Project abstract

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Group homepage: Please visit our website for further information on our research and recent publications.	***https://www.dkfz.de/en/tumor-immunology-and-tumor-immunotherapy***

PROJECT PROPOSAL

Colorectal cancer (CRC) is a common malignancy associated with high mortality, particularly among patients with advanced metastatic disease. Although progress has been made through improved surgical techniques, radiation therapy, local ablation, and chemotherapies, the most significant advancement has come from identifying more relevant biomarkers and corresponding treatments. A stratification tool that has identified an interesting subgroup is the detection of microsatellite instability (MSI) and mismatch-repair deficiency (dMMR). These tumors develop a high number of mutations, potentially offering better neoantigen landscapes, and accumulate numerous tumor-infiltrating lymphocytes (TILs). For the vast majority of cases, the tumors with microsatellite stability (MSS), the role and utility of immunotherapy (in combinations) has been limited so far, although some new approaches apprear to be promising. Combinatorial approaches (with chemotherapy) and novel treatment regimens with new checkpoint-inhibitors have shown some progress. It is yet unclear, which patient has a benefit from these new treatments, especially as there is still a large heterogeneity in terms of responses that can be observed: liver and peritoneal metastases so far have not responded. This large unmet medical need also applies to other gastrointestinal malignancies, namely pancreatic cancer. In our group, we have devised novel model systems (expant models, bioprints) that helped to improve our understanding. Together with clinical material, trial data and cutting-edge tools for biomarker identification (microbiome diagnostics, targeted proteomics, etc.), the systematic landscapes of „resistance“ to immunotherapies at different organ sites will be explored to pave the way forward for future successfull intervemtions. This translational effort clearly bridges from clinical expertise to immunobiology of the tumor microenvironment.