GENETICS

Partners in crime

> Three genome-wide association studies recently reported in the same issue of *Nature Genetics* identify several new susceptibility loci for breast and ovarian cancer.

Over the past few years, genome-wide association studies (GWAS) have been useful in identifying genetic variations that are associated with risk for several types of cancer. Three GWAS recently reported in the same issue of *Nature Genetics* identify several new susceptibility loci for breast and ovarian cancer.

Gayther, Pharoah, Easton and collaborators re-analysed the data from a previous GWAS that had allowed them to identify an ovarian cancer susceptibility locus. This time they stratified cases by histological subtype and specifically considered risks associated with the serous subtype of ovarian cancer. They identified single nucleotide polymorphisms (SNPs) in four different loci that were associated with ovarian cancer risk, one with decreased risk (at 8q24) and three with an increased risk (at 2q31, 3q25 and 7q21). The authors examined the expression of the candidate genes in these loci: *MYC*, *TIPARP* (which encodes a poly(ADP-ribose) polymerase (PARP)), *HOXD1* and *HOXD3* (which are involved in embryogenesis and organogenesis) and *SKAP1* (which encodes a Src-related phosphoprotein). There were significant differences in the patterns of expression of all of these candidate genes between normal and ovarian cancer cells, suggesting that they may have functional roles in the development of ovarian cancer.

These authors also led an independent three-phase GWAS to identify genes associated with ovarian cancer survival. In the first two phases of this study, they identified two SNPs that were associated with survival and located at 19p13. Data from the third phase, however, revealed that these SNPs were more significantly associated with susceptibility to ovarian cancer than survival, especially when the analysis was restricted to patients with the serous subtype of ovarian cancer. One SNP is located in *C19orf62* (also known as *MERIT40*), which encodes a protein that regulates the stability of BRCA1 at sites of DNA damage, and the other SNP lies in *ANKLE1*. Although *MERIT40* was significantly overexpressed in ovarian cancer cell lines, there was no difference in the expression of *ANKLE1* between normal and ovarian cancer cells.

In a separate study, Easton, Couch and collaborators also identified an association between 19p13 and breast cancer risk in women carrying mutations in the well-known breast cancer susceptibility gene *BRCA1*. The authors identified a cluster of five SNPs on chromosome 19. Two of these SNPs were located in coding regions that contained the genes *ABHD8*, *ANKLE1* and *MERIT40*. Further studies of the SNPs in the general population identified associations with risk of oestrogen receptor-negative breast cancer and triple-negative (oestrogen receptor-negative, progesterone receptor-negative and ERBB2-negative) breast cancer. The authors speculate that genetic variations that affect MERIT40 expression could modify BRCA1-dependent DNA repair. These three studies indicate that focusing on particular subtypes of cancer can allow the identification of genetic variations that might contribute to different types of cancer, such as the associations of *ANKLE1* and *MERIT40* with both ovarian and breast cancer.

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ORIGINAL RESEARCH PAPERS Goode, E. L. *et al.* A genome-wide association study identifies susceptibility loci for ovarian cancer at 2q31 and 8q24. *Nature Genet.* **42**, 874–879 (2010) | Bolton, K. L. *et al.* Common variants at 19p13 are associated with susceptibility to ovarian cancer. *Nature Genet.* **42**, 880–884 (2010) | Antonio, A. C. *et al.* A locus on 19p13 modifies risk of breast cancer in *BRCA1* mutation carriers and is associated with hormone receptor–negative breast cancer in the general population. *Nature Genet.* **42**, 885–892 (2010)