MAPPING NOVEL BREAST CANCER SUSCEPTIBILITY GENES BY LINKAGE ANALYSIS OF AUSTRALIAN MULTIPLE CASE KINDREDS

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We have been using the resources of the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer (kConFab) and of the Australian Breast Cancer Family Study (ABCFS) to identify kindreds suitable for mapping high penetrance breast cancer susceptibility loci other than BRCA1 and BRCA2. A 10 cM genomewide search was carried out in 40 families in which BRCA1 and BRCA2 mutations had been excluded with high probability. The highest LOD score under heterogeneity (HLOD) was 2.16 (non-parametric LOD 1.83, P = 0.04) at the 11p telomere; several other regions with HLODs = 1.5–2.0 also merited investigation using fine mapping but have so far neither been confirmed or rejected by these analyses. Subsets based on age of onset and presence of other cancers correlated to some extent with particular linkage peaks and several regions (notably 2q and 13q) corresponded to areas of suggestive linkage reported recently in more limited studies of other cohorts. A large collaborative analysis of these data together with those from similar studies undertaken by members of the international Breast Cancer Linkage Consortium (BCLC) is under way. It is therefore likely that further major breast cancer susceptibility loci will be localised in the near future. The complementarity of these studies with genetic association, candidate gene and tumour-based approaches will be discussed.

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