

Short Communication

Molecular Cancer Genetics in Eastern and Central Europe

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Over the last 10 years 25 different hereditary cancer syndromes have been identified and attributed to specific germline mutations in various inherited cancer genes. Though hereditary cancer syndromes are rare, their investigation has begun to provide unprecedented insights into the molecular origin and pathogenesis of various forms of cancer [3]. With the cloning of cancer-predisposing genes it has become possible to offer predictive DNA testing to family members at risk. For some well-defined, but uncommon inherited cancer syndromes (FAP, MEN2A, Retinoblastoma, VHL and Neurofibromatosis 1 and 2) genetic testing for cancer susceptibility is already part of the clinical management of families affected with cancer. For those inherited cancer syndromes where the risks associated with a predisposing mutation are less certain or effectiveness of preventive strategies are not confirmed, the use of genetic testing for cancer risk is not without controversies [11]. This second group includes the most common inherited cancer syndromes (such as hereditary breast cancers and hereditary non-polyposis colorectal cancers). At least five genes have been identified which may predispose to breast cancer. Germline mutations of BRCA1 and BRCA2 are thought to be responsible for the vast majority of inherited breast cancers [4].

Since the recent identification of BRCA1/BRCA2 genes [7,18], more than 600 distinct mutations in BRCA1 (and close to 600 in BRCA2) have been described (Breast Cancer Information Core (BIC) database: http://www.nhgri.nih.gov/Intramural_research/Lab_transfer/Bic/).

MOLECULAR CANCER GENETIC CENTERS IN EASTERN- AND CENTRAL EUROPE

Centers specializing in the study of inherited predisposition to cancer — particularly breast cancer — have been established in Hungary [1,2,8,9,12], in Poland [6,14] and in Austria [17]. In eight other countries (Czech Republic, Latvia, Slovakia, Slovenia, Russia, Turkey, Ukraine, Yugoslavia) genetic centers are being developed, and molecular cancer genetic studies are carried out in international collaboration. (This information is from cancer centers registered by the European Association for Cancer Research.)

MOLECULAR CANCER GENETIC SERVICE IN HUNGARY

A Clinical Cancer Genetic Center has been developed at the National Institute of Oncology, Budapest as part of research projects. The patients are usually referred by oncologists, surgeons, gynecologists and radiodiagnostics,

and are seen by a clinical cancer geneticist, oncologist and trained nurses. The family history of cancer is collected first, and verified by reviewing the clinical and histological data. The risk is calculated. The indications for BRCA testing include:

- First degree relative, age at diagnosis of breast cancer < 35 years,
- two first degree relatives with breast cancer, mean age at diagnosis < 50 years, or with ovarian cancer at any age,
- three close relatives with breast/ovarian cancer in two successive generations,
- one male breast cancer at any age.

It takes 3–6 months to perform standard DNA testing for BRCA1 and BRCA2 genes.

BRCA1/BRCA2 MUTATION STUDIES IN CENTRAL- AND EASTERN EUROPE

The proportion of recurrent BRCA1/BRCA2 mutations varies widely among populations (reviewed in [15]). Several mutations in BRCA1 and BRCA2 genes have been reported worldwide indicating migrations from Eastern and Central Europe, however the pattern of BRCA1/BRCA2 mutations in this region is just beginning to emerge [1,2,5,8,9,12,13,14].

In order to evaluate the role of inherited BRCA1/BRCA2 mutations in Eastern and Central Europe, we are conducting an international collaborative study on patients from eight Eastern European cancer centers (Olah et al., 1999 in preparation). Until now 150 breast/ovarian cancer families were screened for mutations in the BRCA genes by combined SSCP/HD analysis, PTT and direct sequencing. Only a small number of founder mutations accounted for the vast majority of all BRCA1 mutations in each population [2,6,8,10,16]. Unlike the case of BRCA1, no such recurrent mutation patterns were observed for the BRCA2 gene. Further molecular genetic studies will help to better understand the pathogenesis of breast cancer.

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