GENETICS

BRCA2 mutation offers response and survival advantages

Women with *BRCA1* or *BRCA2* mutations have an increased risk of developing ovarian cancer. Therefore, as part of The Cancer Genome Atlas (TCGA) project, Wei Zhang and colleagues undertook a “comprehensive analysis of genomic, epigenetic, and clinical data in the TCGA database to identify not only clinically important associations with *BRCA1* and *BRCA2* mutations but also gain genomic insight into the mechanisms,” explains Zhang. The researchers evaluated the association between *BRCA1* and *BRCA2* mutations and overall survival, progression-free survival, and chemotherapy response in 316 patients with high-grade serous ovarian cancer.

“The most significant finding was that mutations in *BRCA2* but not in *BRCA1* are associated with better progression-free and overall survival and better response to DNA-damaging platinum chemotherapy in patients with ovarian cancer,” highlights Zhang. Using whole-exome deep-sequencing Zhang’s team also showed

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that patients with mutations in *BRCA2* but not in *BRCA1* exhibited a ‘mutator phenotype’ that contained significantly more mutations than wild-type cases. Zhang elaborates, “the better responses of *BRCA2*-mutated cases are likely due to the highly mutated genome, or hypermutator phenotype, which not only provides tumors with a growth advantage but also exposes them to drug-induced DNA

damage and cell death.” Further work is needed to study *BRCA1* and *BRCA2*, which seem to work differently in the DNA-repair process.

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Original article Yang, D. *et al.* Association of *BRCA1* and *BRCA2* mutations with survival, chemotherapy sensitivity, and gene mutator phenotype in patients with ovarian cancer. *JAMA* 306, 1557–1565 (2011)