unlimited proliferation potential.

Potential projects for a postdoctoral fellow: The formation of chromatin “condensates” in the nucleus with dimensions on the 0.1-1 µm scale is emerging as an important regulatory layer for genome associated activities. However, it remains enigmatic how imaging-derived phenotypes that describe the organization of membraneless nuclear subcompartments are linked to functionally relevant molecular profiles like the transcriptome. We address this issue by applying and further developing spatially resolved transcriptomics approaches with novel fluorescence microscopy-based readouts to reveal the underlying structure-function relationships. The work addresses the fundamental research question how the genome is partitioned into transcriptionally active or silenced chromatin subcompartments in a cell type specific manner and how the deregulation of this process is linked to cancer. It provides

a novel approach for dissecting tumor heterogeneity and molecular resistance mechanisms from the analysis of longitudinal patient samples.