Finland 18 different *BRCA1/2* mutations have been found. Eleven of these mutations are recurrent (including four founder mutations unique to Finland) and one of 18 is unique to one family (4081insA). We have studied 38 Eastern Finnish breast/ovarian cancer families for *BRCA1* and *BRCA2* germline mutations. The 4081insA mutation was detected in PTT analysis and it was confirmed by heteroduplex, sequencing and haplotype analysis. The insertion of an adenine causes frameshift, which leads to a translation terminating signal and protein truncation at codon 1288. The 4081insA mutation is in the *BRCA2* gene ovarian cancer cluster region (OCCR) in exon 11. We screened a family of the index patient, her three brothers and four sisters. Mutation was found in three sisters and one brother, in addition to the index patient and one of her three sons. The 4081insA mutation is rare and has a high penetrance; four of six mutation carriers in the family are affected with breast (two cases) or ovarian cancer (two cases). There were no other cancer cases in the family. Two mutation carriers, both males, at the age of 76 and 59 years, are so far apparently healthy with no symptoms. The four sisters each had an advanced type of breast or ovarian cancer with a poor prognosis. However, they all had a good response to treatment and after 9 to 19 years follow-up time no recurrence has been seen and all are alive and well. Although the mutation is highly penetrant, the breast and ovarian cancer patients carrying it, in this family, seem to have an exceptionally good clinical course.

PI-04 Breast cancer in young women: prevalence of LOH at *p53*, *BRCA1* and *BRCA2*

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Previous studies have shown that breast cancers show more aggressive pathological features in younger women than those occurring in older women. These findings have raised the question whether differences are present at the molecular level. In order to examine genetic alterations associated with early onset breast cancer 31 cases, selected for age under 35 at diagnosis, were examined for loss of heterozygosity (LOH) and microsatellite instability (MI) in three key chromosomal intervals: 17p13 (p53), 17q11–22 (*BRCA1*) and 13q12–14 (*BRCA2*). The cases selected had no obvious family history. DNA was extracted from formalin-fixed paraffin embedded normal and tumour tissue (whole section and microdissected DNA) and analysed by PCR amplification of microsatellite repeat markers. Products were resolved on 10% non-denaturing polyacrylamide gels and silver stained.

28/31 (90%) cases exhibited LOH for at least one marker and 19 (61%) cases showed LOH at 2 or more markers. There was no MI detected. The frequency of LOH detected for each of the markers was as follows: 17p, D17S796 (37%) and D17S799 (61%); 17q, D17S855 (65%) and THRA1 (41%); and 13q, D13S171 (48%). These frequencies are higher (apart from THRA1) than those previously reported for unselected series of breast cancer. Other markers are currently being investigated. These results suggest that LOH at these regions could be related to early onset breast cancer and to poor tumour prognosis.

PI-05 *BRCA1* mutation analysis in breast and ovarian cancer families from Greece

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We have been constructing a genomic DNA database from breast/ovarian cancer patients with a family history, in collaboration with several Greek hospitals. The criteria used for the selection of high-risk families are those accepted universally. In the present study we report three frameshift mutations in *BRCA1*. These mutations were found in female patients with a family history of breast/ovarian cancer, and are all located in exon 11. Mutation identification was made using PTT and direct sequencing. The first mutation identified is 3741insA (codon 1208), carried by a woman who developed bilateral breast cancer at age 31 with her mother's sister affected with breast cancer at age 35. This mutation is reported only once in the BIC database. The second case is a woman with ovarian cancer carrying the mutation 1623del5-TTAAA (codon 502). Her daughter developed breast cancer and her mother endometrial cancer. This mutation has been reported 6 times in the BIC database. The third *BRCA1* mutation, 3099delT (codon 994) is a novel mutation and was found in a woman with ovarian cancer at age 33, with her sister and mother affected with ovarian cancer at different ages. Her grandmother was also affected with breast and ovarian cancer. We have also screened breast/ovarian patients with a family history for two mutations with strong founder effects, 22 patients for 185delAG and 26 patients for 5382insC. None of these mutations was found, indicating that their frequency in Greece might be quite different from those reported by