Research profile for applicants

Name of DKFZ research division/group:	***B380***
Contact person:	***Ana Banito*** ***a.banito@kitz-heidelberg.de***
Group homepage: *Visit this website for further information on current research and recent publications.*	*https://www.dkfz.de/en/soft-tissue-sarcoma* *https://www.kitz-heidelberg.de/en/research/research-groups/sarcoma/jrg-soft-tissue-sarcoma*

RESEARCH PROFILE AND PROJECT TOPICS

Sarcomas are aggressive cancers of mesenchymal origin. They are rare in adults but account for up to 13% of childhood cancers, and they remain a leading cause of life-years lost in young patients. Unlike most adult tumours, many pediatric sarcomas have few mutations and are driven by a single gene fusion. Many of these fusion proteins act as chromatin regulators rather than classic signalling proteins, which makes sarcomas a striking example of cancer caused by epigenetic dysregulation. It also means these drivers have so far been considered "undruggable." Our lab studies how these fusion oncoproteins rewire the epigenome to transform cells. We combine functional genomics (CRISPR screens), chromatin profiling (CUT&RUN/ChIP-seq, ATAC-seq, DNA methylation), proteomics, single-cell and spatial transcriptomics, and in vivo models. To study these questions in vivo, we developed a flexible platform of genetically engineered mouse models based on electroporation. It combines transposons, CRISPR and inducible protein degradation (dTAG) to model more than ten sarcoma types in immunocompetent mice. Current projects ask: 1. whether oncogenic chromatin states can be reversed by acute removal of the fusion protein, 2.which cells sarcomas originate from and how oncofusions initiate tumorigenesis. 3. how tumours become resistant to therapy