LINK TO ORIGINAL ARTICLE

Breast and prostate cancer: familial associations

Kari Hemminki, Asta Försti and Bowang Chen

Kari Hemminki, Asta Försti and Bowang Chen are at the Division of Molecular Genetic Epidemiology, German Cancer Research Center (DKFZ), Im Neuenheimer Feld 580, 69120 Heidelberg, Germany.

Kari Hemminki and Asta Försti are also at the Center for Primary Care Research, Lund University, Malmö 20502, Sweden.

Kari Hemminki is also at the Center for Family and Community Medicine, Karolinska Institute, Huddinge 14183, Sweden.

Correspondence to K.H.
e-mail: K.Hemminki@dkfz.de

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In a recent Opinion article by Gail Risbridger and colleagues, Breast and prostate cancer: more similar than different (*Nature Rev. Cancer* **10**, 205–212 (2010)), the extensive biological similarities of the hormone-dependant pathways of breast and prostate cancers were discussed[1]. They also pointed out that mutation of *BRCA2* predisposes to both breast and prostate cancer, and that mutation carriers with prostate cancer have a poorer survival rate than patients with prostate cancer who do not have *BRCA2* mutations[2]. However, whether the biological similarities would lead to a familial aggregation of these cancers was not discussed. Familial associations between breast and prostate cancer would imply a shared genetic susceptibility that might go beyond mutations in *BRCA2*. The recently characterized low-penetrance genes for these cancers provide few clues about a possible shared susceptibility, with the exception of the 8q24 locus. However, the associated single nucleotide polymorphisms found at this locus are not concordant[3–6].

We have used the nationwide Swedish Family Cancer Database, the world's largest data set of its kind[7], to study shared familial clustering of various cancers, including breast cancer with prostate cancer[8]. This study identified 10,553 sons (0 to 70 years old) and 107,518 fathers (unlimited age) with prostate cancer, among a total of 170,000 cancer patients in the offspring generation and more than 800,000 cancer patients in the parental generation. We calculated familial standardized incidence ratios (SIRs) and confidence intervals (CIs) for prostate cancers and other cancers in family members[8,9]. Separate proband groups were used: affected parents only, affected siblings only, and affected parents and siblings, to suggest genetic modes of inheritance and level of penetrance[10]. The methods of calculation have been described.

For breast cancer, we found that the SIRs were 1.64, when the mother was diagnosed with breast cancer, 1.91 when the sister was diagnosed and 3.83 when both mother and sister were diagnosed. In discordant analysis when probands were diagnosed with prostate cancer, the SIRs for breast cancer were 1.11, 0.96 and 1.62. For prostate cancer, each of the concordant risks was higher, particularly for brothers (3.40), and fathers and brothers (6.71); the corresponding SIRs for prostate cancer in breast cancer families were 1.19 when the mother was diagnosed with breast cancer, 1.07 when the sister was diagnosed and 1.55 when both mother and sister were diagnosed. All these discordant SIRs were significant at a 5% level (TABLE 1), except those among siblings; many were significant even at a 1% level. When prostate cancer was diagnosed before the age of 60 years in sons of a mother with breast cancer the SIR was 1.47 ($n = 41$, 95% CI 1.17–1.82)[8].

Considering that *BRCA2* mutations account for only a small proportion of familial breast cancers in Sweden it is unlikely that the common parent–offspring aggregation of breast and prostate cancers would be explained by these mutations, except in the high-risk families of parent and sibling probands[11]. However, the median diagnostic age of breast cancer was 54 years in families with both father and brother diagnosed with prostate cancer, and this was higher than that found in *BRCA2* mutation carriers (<50 years)[12]. Therefore, these data suggest that only a small proportion of the prostate–breast aggregation in families was explained by *BRCA2* mutation and that new shared susceptibility genes are likely to exist.

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Competing Interests
The authors declare no competing financial interests.

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Table 1 | **Familial risk of breast and prostate cancer**

Site	Parent proband			Sibling proband			Parent and sibling proband		
	O	SIR	95% CI	O	SIR	95% CI	O	SIR	95% CI
Familial risk for concordant prostate and breast cancer									
Breast*	3656	1.64‡§	1.59–1.70	1855	1.91‡§	1.79–2.04	248	3.83‡§	3.38–4.33
Prostate	1481	1.97‡§	1.87–2.07	355	3.40‡§	3.06–3.78	117	6.71‡§	5.55–8.05
Risk of breast cancer in families with patients with prostate cancer									
Breast	2281	1.11‡§	1.06–1.15	179	0.96	0.82–1.11	53	1.62‡§	1.21–2.11
Risk of prostate cancer in families with patients with breast cancer									
Prostate	604	1.19‡§	1.09–1.29	284	1.07	0.95–1.20	32	1.55§	1.06–2.20

CI, confidence interval; O, number of observed cases; SIR, standardized incidence ratio.*All data were taken from REF. 8, except the Breast* row, which originates from REF. 10. ‡99% CI does not include 1.00. §95% CI does not include 1.00.