## P3

### Molecular diagnosis methods of BRCA mutations in breast cancer

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Breast cancer is the most common malignancy among females in the world. It results from genetic and environmental factors leading to accumulation of mutations in essential genes. Approximately 5%–10% of all breast cancers are associated with hereditary susceptibility due to mutations in autosomal dominant genes, such as BRCA1 and BRCA2, p53, PTEN, and STK11/LKB1 in women. The molecular analysis of breast cancer relies on several technical approaches, which allow genetic and physical mapping, characterization of the gene structure, expression studies, and identification of disease-causing mutations. The most common gene changes in breast cancer are those of the BRCA1 and BRCA2 genes. Women who know they carry the mutated gene may use this information to make more informed decisions about their health care, including whether to use tamoxifen and/or prophylactic surgery to delay or prevent the onset of cancer. Mutation screening methods vary in their sensitivity for BRCA1 and BRCA2. Nearly 2,000 distinct mutations and sequence variations in BRCA1 and BRCA2 have already been described. Methods widely used in research laboratories miss nearly a third of the mutations that are detected by DNA sequencing. In addition, large genomic rearrangements are missed by most of the techniques, including direct DNA sequencing, currently used for clinical testing. Such rearrangements are believed to be responsible for 10% to 15% of BRCA1 inactivating mutations. There is no single perfect method to screen for unknown mutations; combinations of these methods may be necessary for accurate genetic diagnosis. This overview will consider the nature of breast-cancer susceptibility genes, theirs function in breast cancer and comparison of novel molecular diagnosis methods for mutation detection in these genes. It covers the methods used for detection of unknown and known BRCA mutations, namely the Two-Dimensional Gene Scanning (TDGS), single-strand conformation polymorphism (SSCP), heteroduplex analysis (HDA), Denaturing High-Performance liquid chromatography (DHPLC), DNA microarray technology, Real time PCR, Mass spectrometry, Allele-specific PCR, Multiplex mutagenically separated PCR, and the Protein truncation test. The methods such as allele-specific amplification (ASA) and multiplex mutagenically separated PCR can detect one mutant allele in a background of 104–106 wild-type alleles but they are not amenable to automated, high-throughput, and multiplexed applications.

## P4

### BRCA1 gene mutation in exon 20 (5382insC) is frequent in patients from breast and/or ovarian cancer families from Eastern part of Poland

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Mutations in BRCA1 gene predispose a carrier to breast and/or ovarian cancer development. It is known, that mutations in this gene very rare occur de novo and have founder character. This peculiarity makes the identification of patients with mutations and consequently increased risk of breast and ovarian cancer development much easier. For Polish population there were discovered 5 the most frequent mutations in BRCA1 gene: 5382insC (exon 20), C61G (exon 5), 4153delA (11p region of exon 11), 185delAG (exon 2), and 3819del5 (11o region of exon 11). Still there is no enough information about founder mutations in BRCA1 gene for population from Eastern part of Poland.

**The aim of the study:** To seek three - 5382insC, C61G, 4153delA - polish recurrent mutations of BRCA1 gene in patients from Eastern region of Poland.

**Material and methods:** The studied group (168 patients from 143 families) consisted of breast cancer patients and healthy persons with breast and/or ovarian cancer aggregation in family history, who live in Eastern part of Poland.

DNA of patients was isolated from peripheral blood cells, and then was subjected to analysis with the help of MULTIPLEX method (patent: PL 185957) based on simultaneous amplification of three examined BRCA1 regions. Amplification of exon 20 and exon 11p was mutation specific and was yielded only in presence of the mutations; while PCR products of exon 5 was obtained in all probes and subjected to digestion with enzyme AvaII in order to reveal the mutation.

**Results and conclusions:** We detected 5 (3.5%) families with mutation in BRCA1 gene and all mutations were 5382insC (exon 20), that let us to conclude this BRCA1 mutation the most frequent in patients from Eastern part of Poland.

Among mutation carriers' families there were families with the only breast cancer (3 families) and the only ovarian cancer (1 family) as well as both cancers (1 family) presence in family history. In these families except breast and ovarian cancers also malignancies of lung, uterus and liver were found.

The lack of histopathological data of all breast cancer patients with mutation in BRCA1 gene did not allow to perform statistical analysis of dependence of histological breast cancer origin upon the presence of 5382insC mutation. Nevertheless, it is worth to note, that in our study patients with BRCA1 gene mutation developed breast cancer of ductal and lobular origin.

## P5

### Family syndromes of cancer of female reproductive organs in Chernivtsi region

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The features of pathogenesis of cancer of female reproductive organs are defined by the endogenous factors – endocrine metabolic impairments and genetic factors. The study of the