the program were compared with breast carcinomas detected in 313 female relatives outside the program and with a standard population documented in the local tumor registry.

Results: The acceptance rate for the surveillance program was 85%. Overall, 41 primary or secondary breast carcinomas were detected. The average detection rates were 89.6/1000 for mutation carriers, 47/1000 for high risk and 24.7/1000 for moderate risk women compared to 1/1000 in the local tumor registry. In a retrospective analysis these tumors were compared with tumors detected in relatives of these women outside the program and tumors documented in the local registry. Overall, 83% of the screen detected tumors were node negative and 85.4% were pre-invasive or smaller than 2 cm. In comparison, of the tumors detected in female relatives outside the program only 48% (p=0,0003) were node negative and 44% (p<0,0001) were pre-invasive or smaller than 2 cm. Of tumors gathered in the local tumor registry 56% (p=0,003) were node negative and 42% (p<0,0001) were pre-invasive or smaller than 2 cm.

Discussion: Prospective cancer detection rates in proven or suspected carriers of mutations in the BRCA1 or BRCA2 gene were significantly greater than expected in the average-risk population. A structured screening program including CBE, US, MG and MRI is effective in the early detection of breast carcinomas in this risk group and should be offered to these women as a matter of routine.

P4

The presence of hereditary BRCA1 gene mutations in women with familial breast cancer or familial ovarian cancer and the frequency of the occurrence of these tumours in their relatives

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In 48 women with familial breast cancer as well as in 22 women with familial ovarian cancer, the presence of patogenic mutations in BRCA1 gene were found in 35.4% or 54.6% of patients respectively. From the patients possessing mutations we created two groups: the CaM - probands with breast cancer and CaOv - with ovarian cancer. The probands with breast cancer were younger by a mean of 5 years, then the probands with ovarian cancer (p=0.048).

Methods: The PCR-SSCP procedure was used for seeking mutations in the BRCA1 gene. Fragments suspected of mutation presence were subjected to nucleotide sequencing.

Results: In the CaM group, which consisted of 17 women with breast cancer the following mutations in the BRCA1 gene were detected: 5382insC, T300G, 3819del5 and IVS20+60ins12. The probands of the CaM group, and their relatives, developed a total of 49 breast and ovarian cancers. Among all these tumours the breast cancers of probands made up 34.7%, the breast cancers of probands' relatives made up 57.1% and the ovarian cancers of probands and their relatives made up only 8.2%. The CaOv group consisted of 12 probands with ovarian cancers in whom we detected only 2 kinds of mutations: 5382insC and 185delAG. The probands of the CaOv group, and their relatives, developed a total of 38 ovarian and breast cancers. Among all these tumours the ovarian cancers of the probands made up 31.6%, the ovarian cancers of their relatives made up 34.2% and the breast cancers of the relatives 34.2% of tumours. In probands with breast or ovarian cancer the predominant mutation was the 5382insC – in the BRCA1 gene detected in 76.5%, and in 91.7%. Despite the predominant presence of the same mutation in probands from both groups the ratio of the number of breast cancers to the number of ovarian cancers in their relatives differed significantly (p=0.0003).

Conclusion: This data shows, that the presence of the 5382insC mutation in the BRCA1 gene is not always associated with the development of ovarian cancer. It is very likely that the development of ovarian cancer requires some additional factor, which is common among the familial ovarian cancer patients, and is almost inexistent among the familial breast cancer group of patients. On the other hand the development of ovarian cancer at a later age than breast cancer in probands suggests that there exist some factors, which slow down the development of ovarian cancer, or which accelerate the development of breast cancer.

P5

The analysis of genetic polymorphisms in CYP1B1 and COMT genes in breast and endometrial cancer patients

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Breast (BC) and endometrial (EC) cancer are known to be severe malignant diseases, characterized by unfavorable consequences for women's health. We focused our comparative study on the impact of genetic polymorphisms in CYP1B1 and COMT genes into the individual predisposition for the development BC or EC. CYP1B1 and COMT are two enzymes responsible for the synthesis and inactivation of catecholestrogens. Polymorphic forms of these enzymes were shown to differ in their enzymatic activities. Hence, inherited alterations in the activity of COMT and CYP1B1 hold the potential to define differences in cancer risk associated with estrogen-induced carcinogenesis. We analysed 3 polymorphisms in CYP1B1 gene: Arg48Gly, Ala119Ser, Val432Leu and Val158Met polymorphism in COMT gene. By using standard RFLP (restriction fragments length polymorphism) method we have analysed breast cancer patients (N=210), endometrial cancer patients (N=138) and control individuals (N=152). Neither for breast cancer nor for endometrial cancer we have found statistically significant association with COMT polymorphism. At the same time we have demonstrated that Arg48 CYP1B1 polymorphic form, characterised by Shimada et al., as a form with the highest activity for the 4-hydroxylation of the estrogens, is strongly

