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## microRNAs as prognosticators and predictive factors in breast cancer

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Despite progress in understanding breast cancer, we are still left with two important controversies. First, a disappointingly small number of reliable and reproducible prognostic and predictive factors have been developed that can meet the demand for the clinical setting, even though more than 100 prognostic factors are known. As an example of the urgent need for more knowledge in this field is the recent extension from the 5-year tamoxifen treatment schedule to 10-year adjuvant tamoxifen treatment for estrogen receptor (ER) positive breast cancers. Due to the lack of predictive markers, the clinicians are not able to decide who will benefit from this extension as only 2-3% of the patients will experience a long term overall survival benefit. This further supports the St. Gallen guidelines, where over and under treatment is estimated to occur in 85% and 20% of the lymph node negative patients. Secondly, there has been a substantial focus on personalized systemic treatment in the primary/adjuvant setting. However, when the primary treatment has been completed, the systematic follow-up is only focused upon early detection of local relapse (i.e. mammogram/ultrasound and clinical examination). Paradoxically, there is no search for early systemic relapse even though the distant metastatic lesions will kill the patient if they become clinically overt. In this lecture, the role of microRNAs as prognostic and predictive biomarkers in breast cancer will be discussed, as well as the use of microRNAs in therapy.

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## Identifying predictors of taxane-induced peripheral neuropathy using mass spectrometry based proteomics technology

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Major advances in early detection and therapy have significantly increased the survival of breast cancer patients. Unfortunately, most cancer therapies are known to carry a substantial risk of adverse long-term treatment-related effects such as chemotherapy-induced peripheral neuropathy (CIPN). Little is known about patient susceptibility to severe side effects after chemotherapy. Thus, for those at high risk for disease recurrence, a major concern is the patient's inability to tolerate the full dose/duration of therapy to improve outcome. Recent advances in proteomic technologies incorporating mass spectrometry (MS) for biomarker discovery show great promise to provide clinically relevant protein biomarkers. In this study, we evaluated the association between protein content in serum exosomes and severity of CIPN. Women with early stage breast cancer receiving adjuvant taxane chemotherapy were assessed with the FACT-Ntx score and serum was collected before and after the taxane treatment. Based on the change in FACT-Ntx score from baseline to 12 month follow-up, we separated patients into two groups: those who had no change (Group 1) and those who had a >20% worsening (Group 2). MS-based proteomics technology was used to identify proteins present in serum exosomes to determine potential biomarkers. Statistical analysis revealed a 12-protein signature that resulted in a distinct separation between baseline serum samples of both groups (FDR<0.2) suggesting that the baseline samples can predict subsequent neurotoxicity. Since we found more distinct exosomal proteins at baseline between these two groups of patients we speculate that there are host-factors that could predispose patients to this toxicity.

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