Results: By XmaI-RRBS we have identified 10 genes the states of methylation of which most effectively mark BC luminal B sensitivity to anthracycline based NAC. For locus specific assessment of these markers we have developed a multi-locus methylation sensitive PCR system. Based on the methylotyping results obtained for the 40 samples of the validating cohort, the diagnostic properties of the system were estimated: the area under the ROC curve was 84%, with the sensitivity of 82% and the specificity of 80%.

Conclusions: The system including a limited number of methylation markers makes it possible to effectively predict the response of luminal B subtype BC to anthracycline based NAC by an analysis of biopsy material obtained before the treatment. Reasonable diagnostic sensitivity and specificity values are achieved only when the markers are evaluated in complex; in separate the differences in gene methylation frequencies between responding and non-responding tumors may be negligible (Table).

Table: 80P Methylation frequencies of selected genes in tumors responding and not responding to anthracycline based NAC

Gene	Responders, %	Non-responders, %
SLC9A3	28 (7/25)	27 (4/15)
C1QL2	20 (5/25)	13 (2/15)
DPYS	60 (15/25)	47 (7/15)
IRF4	72 (18/25)	33 (5/15)
ADCY8	64 (16/25)	40 (6/15)
KCNQ2	48 (12/25)	40 (6/15)
TERT	80 (20/25)	60 (9/15)
SYNDIG1	20 (5/25)	20 (3/15)
SKOR2	56 (14/25)	67 (10/15)
GRIK1	84 (21/25)	87 (13/15)

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80P DNA methylation markers of breast cancer response to anthracycline based neoadjuvant chemotherapy

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Background: Neoadjuvant chemotherapy (NAC) is intensively used for the treatment of locally advanced breast cancer (BC). The aim of this study is to provide a better insight into BC response to neoadjuvant anthracycline based chemotherapy.

Methods: Genome-wide methylation analysis of 27 BC biopsy specimens of the luminal B subtype taken before the treatment was performed using the XmaI-RRBS method. Methylation status of the selected markers was next determined by methylation sensitive restriction enzyme PCR in a validating sample of 40 BC biopsy specimens.