TGFB1–509TT genotypes were showed in the patient group in comparison to the controls ($p = 0.008$ and $p = 0.03$ respectively). We have observed an increased frequency in the VEGF-2578A/A genotype among women with positive regional lymph node metastases compared to patients with negative regional lymph node metastases ($p = 0.02$). A significant difference was found between the luminal B and luminal A subtype tumor of patients carrying the VEGF-2578C/C genotype ($p = 0.04$). In addition, patients with the FGFR2A/A genotype exhibited a non-statistically significant better response to neoadjuvant chemotherapy ($p = 0.06$). There was also trend for association between FGFR2G/G genotype and worse response to neoadjuvant chemotherapy in infiltrating ductal breast carcinoma patients ($p = 0.08$).

Conclusions: These findings indicate that genetic variants in VEGF-2578A/A, FGFR2G/G and IL10–592A/A are associated with infiltrating ductal breast carcinoma risk. Polymorphism in VEGF gene may serve as molecular marker related with regional metastasis and molecular subtype of tumor. The polymorphic variants of FGFR2 gene may be a potential prognostic factor for response to neoadjuvant chemotherapy in infiltrating ductal breast carcinoma patients.

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In patients with early breast cancer, populations of immature, cytokine producing plasmacytoid dendritic cells (PDC) decrease in tumour draining lymph nodes and express TLR9

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Background: Plasmacytoid dendritic cells (PDC) represent a distinct subset of dendritic cells (DC) capable of producing large amounts of type-1 interferons after stimulation of toll-like receptors (TLR)-7 and 9. In breast cancer draining LN, PDC secrete cytokines such as IL-10 and IL-12 with the potential to polarise local T cell responses. Despite being frequently identified within the tumour microenvironment, PDC remain poorly characterised in human cancer.

Materials and Methods: Plasmacytoid DC and myeloid DC (MDC) were identified using flow cytometry in cell suspensions of control LN and good and poor prognosis breast tumour draining axillary LN (TDLN) as defined by the Nottingham Prognostic Index (NPI). Immunohistochemistry and immunofluorescent microscopy was performed on frozen Control LN and TDLN sections to localise PDC and determine IL-10 and IL-12 expression. Immunofluorescence microscopy of magnetically sorted PDC populations was undertaken to determine TLR-9 expression.

Results: PDC constituted a prominent immature population in all LN studied. In both control and TDLN the maturation status of PDC and MDC subset populations was similar. When compared to poor prognosis LN, PDC proportions decreased in LN draining good prognosis breast cancer ($p < 0.05$). Immunohistochemistry identified CD123+ BDCA-2+ PDC within the cortex and sinus system of control and tumour draining LN. In LN containing metastatic breast cancer, CD123+ BDCA-2+ PDC were found within and at the cancer periphery. Immunofluorescence microscopy localised BDCA-2^+ PDC co-expressing IL-10 or IL-12 to the T cell areas of control and tumour draining LN. TLR-9 expression was identified on PDC sorted from control and tumour draining LN.

Conclusions: PDC were found in close proximity to malignant cells in metastatic LN as well as T cells in control LN and TDLN. The identification of PDC in the sinus system of control LN and TDLN suggests that they can gain access to tissue afferent lymphatics. The expression of IL-10 and IL-12 by PDC in the T cell areas of control LN and TDLN confirms that PDC are able to produce polarising cytokines. In patients with breast cancer, the migration and cytokine secretion of PDC populations may play a pivotal role in anti-tumour responses. The expression of TLR-9 by PDC also makes them a target for therapeutic intervention.

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Relation between methylation promoters gene and estrogen receptor (ERS1) and her2/neu status in breast cancer patients

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The CpG island metylator phenotype is associated with distinct clinicopathological caracteristics as Estrogen Receptor (ESR1) positive and amplification HER2 in breast cancer.

Objective: To investigate the relation between DNA promoter methylation and the prognostic clinico-pathological features of breast cancer, including diagnosis and treatment response and to evaluate epigenetics differences in tumor-related genes to ESR1 and HER2/neu status in primary breast cancer.

Material and Methods: We quantified methylation levels of promoter of 5 genes (ERS1, RAR-β, 14-3-3 sigma, APC, E-Cadherin) which are to confer growth advantage to cells in 107 women with breast cancer and 108 control subjects. Real Time QMS-PCR SYBR green (methylation-specific PCR) was used to analyze the hypermethylation. Tumours were classified as phenotype basal, luminal A, Luminal B and phenotype HER2+.

Results: Ours analyses revealed low or absent methylation *ESR1*and *14-3-3*σ in healthy controls and significant differences between breast cancer patients (pts) and healthy controls in relative serum levels of methylated gene promoters *ESR1* ($p = 0.0112$) and *14-3-3*s ($p = 0.0047$). Presence of methylated *ESR1* in serum of breast cancer patients was associated with ER-negative phenotype ($p = 0.0179$). Of the available cases, 60 pts (56%) were Luminal A, 10 pts (9.3%) Luminal B, 13 pts (12%) Basal like and 9 pts (8.4%) HER2+. We observed that methylated ERS1 was preferably associated with phenotype Basal Like and worse interval progression free and survival global though $p > 0.05$ and the amplification HER2+ was correlation with significant more frequent methylation gene ($p < 0.05$). Thet hypermethylation of normal ERS1 and 14-3-3σ combined differentiated between breast cancer patients and healthy controls ($p = 0.0001$) with a sensitivity of 81% (95% CI: 72−88%) and specificity of 88% (95% CI: 78−94%).

Conclusions: This study identifies the presence of variations in global levels of methylation promoters genes in healthy controls and breast cancer with different phenotype classes and shows that these differences have clinical significance. These showed that frequent methylation had a strong association with molecular phenotype of breast cancer and perhaps in the future can explain therapy resistance related to RE and HER2/neu status in breast cancer patients.

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Novel germline mutations in BRCA2 gene among breast and breast-ovarian cancer families from Poland

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Background: The aim of our study was an assessment of the spectrum of *BRCA2* gene mutations and their frequency in women and men with familial breast cancer and ovarian cancer, in whom no mutations were found in *BRCA1* gene.

Material and Methods: 105 probands were selected (97 women and 8 men) and treated in the Oncology Center in Warsaw and the Oncology Center − Branch in Cracow in the years 1998–2008 and remain in care of the Genetic Counselling Clinic, Oncology Center in Warsaw. The patients were aged 17−67 years; (median age 46 years). The presence of molecular changes was examined in DNA isolated from peripheral blood lymphocytes. Germline mutations in 27 exons of the *BRCA2* gene were screened by "touchdown" PCR amplification, DHPLC and sequencing. Missense mutations were classified by multiple-sequences alignments of orthologous BRCA2 protein sequences with T-Coffee software.

Results: Thirty-nine molecular variants were identified in the study group, including eight changes determined for the first time (five pathogenic