Exploration of new potential predictive and prognostic biomarkers, such as RTKs and CTCs, for future targeted medical therapy in breast cancer patients, with a special focus on triple-negative breast cancer

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Background

More than 8000 Swedish women are diagnosed with breast cancer (BC) every year. The 5-year survival rate is almost 90%. Still, 1500 women develop metastatic disease each year and approximately 5000 live with metastatic BC. The triple negative breast cancer (TNBC) subgroup remains a challenge to treat with no targeted therapy available. The aim of projects 1 and 2 is to explore tumor cell and stromal expression of receptor tyrosine kinases (RTKs) involved in cell growth and proliferation, as they are possible future targets for BC therapy; especially in the difficult to treat TNBC.

Another important challenge in BC is to ensure that the appropriate treatment is chosen and to effectively monitor treatment response. Enumeration of circulating tumor cells (CTCs) in patients with metastasized cancer has been shown to carry additional prognostic information to standard clinical tumor and patient characteristics. The aim of projects 3 and 4 is to elucidate if the prognostic information offered by CTCs can be further refined by morphologic assessment of these cells.

Methods

Women with primary BC (n=500+) were included in projects 1 and 2. Protein expression was evaluated by immunohistochemistry and gene copy number by fluorescence in situ hybridization.

Women with first diagnosis of metastatic BC (n=52) were included in projects 3 and 4. CTCs were captured by the CellSearch® system and morphologic characterization was performed on scanned microscopy images from this system.
Results and future perspectives

TNBC had inferior prognosis compared to non-TNBC in primary and metastatic BC[1, 3].

Project 1. The RTKs investigated (c-KIT, VEGFR2 and PDGFR-α) showed high expression in TNBC. Survival analyses showed no difference in BC mortality for TNBC patients with high vs. low RTK expression[1]

Project 2. The importance of the PDGF-family in primary breast tumors, synchronous lymph node metastases and asynchronous distant metastases is explored[2].

Project 3. CTC clusters were present more often in HER2-positive and TNBC compared to hormone receptor positive BC. CTC clusters and apoptosis in follow-up blood samples during treatment were associated to significantly worse prognosis[3].

Project 4. CTC size, shape, cytokeratin staining intensity and nuclear-to-cytoplasmic ratio are investigated in relation to BC prognosis, metastatic site, and BC subtype.

Publications


2. Jansson S…. Importance of PDGFR-alpha, PDGFR-beta and PDGF-CC expression in breast cancer (manuscript in preparation)