Project abstract

Name of DKFZ research division/group:	***Metabolic crosstalk in cancer (B350)***
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Group homepage: Please visit our website for further information on our research and recent publications.	***https://www.dkfz.de/en/brain-cancer-metabolism/***

PROJECT PROPOSAL

The major goal of the division of metabolic crosstalk in cancer is to unravel how metabolites function as signaling molecules in the crosstalk between tumor cells and the tumor microenvironment, thereby contributing to the malignant properties of tumor cells and/or the suppression of anti-tumor immune responses. Moreover, we apply metabolomics in clinical cohorts to systematically profile small-molecule signatures and enable the discovery and validation of diagnostic, prognostic, and predictive biomarkers.

Survivorship research project

Breast cancer (BC) is the most common cancer in women, with 2.3 million diagnoses annually worldwide (WHO). In developed countries, one in eight women is affected during their lifetime. 75% of BCs are hormone receptor-positive (HR+) and are treated with endocrine therapies (ET) to inhibit hormone-driven tumor growth. Advances in detection and treatment have improved survival rates, increasing the focus on quality of life (QoL). While being less toxic than chemotherapy, ET often causes menopause-like symptoms, fatigue, and neuropsychological issues, strongly affecting QoL, and leading to significant morbidity and costs. HR+BC recurrence rates remain low but persist for more than 20 years, with no routine molecular markers to detect relapse early.

Despite extensive efforts to identify new targets and biomarkers for BC, metabolism remains largely overlooked. Our prior work on HR+BC highlighted the importance of amino acid metabolism, particularly for amino acid metabolism in ET response.

The goal of this survivorship research project is to identify metabolites, proteins and nucleic acids that could serve as biomarkers predicting long-term outcomes, incl. recurrence, metabolic status, menopause-like symptoms, fatigue, and depression >5 years after ET.

Metabolism-linked molecular biomarker discovery presents high added value for risk stratification and tertiary prevention in HR+BC: Our biomarker panels will open new avenues for personalized therapies by guiding the duration and dosage of ET to prevent overtreatment, control adverse events and optimize safety by predicting relapse early. It can also guide ET combination with new therapy options including exercise interventions or pharmacological drugs directly targeting metabolism.