Project abstract

Name of DKFZ research division/group:	***Division of Genome Instability (B420)***
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Group homepage: Please visit our website for further information on our research and recent publications.	***https://www.dkfz.de/genominstabilitaet-in-tumoren***

PROJECT PROPOSAL

Unknown before the next-generation sequencing era, chromothripsis is a new phenomenon of genome instability, by which a presumably single catastrophic event generates extensive genomic rearrangements of one or a few chromosome(s) (see Simovic and Ernst, Nature Reviews Cancer 2025, https://www.nature.com/articles/s41568-024-00769-5). We and others discovered that chromothripsis is one of the most frequent events in cancer, affecting 30-50% of all cancers. In addition, chromothripsis is linked with poor prognosis for cancer patients. Our laboratory aims at elucidating how chromothripsis arises and at systematically deciphering the molecular and cellular consequences of chromosome instability. We have leveraged state-of-the-art technologies as well as newly developed in vitro and in vivo models to make several fundamental discoveries on how instability contributes to cancer development. In the coming years, our research will further develop its three essential basic and translational areas of investigation to elucidate how chromosome instability leads to massive genome rearrangements:

1. The somatic (epi)genome evolution in time and space: evolutionary dynamics of chromosomally unstable tumors
2. The molecular mechanisms underlying chromothripsis and chromosome instability
3. The pre-cancer landscape, to pioneer novel approaches to detect, prevent and treat chromosomally unstable tumors

We are looking for a highly motivated clinician scientist, who would like to work on a fascinating newly discovered phenomenon. Our work goes from basic research aiming at a better understanding of the mechanisms underlying chromothripsis to pre-clinical studies in mouse models. Within this framework, there is a broad range of possible projects for the candidate, depending on individual predilections and aptitudes. Next-generation sequencing, single-cell, long-read and spatial technologies are core methods used in our group. Projects combining wet lab and computational approaches are possible.