Genomics and proteomic analysis of breast cancer

**EVOLUTIONARY PATTERNS OF MICRORNA EXPRESSION THROUGH THE COURSE OF DISEASE AND THERAPY IN RECURRENT BREAST CANCER**


1Cancer Research Center, Chaim Sheba Medical Center, Ramat Gan, ISRAEL
2Physics of Complex Systems, Weizmann Institute of Science, Rehovot, ISRAEL
3Oncology Institute, Chaim Sheba Medical Center, Ramat Gan, ISRAEL
4Pathology Institute, Chaim Sheba Medical Center, Ramat Gan, ISRAEL
5Division of Oncology, Chaim Sheba Medical Center, Ramat Gan, ISRAEL

**Background:** Although metastatic disease is the cause of death in breast cancer, most studies are focused on primary tumors. However, intra-tumoral heterogeneity frequently develops through the course of disease. This molecular evolution is clinically challenging and is the main reason for resistance to therapy.

**Aim:** To explore alterations through the course of disease and therapy by molecular profiling of individual breast cancer patients.

**Methods:** A prospective dataset of all the patients who have undergone uniform neo-adjuvant treatment in Sheba Medical Center from 2003 was analyzed. The neo-adjuvant setting enabled sampling of residual tumors post-treatment. We assembled a unique cohort of patients having matched samples from pre-treatment, post-treatment and recurrence. We collected FFPE (Formalin-Fixed Paraffin-Embedded) samples of tumors, lymph nodes and metastasis and extracted total RNA and DNA. We profiled miRNA expression across all samples for each patient (total of 71 samples for 20 patients), using NanoString analysis. The results were validated by qRT-PCR.

**Results:** We clustered the miRNAs according to their patterns through the disease course for each individual patient. The different miRNAs patterns were divided into categories that were served to identify shared miRNAs that dictates the tumor evolution. We found a good agreement between the expected pattern, calculated according to the Caldas dataset, and the observed trend. For example, miRNAs known to be down-regulated in breast cancer showed an increase in expression post treatment, but not in involved lymph node, and a significant reduction at recurrence.

Interestingly, we identified unique patterns for individual patients that suggested either clonal selection or response to treatment and were in agreement with the clinical outcome.

**Conclusions:** This longitudinal observation enabled us to profile the pattern of expression for each patient and provided a hint into the mechanism of disease progression. This approach of serial assessments through the course of disease in individual patients may have important consequences for personalized medicine.

**Disclosure:** All authors have declared no conflicts of interest.