Editorial: Genotype matters—tailored screening for germline CHEK2 variants

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A recent editorial was published in *Oncotarget*, titled "Genotype matters: Personalized screening recommendations for germline CHEK2 variants."

Recognized as a moderate-risk gene, CHEK2—responsible for encoding the CHK2 protein, which plays a crucial role in the repair of DNA double-strand breaks—is associated with a 20–40% lifetime risk of breast cancer (BC) by age 85. While CHEK2 pathogenic variants (PVs)

were previously linked to an increased risk of colorectal cancer (CRC), two recent studies have not observed this association.

In their recent work, researchers Adela Rodriguez Hernandez, Rochelle Scheib, Judy E. Garber, Huma Q. Rana and Brittany L. Bychkovsky from Dana-Farber Cancer Institute and Harvard Medical School in Boston, found that a CHEK2 PV does not increase the CRC risk compared with controls (odds ratio 0.62 (0.51–0.76), p

The cancer risks associated with CHEK2 PVs vary depending on the variant type, and risk management strategies should reflect this variability. The CHEK2 c.1100del is the most studied truncating variant and has been crucial to our understanding of the cancer phenotype. Cancer risks seem to be higher with truncating variants compared to missense variants.

"In our study, we postulated that these differences were driven by three common low-risk (LR) missense variants: p.I157T, p.S428F, and p.T476M, all of which have a BC odds ratio of