associated with increased breast cancer risk (OR 3.22, 95% CI 2.34-4.43) and endometrial cancer risk (OR 2.43, 95% CI 1.72-3.44). An increased risk for the development both breast cancer (OR=2.18, 95% CI 1.58-3.01) and endometrial cancer (OR=2.52, 95% CI 1.78-3.56) was associated also with another CYP1B1 polymorphic form – Ala119 CYP1B1. Statistically significant increase of risk for the development of endometrial but not breast cancer was shown to be associated with CYP1B1 Val432Leu polymorphism. This finding can be considered as a result of a higher estrogen-dependency of the endometrial tissue compared to breast tissue, and hence higher sensitivity of the endometrium tissue to the genotoxic action of catecholestrogens. We consider our results to be useful for further analysis of these two diseases regarding their estrogen-dependency and prevention. Also, the revealed associations provide a new detail to the whole picture, illustrating the impact of genetic variations in the genes of estrogen metabolizing enzymes to the individual breast and endometrial cancer susceptibility. Partly supported by the Norwegian Cancer Society and RFBR (03-04-49282).

P6

A new family of KIAA1245 genes with and without the HERV-K LTRs in their introns

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A transcript containing the long terminal repeat (LTR) and the sequence homologous to the KIAA1245 mRNA fragment were revealed among the transcribed LTRs of human endogenous viruses of the K family in normal and tumor tissues. Ten other sequences with a high level of homology to the KIAA1245 mRNA were found in the GenBank. The intron-exon structures were determined for all the sequences, and their exon sequences were compared. The comparison showed that they differ both in the extent of the exon homology and in the presence or absence of the HERV-K LTR in the third intron. The revealed sequences form a new gene family that comprises at least four subfamilies. Two of these subfamilies have the LTR, and the other two do not. We showed by PCR that the LTR was integrated into the introns after the divergence of the orangutan evolutionary branch from other hominoids but before the divergence of the gorilla branch, i.e., 8-13 million years ago. The total expression of the genes of this family was examined in a number of tissues. It was shown that LTR-containing genes of this family expressed in tumor, embryonic tissues and in transformed human cell cultures, in explored normal tissues of the mature organism the expression of genes of this family was not detected.

P7

The genetic consultation of the girls from risk groups of developing tumors of reproductive organs

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The diagnosis of ovarian tumors in girls is made at present as a chance finding. Taking into account that the doctors have not so extensive clinical experience we may conclude that mistakes in diagnostics of ovarian tumors on early stages have reached rather considerable figures. The problem is still more urgent because of increasing number of ovarian cancer cases in women. That is why special attention should be paid to the question of finding tumors of this localization in children's age. The comprehensive study of genetic and hereditary factors, which determine the origin of ovarian tumors in girls, can promote the solving of this problem. It is known, the younger is the patient with tumor the bigger is hereditary contribution in its occurrence (H. Lynch, 1984). First of all in our research we performed clinico-genealogical analysis of 21 girls who were operated on ovarian tumors. Their age was from 4 to 16. Teratomas were found in 10 girls, serose cilioepithelial formations - in 11. The clinico-genealogical investigation resulted in interesting data: there were cases of ovarian cancer, cancer of mammary gland and uterus in close relatives (a mother, a sister, a grandmother) in 14 out of 21 genealogies. Those 14 girls primordially had a high genetic risk for developing tumors of the reproductive sphere. Working out the problem of active diagnostics of ovarian tumors in girls, we made genealogical analysis of 520 probands - women with ovarian cancer. Among their relatives 34 girls were chosen (the 1st stage of relationship) aged from 3 to 15 years who had never been examined by a gynecologist before. Those girls made up the group of high genetic risk. They underwent the following examinations: ultrasound diagnostics of the organs in minor pelvis, computed tomography and rectal-abdominal examination of necessity. This screening program allowed finding out ovarian cysts for the first time (1 teratoma, 2 cystomas) in 3 girls aged 9, 12 and 14. Those cysts had not manifested themselves before the examination. The rest of the girls are under dispensary supervision twice a year. The given data lead to the conclusion that genetic approach may become rather effective in solving the problem of early diagnostics and prevention of ovarian tumors in girls, especially in genetic risk groups. While giving effective preventive help to children with the risk of malignant tumor developing we consider that the following measures are necessary to be taken: – to organize dispensary contingent of persons with high genetic risk of cancer development; – to arrange clinical monitoring of their state of health.