Project abstract

Name of DKFZ research division/group:	***Tumorigenesis and Molecular Cancer Prevention Group (C150)***
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Group homepage: Please visit our website for further information on our research and recent publications.	*https://www.dkfz.de/en/tumorigenesis-and-molecular-cancer-prevention*

PROJECT PROPOSAL

The **Tumorigenesis and Molecular Cancer Prevention Group** investigates the earliest biological changes that drive the transition from normal gastric and oesophageal epithelium to cancer. By the time most solid tumours are diagnosed, they have already undergone clonal expansion from a single cell. While this simplifies tumour analysis, it presents a major challenge for studying the **very early** stages of cancer, when subtle genetic, epigenetic, and environmental changes begin accumulating. At this stage, clonal expansion cannot be leveraged, requiring a unique set of tools to uncover the first steps in cancer development.

To understand the dynamics of cancer initiation, we utilize cutting-edge single-cell technologies, including:

- Single-cell RNA sequencing (transcriptional profiling)
- Single-cell ATAC-seq (epigenetic regulation)
- Single-cell DNA sequencing (genetic alterations)
- A newly developed reduced-representation DNA sequencing technique

We exemplified the utility of these approaches by discovering the cell of origin in oesophageal adenocarcinoma, developing methods to track extrachromosomal DNA at the single-cell level, and designing risk-stratification techniques for patients with gastric and oesophageal precancerous lesions.

Research Opportunities in Our Group

We focus on two major themes:

1. **Advancing our understanding of normal and precancerous tissue biology** – essential for improving early diagnostics and targeted treatments.

2. **Translating knowledge into clinical impact** – applying state-of-the-art technologies to detect early cancers and stratify patients who are at increased risk but currently fall below treatment thresholds.

Potential projects include:

- Risk stratification of Barrett's Oesophagus and Gastric Intestinal Metaplasia
- Early detection of dysplastic and carcinoma in situ lesions in gastric and oesophageal cancer
- Application of single-cell RNA sequencing, spatial transcriptomics, and genome-wide genetic studies to refine diagnostic approaches

If you are passionate about cancer research and want to work on projects with direct clinical relevance, we encourage you to get in touch!