processed immediately after collection to avoid interference of the *in vivo* gene expression signature with ex vivo stress responses. An alternative is the use of an integrated system for collection, stabilization, and purification of intracellular RNA from whole blood like PAXgene (Qiagen) or Tempus Blood RNA tubes (Applied Biosystems). RNA profiles will be stabilised for up to 5 days at room temperature.

300 POSTER

Importance of XRCC1 Arg399Gln polymorphism in the development of breast carcinoma in women with and without breast cancer family history

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Background: Breast cancer is the neoplasia with higher incidence and mortality in women all over the world. Many environmental factors have been associated with risk of breast cancer development, such as radiation, diet and endogenous and exogenous estrogens. Several studies have reported that the genes involved in DNA repair and maintenance of genome integrity are implicated in protecting against mutations that lead to cancer. Epidemiologic evidence has shown that inheritance of genetic variants (polymorphism) at one or more loci results in reduced DNA repair capacity and increased cancer risk. Base excision repair (BER) is a crucial pathway in the maintenance of genome stability. Variants of several DNA repair genes, including *XRCC1* gene, have been described, but the influence of these genetic variants in repair phenotype and cancer risk remains unclarified.
Aim: The purpose of this study was to evaluate the role of *XRCC1 Arg399Gln* polymorphism as genetic susceptibility markers to familiar and sporadic breast cancer.
Materials and methods: We have used a case-control study. We analysed 630 DNA samples from Portuguese individuals: 71 breast cancer patients with family history (FH) of breast cancer, 219 patients without FH and 340 control subjects, for *XRCC1 Arg399Gln* polymorphism using PCR-RFLP.
Results: We found *Arg/Arg* genotype in 33.8% breast cancer patients with FH, in 43.8% of patients without FH and 34.3% of healthy women. We observed statistically significant differences in *Arg/Arg* genotype of *XRCC1 Arg399Gln* polymorphism between breast cancer patients without FH and control group ($p = 0.025$; OR = 1.49, 95%CI: 1.03–2.14). Furthermore, we found that *Arg/Arg* genotype is more frequent in breast cancer patients without FH (43.8%) than in patients with FH (34.3%).
Conclusions: These preliminary results, in the Portuguese population, show a higher frequency of the *Arg/Arg* genotype of *XRCC1 Arg399Gln* polymorphism in patients without FH of breast cancer than in patients with FH and control groups, suggesting this genotype in women with no FH of breast carcinoma as a susceptibility factor to the breast carcinoma development.

301 POSTER

Very high frequency of BRCA1 5382insC founder mutation in Russian "hereditary-like" breast cancers

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Background: BRCA1 5382insC is a rare founder mutation described in Ashkenazi Jews. Some studies indicate that it may play a certain role in breast cancer (BC) incidence in Eastern Europe.
Material and methods: We analyzed the impact of BRCA1 5382insC founder mutation in BC predisposition in St.-Petersburg, Russia. In order to enhance the design of the study, we recruited a significant number of patients with "extreme" level of BC susceptibility (bilateral breast cancer (biBC) patients and/or cases with affected first-degree relative(s) and/or young BC cases) as well as an additional "cancer tolerant" control group consisting of elderly tumor-free women. BRCA1 5382insC allele was detected by allele-specific PCR.
Results: The BRCA1 5382insC carriers constituted as many as 16/184 (9%) familial and/or early-onset ($\leqslant 40$ years) BC cases and 15/144 (10%) biBC patients. The remaining BC cases, i.e. those selected against the early onset, bilaterality, and history of the disease in first-degree relative(s), showed the 5382insC mutation in 18/709 patients (2.5%). Strikingly, the 5382insC variant was not observed in any of 478 middle-aged healthy female donors or 350 elderly ($\geqslant 75$ years) non-affected women.
Conclusions: When taken together with the literature data, several aspects of this study deserve a critical discussion. 1) Unexpectedly for such a numerous nation as Russians, BRCA1 5382insC founder mutation constitute an indeed significant proportion of "hereditary-like" BC cases; 2) Since high BRCA1 5382insC occurrence was also repeatedly observed in BC-affected subjects from other Slavic countries, one may suspect that an initial allocation of this variant to the Jewish ancestry could have been wrong; 3) If the estimates found in this study are coupled together with our results on the frequency of CHEK2 1100delC (6%) and NBS1 657del5 (1%) variants in "hereditary-like" BC, 2 conclusions can be made: a) 3 simple PCR tests may reveal the genetic cause in 1 out of 6 familial and/or bilateral and/or early-onset BC in Russia; b) "comparison of extremes" approach provides a straightforward tool for the disease association analysis of rare genetic variants.

302 POSTER

Chromosome 22 array-CGH profiling of breast cancer reveals tumor heterogeneity and 340 kb shared region of loss with ovarian cancer

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Breast cancer is the leading cause of death among women in developed countries. Loss of chromosome 22q has been previously established as a common event in breast malignancy, with a frequency of up to 66%. However, despite the number of studies (LOH, metaphase CGH), the identity of putative gene(s) on 22q involved in initiation and/or progression of this tumor remains unknown.
To address this issue, we have performed gene copy number profiling in a set of various stage breast cancers, corresponding surrounding healthy tissue and peripheral blood lymphocytes using a tiling-path chromosome 22 genomic microarray, with an average resolution of 75 kb. The major aberration observed was heterozygous interstitial deletions of various sizes in the telomeric part of 22q. The extent of these deletions varied from 340 kb to 12 Mb. Interestingly, the smallest 340 kb segment is shared with the region of allelic loss previously identified in ovarian carcinoma.
This finding suggests the existence of a common region of 22q, involved in the pathogenesis of these female cancers. The second prevailing type of finding was a complex pattern of low-copy-number amplifications/gains within the proximal half of 22q which were always accompanied by a loss of genetic material in the telomeric part of the chromosome. Our analysis also revealed small deletions in the centromeric region that have been previously reported as normal polymorphisms. Another aim of our project was to identify genetic heterogeneity within the studied tumors. The most remarkable finding was the presence of distinct aberrations in the two samples derived from different locations of the same large tumor.
This clearly demonstrates the co-existence of separate cell populations within the tumor mass and may reflect evolving steps of tumor progression.

303 POSTER

Bilateral breast cancer – clinical features and BRCA1, BRCA2, CHEK2 mutations

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Purpose: The aim of the study was to analyze clinical features of patients with bilateral breast cancer and to determine the contribution of BRCA1, BRCA2 and CHEK2 mutations in analyzed group.
Material and methods: Five hundred and nineteen case history of bilateral breast cancer patients (pts) treated at Cancer Center, Warsaw, Poland were analyzed and genetic mutations were evaluated in 120 of them. The time of observation was 1–56 years, median 24 years. There were 193 (34%) of synchronous (SBC) and 326 (66%) of metachronous (MBC) breast cancers. Mean age of diagnosis of SBC and MBC breast cancer was respectively 57 and 48 years ($p < 0.001$). In pts with MBC median time between detection of cancers were 5 years (range 1–54 years). Family history of breast or/ and ovarian cancer was verified in 37.5% of pts. Kaplan-Meier survival analysis was performed. Kohen-kappa homogeneity test was used regarding histological type and grade of cancers in both breasts of each patient.
Results: The probability of 5-year, 10-year and 20-year overall survival in MBC was 93%, 85% and 64% and in SBC– 82%, 71% and 46%