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Founder Mutations of BRCA1 and BRCA2 in North American Families of Polish Origin That Are Affected with Breast Cancer

To the Editor:

We have recently identified five founder mutations in a panel of 66 families with breast/ovarian cancer who were ascertained in western Poland (Górski et al. 2000). Of the 35 families with mutations, 33 had one of the five recurrent BRCA1 mutations, including 18 families with the 5382 insC mutation. Only one BRCA2 mutation was found in the 66 families.

A significant proportion of North American families claim Polish ancestry. We were interested to see whether the same mutations were present in families residing in North America who claimed Polish ancestry. This information might be useful for genetic counseling and to facilitate mutation detection.

We attempt to record ethnicity for all families affected by breast cancer listed in our database. From a source of 1,010 families who underwent genetic evaluation, we identified 23 families of Polish ancestry. All families were tested for the five Polish founder mutations. We also completed the protein truncation test (PTT) of exon 11 of BRCA1 and exons 10 and 11 of BRCA2. A few families had mutations identified through an earlier study (Serova et al. 1997).

No BRCA2 mutation was seen in the 23 families, but 10 BRCA1 mutations were found (43%), including 6 5382insC mutations. The other mutations included one instance each of 964del4, IVS16-581del1014, C1806T, and 4184del4. None of these were present in the original panel of Polish families (Górski et al. 2000). We identified four other families in our database who did have one of the putative Polish founder mutations (other than 5382insC and 185delAG)—but none of these families were Polish. There were two unrelated Czech families with the 3819del5 mutation, one Lithuanian family with the 4153delA mutation, and one family of mixed European ancestry with the T300G mutation. These three mutations have been reported to the Breast Cancer Information Core database 13 times, 7 times, and 46 times, respectively. Only two of the families reported to BIC were said to be Polish (both had the 3819del5 mutation). The 4154delA mutation is common in Russia (Gayther et al. 1997). In summary, none of the mutations that are common in Poland appear to be specific to the population.

Our results support the claim that the majority of mutation-carrying families with Polish ancestry carry the BRCA1 5382insC mutation, in Poland and in North America. We believe that, when resources are limited, it may be efficient to offer testing for this mutation prior to undertaking a complete evaluation for Polish families seeking genetic testing. The low frequency of BRCA2 mutations in Polish families, in Poland and in North America, remains to be explained.

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Vacuoliting Megalencephalic Leukoencephalopathy

To the Editor:

In a report in the February 2000 issue of the *Journal,* Topçu et al. (2000) reported on the mapping of vacuoliting megalencephalic leukoencephalopathy with subcortical cysts to chromosome 22q, in a 3-cM interval between the markers D22S1161 and n66c4. The centromeric boundary was defined by a recombination event with the marker D22S1161. However, how n66c4 was determined as the telomeric boundary is not clear. n66c4 reaches its maximal LOD score at $\theta = .00$. The

highest multipoint LOD score was also reached with that marker, and the haplotypes shown in figure 2 of the report do not reveal any recombination events with this marker, either in the patients or in the unaffected sibs. The interval containing the gene should therefore be defined as being between D22S1161 and the telomere.

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