breast care
a ctmm project

Center for Translational Molecular Medicine

Breast Cancer Response study BREAST CARE

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Disease area: Oncology

Introduction

Patients with breast cancer rarely die of their local tumor but usually succumb to distant metastases. Many treatment choices are available and in each individual case a choice must be made with regard to the combination, the sequence and the duration of treatment. This project employs a setting in which preoperative ('neoadjuvant') chemotherapy is administered to patients with a primary breast tumor in situ. Using a range of different approaches, response prediction and response monitoring are being studied.

Technologies / products to be developed

1. Response prediction in Breast Cancer
2. Monitoring of response during or following (neo)adjuvant therapy
3. (Neo)adjuvant treatment strategies based on relevant animal models

Approach

- Genetically engineered mouse models
- High though-put high complexity gene expression analyses on human and animal tumors in the context of neoadjuvant chemotherapy; aCGH
- Functional imaging in both animals and patients
- Differential activity measurements of progesterone antagonists in pertinent genetically defined mouse tumors
- Comparative proteome profiling of laser microdissected breast cancer tumor cells using Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS) in the context of advanced chemotherapy
- Multimodality imaging (fused MRI plus PET/CT [high resolution time of flight system]) to monitor chemotherapy in humans and to tailor radiotherapy

Results continued

Correlation of intrinsic breast cancer subtypes with standard pathology and immunohistochemistry studied in 195 tumors

Indicators of homologous recombination deficiency defined in human breast cancer specimens

Microdissection of 50 advanced breast tumor tissues and method optimization of sample preparation for proteome analysis

Gene expression profiling of untreated *Brca1-/-; p53-/-*mouse mammary tumors does not result in a signature that could predict response to docetaxel

Mdr1-/-;Brca1-/-;p53-/- mouse mammary tumors are hypersensitive to docetaxel and doxorubicin, and hardly acquire drug resistance.

Estrogen alone can fully restore mammary tumor formation in ovariectomized BRCA1 female mice → BRCA1-associated tumorigenesis is estrogen-dependent

Progesterone can only partly restore mammary tumor formation in ovariectomized BRCA1 female mice → BRCA1-associated tumorigenesis is partly progesterone-dependent

Optimization of sample preparation protocol for proteomics analyses reducing preparation time from 2 days → <30 minutes

MRI diffusion package transferred

Setup of prone breast support device at PET optimized

DWI Distortion correction proven feasible

18 patients included with MRI and PET prior and during neoadjuvant chemotherapy

Feasibility of response monitoring using Annexin V investigated in preclinical setting

Participants

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