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Frequency of pathogenic and likely pathogenic variants in genes associated with an increased risk for cancer in patients undergoing population-based carrier screening

Erika Cooper, MS, CGC; Lauren Petrarca, MS, CGC
Labcorp Women's Health and Genetics, Labcorp, Westborough, MA

Introduction

Carrier screening is used to identify individuals at risk for having children with autosomal recessive or X-linked genetic disorders. In some instances, carrier testing may reveal unintended findings, including identifying individuals who have an increased risk of developing cancer. The objective of this study was to investigate the frequency at which individuals test positive on carrier screening for pathogenic and likely pathogenic variants in genes associated with a risk for malignancies. These types of results highlight the need for appropriate pre- and post-test counseling.

Methods

Carrier screens (n=1581), collected from July to November 2021, were analyzed to identify carriers of 4 conditions (6 genes) associated with cancer predisposition: Ataxia-telangiectasia (ATM), Bloom syndrome (BLM), Fanconi anemia (*FANCL*, *BRIP1*, *FANCC*), and Nijmegen breakage syndrome (NBN). All patients had the same carrier screening panel drawn, which included over 500 genes.

Results

Out of the 1581 carrier screens, we identified 20 patients (1.3%) who were carriers for one or more genes associated with cancer predisposition. The number of carriers for each gene is as follows: ATM (8), BLM (3), *FANCL* (3), *BRIP1* (2), *FANCC* (2), NBN (2).

Conclusions

These data suggest that approximately 1.3% of individuals who undergo a carrier screening panel of this size are positive for a variant that may increase their risk to develop cancer. These findings are outside the original intention of carrier screening which is to identify reproductive risks. Additionally, they underscore the need for appropriate pre-test counseling that includes a discussion of the possibility of identifying a variant associated with an increased risk for malignancy. Post-test counseling regarding these results is critical, not only to review reproductive risks, but also to review potential implications for one's own healthcare.

Figures

Table 1. Identified carriers and associated cancer risk

Genes	Number of identified carriers	Associated cancer risks
ATM	8	Breast, ovarian, and pancreatic; emerging evidence suggests an association with prostate cancer
BLM	3	Possible association with colorectal cancer
FANCL	3	Possible association with prostate cancer
BRIP1	2	Ovarian cancer; possible association with female breast cancer
FANCC	2	Possible association with pancreatic cancer
NBN	2	Possible association with prostate cancer

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