GENETICS

All in the family

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URLs

PALB2
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=full_report&list_uids=79728

BRCA2
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=full_report&list_uids=675

Breast cancer
http://www.cancer.gov/cancertopics/types/breast/

BRCA1
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=full_report&list_uids=672

Partner and localizer of BRCA2 (PALB2) binds to and promotes the localization of BRCA2 to DNA double-strand breaks, enabling proper homologous recombination-mediated DNA repair. Given that mutations in *BRCA2* and other breast cancer susceptibility genes account for less than half of familial breast cancers, Robert Winqvist, David Livingston, Hannele Erkko, Bing Xia and colleagues investigated whether *PALB2* mutations also increase breast cancer susceptibility.

The authors identified an exonic *PALB2* mutation, c.1592delT, that occurred at a significantly higher rate in Finnish *BRCA1* and *BRCA2* mutation-negative breast cancer families than in controls. Functional testing in cell lines indicated that this mutation produced a truncated protein with true loss of function — decreased binding affinity for BRCA2 and loss of homologous recombination and DNA crosslink repair were observed.

PALB2 c.1592delT mutations were also observed in 18 of 1,918 cases (about 1%) of unselected female breast cancers. This is about fourfold more than the mutation rate in controls, and is noteworthy given that *BRCA1* and *BRCA2* mutations in Finnish breast cancer together account for 1.8% of cases. Furthermore, many of these 18 cases had a family history of breast and other cancers.

The authors also looked at Finnish prostate cancer cases and found one family in which all male carriers of *PALB2* c.1592delT developed prostate cancer (with the exception of one carrier who died early at 52 years of age).

These data argue that *PALB2* is a significant breast cancer susceptibility gene that might also be associated with some cases of familial prostate cancer.

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ORIGINAL RESEARCH PAPERS Erkko H. *et al.* A recurrent mutation in *PALB2* in Finnish cancer families. *Nature*, 7 Feb 2007 (doi:10.1038/nature05609)