Population Screening of CHEK2 Mutations in Poland

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Mutations in the CHEK2 gene confer an approximately two-fold increase in the risk of cancer in many organs including the breast, colon, kidney, prostate and thyroid. In addition, we have recently identified a positive association of similar magnitude between a CHEK2 mutation and bladder cancer, endometrial cancer and low-grade ovarian cancer (unpublished data). Surveillance is available for most CHEK2-associated cancers. CHEK2 is not a high-risk gene, but it is associated with multi-cancer susceptibility, and founder alleles in CHEK2 are common in Poland (5.5% of the general population); therefore CHEK2 is responsible for development of more cases of cancer in Poland than founder mutations known to date in high-risk genes (including those in BRCA1, MSH2 and MLH1).

In 2005 in cooperation with the Center of Medical Diagnosis and Hematology (BIOS) and the journal Wprost we performed population screening of CHEK2 mutations in Warsaw. This study was started by publication of an article describing the association of the CHEK2 gene and multi-site cancer predisposition. Readers of Wprost journal were invited for genetic consultation and CHEK2 gene testing. Patients who responded to the invitation were interviewed in the BIOS centre. During the interview the goals of the study were explained, informed consent was obtained, a first session of genetic counselling was given and a blood sample was obtained for DNA analysis. A detailed family history of cancer was taken from all patients (first- and second-degree relatives included).

During a period of 6 months, 3,826 individuals participated in this study. We identified: 192 carriers of a CHEK2 mutation, 240 families with hereditary susceptibility to breast and/or ovarian cancer, 62 families with familial colorectal cancer (including HNPCC). In addition, BRAC1 testing was performed in all individuals with a positive family history of breast or ovarian cancer. Twenty-one BRCA1 mutation carriers were identified. CHEK2 and BRCA1 mutation status was investigated using two independent blood samples. Then, all patients were invited for a second session and final genetic counselling was given. Appropriate surveillance was recommended for patients with familial cancer aggregations, as well as for BRAC1 and CHEK2 mutation carriers. We believe that this action broadened the knowledge about the role of genetic counselling and DNA testing in cancer prevention in Poland. It has also shown that many people in our population need such counselling and surveillance. We believe that this action will help reduce cancer morbidity and mortality in Poland.