Research profile for applicants

Name of DKFZ research division/group:	***Molecular Neurobiology (A290)***
Contact person:	***Prof. Ana Martin-Villalba***
Group homepage: *Visit this website for further information on current research and recent publications.*	***https://www.dkfz.de/molekulare-neurobiologie*** *https://martin-villalba-lab.github.io/index.html*

RESEARCH PROFILE AND PROJECT TOPICS

The Martin-Villalba lab's research spans two organs, the brain and the pancreas, joined by a common question: how do tissues balance quiescence, regeneration, and the risk of disease that regeneration itself creates.
In the brain, Ana's team has shown that neural stem cell identity is encoded in the DNA methylome. Using single-cell triple-omics (NMT-seq) to jointly profile the transcriptome, DNA methylome and chromatin accessibility of astrocytes and the neural stem cell lineage, they found that stemness is conferred less by transcription than by a specific methylation signature: methylation silences astrocyte genes while demethylation licenses neurogenic genes ahead of their expression. Ischemic injury unlocks this stemness-methylome in ordinary astrocytes, enabling them to generate new neurons (Kremer et al., Nature, 2024). Together with her lab's pioneering single-cell technologies (Llorens-Bobadilla et al., Cell Stem Cell, 2015; Kremer et al., Nature 2024; Kremer et al., Nature-Methods, 2024), the use of AAV technologies for targeting adult neural stem cells (Kremer et al., Molecular Therapy Methods & Clinical Development), and its work on stem cell quiescence, interferons and Wnt activity, this reshapes the understanding of how the aging brain retains, and restricts, its regenerative potential.
In the pancreas, her lab studies how polyploid acinar cells, which normally boost secretory capacity, become a liability during tissue repair. Its latest bioRxiv preprint shows that upon inflammatory injury, polyploid acinar cells contribute to regeneration via acinar-to-ductal metaplasia and thereby run the risk of acquiring chromosomal instability (CIN). The findings establish a direct physiological link between polyploidy, tissue repair and chromosomal instability (CIN), offering a new explanation for the elevated cancer risk long observed after pancreatic inflammation (Brunken et al., bioRxiv, 2026). The lab has also studied the molecular changes leading to ADM via triple-omics and found out how acinar cells gain facultative stemness.
The postdoctoral fellow should through the parallel study of regeneration in the pancreas and the brain find out what is important to gain facultative stemness, how to activate it and

how to avoid cancer while doing this. Lessons can be also applied to turned a cancer cell into a quiescent one (see Nature Communication, 2025).