

**POSTER SESSION 7: Early diagnosis of cancer**

**P7.1**

**Breast Tissue Dynamics in BRCA1/2 Mutation Carriers**

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**Introduction:** Circulating free DNA (cfDNA) is released to the bloodstream from dead cells in different tissues. Today, most of the detection methods are based on sequencing and pathologic changes in the genetic code. We use a method based on the methylation pattern of cfDNA, thus allowing us to measure normal tissue turnover in various clinical scenarios.

BRCA1/2 gene mutation is a common cause of hereditary breast and ovarian cancer worldwide. Previous data suggests that healthy carriers of the BRCA1/2 mutation have an increased turnover of cells in the breast tissue. Therefore, we believe that increased cell turnover is a potential early mark of tumorigenesis in this population.

**Methods:** Using Illumina methylation array we have identified three sites with breast unique methylation pattern. Then, three cohorts of pre-menopausal United States women were identified: healthy controls (n=27), healthy BRCA1/2 mutation carriers (n=10) and BRCAmut/+ metastatic breast cancer patients (n=5). 20 ml of peripheral blood were drawn during the menstrual cycle at days 1-3 (Time point 1= TP1), days 9-11 (TP2) and days 21-23 (TP3).

**Results:** Average levels of total cfDNA (ng/ml) in healthy controls were: TP1=3.50, TP2=3.64 and TP3=3.23. Average levels of total cfDNA in healthy BRCA1/2 mutation carriers at previously mentioned time points were: 3.45, 2.84, and 3.51, respectively.

Fraction of breast specific cfDNA at different time points in healthy controls were as following: TP1=0.3%, TP2=0.05%, TP3=0.2%. Fraction in healthy BRCAmut/+ women were: TP1=0.3%, TP2=0.1%, TP3=0.6%.

Total cfDNA levels and fraction of breast-specific cfDNA in metastatic breast cancer patients were considerably higher, representing extensive burden of disease in this group.

**Conclusion:** Our data suggests that turnover of body tissues and breast tissue change during the menstrual cycle, with potential variation between healthy women and BRCA1/2 mutation carriers. The difference can reflect differential hormonal sensitivity of tissues.

Surprisingly, we have not identified increased turnover of breast tissue of BRCA1/2 carriers. This finding may imply that BRCA1/2 tumorigenesis is due to damaged cell-removal mechanism (such as apoptosis or senescence) instead of uncontrolled proliferation on the background of DNA repair defect.