

## Project abstract

Name of DKFZ research division/group:	<b>Cancer Progression and Metastasis (A013)</b>
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Group homepage: Please visit our website for further information on our research and recent publications.	<a href="https://www.dkfz.de/en/tumorprogression-metastasierung/index.php">https://www.dkfz.de/en/tumorprogression-metastasierung/index.php</a>

### PROJECT PROPOSAL

Colorectal cancer (CRC) is one of the most prevalent cancer entities in the world and patients presenting at later stages of the disease have a dismal prognosis. This is mainly due to the systemic distribution of cancer cells throughout the body and metastatic cells being resistant to standard-of-care therapies. The Cancer Progression and Metastasis laboratory at DKFZ aims to tackle these problems.

The successful applicant will conduct the reverse translation of a randomized multicenter phase II/III clinical trial TROPHIT1 (<https://www.aio-portal.de/studie/206--trophit1.html>) starting in 2024 targeting TROP2 expressing cells in metastatic CRC (mCRC). Importantly, targeting TROP2 pharmacologically with an antibody drug conjugate (ADC) that is linked with a humanized antibody recognizing TROP2 (Trodelvy; Sacituzumab Govitecan) has been approved for triple negative breast cancer (TNBC) by EMA and FDA in 2021 and makes TROP2 a very promising target. Despite the strong effects in TNBC the role of TROP2 in CRC is only sparsely understood.

The overall goal of the project is to decode the response to Trodelvy treatment in patients with m(CRC). In collaboration with the NCT Heidelberg (Bruno C. Köhler), your role will be the in-depth characterization of clinical specimens sampled at various time points under the umbrella of the TROPHIT1 clinical trial. You will leverage various multiome analyses (bulk, single cell or spatial transcriptomics) to decipher mechanisms of response and resistance to Trodelvy. In addition, patient derived *ex vivo* cultures, of various kinds, will be generated by you to identify and investigate the mechanism of therapy response/resistance. Overall, this multidisciplinary project with highest clinical relevance is designed to decipher mechanisms to enhance future trial design.

We are looking for a highly motivated candidate, who aims to work in a top notch, interactive (many collaborations are involved in the project) and international research team. At HI-STEM/DKFZ/NCT we conduct state-of-the-art and beyond research with excellent technical and intellectual support.



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