Nature Reviews Clinical Oncology **11**, 560 (2014); published online 19 August 2014; doi:10.1038/nrclinonc.2014.142

BREAST CANCER

PALB2—a new player in hereditary breast cancer

Loss-of-function mutations in *PALB2* are associated with an increased risk of breast cancer; however, the lifetime risk of this disease for women who have inherited *PALB2* mutations is not known. Marc Tischkowitz and colleagues have now shown that the risk of breast cancer for *PALB2* mutation carriers can be as high as the risk reported for *BRCA2* carriers.

The investigators collected data on 362 individuals with *PALB2* mutations from 154 eligible families, and used a modified segregation-analysis approach to determine the age-specific risk of breast cancer, considering the effects of *PALB2* genotype and residual familial aggregation.

"This is by far the largest study to date and provides the most accurate risk estimates for *PALB2* mutation carriers," comments Tischkowitz. He continues, "we found that a woman with a *PALB2* mutation has a 35% risk of developing breast cancer by the age of 70 years, rising to 58% if there is a strong family history."

The researchers have also reported that the breast cancer risk associated with *PALB2* mutation is higher in younger women (those born after 1960).

Although a large proportion of hereditary breast cancer cases remains unexplained, this study clearly confirms *PALB2* as an important gene in this pathology, together with *BRCA1* and *BRCA2*. Undoubtedly, "these results will help clinicians to better advise and manage those women with *PALB2* mutations", concludes Tischkowitz.

Alessia Errico

Original article Antoniou, A. C. *et al.* Breast-cancer risk in families with mutations in *PALB2*. *N. Engl. J. Med.* doi:10.1056/NEJMoa1400382