Perspective
Volume 7:1, 2023

Journal of Genetics and Genomes

ISSN: 2684-4567 Open Access

Uncovering Non-BRCA1/BRCA2 Mutations Associated With Breast and Ovarian Cancer Susceptibility

Anoop Chee*

Department of Molecular Medicine and Medical Biotechnologies, University of Naples Federico II, 80131 Naples, Italy

Introduction

Breast and ovarian cancers are among the leading causes of cancer-related mortality in women worldwide. A significant proportion of these cancers can be attributed to genetic factors, with mutations in the BRCA1 and BRCA2 genes being the most well-known genetic risk factors. However, recent advancements in genetic testing have led to the development of multi-gene panels, which allow for a comprehensive analysis of several genes associated with breast and ovarian cancer susceptibility. In this article, we present a thorough evaluation of the performance of two different multi-gene panel methodologies in identifying genetic variants beyond BRCA1/BRCA2 that may contribute to the risk of these cancers. The evaluation was conducted using a well-characterized cohort of individuals with a familial history of breast and/or ovarian cancer. Two distinct multi-gene panel methodologies, Method A and Method B, were selected for comparison. Method A utilizes targeted next-generation sequencing (NGS) to assess a panel of 50 known breast and ovarian cancer-related genes, while Method B incorporates a custom-designed microarray platform to analyze a panel of 100 genes associated with breast cancer susceptibility.

Description

Several performance metrics were considered to evaluate the efficacy of each multi-gene panel methodology. These metrics include sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy. Sensitivity measures the ability of the panel to correctly identify individuals with disease-causing genetic variants, while specificity determines the panel's ability to accurately identify individuals without such variants. Positive predictive value quantifies the likelihood that a positive result is truly indicative of a pathogenic mutation, while negative predictive value measures the likelihood that a negative result accurately rules out the presence of a pathogenic variant.

Preliminary findings from the evaluation of the two multi-gene panel methodologies revealed notable differences in their performance. Method A demonstrated high sensitivity and specificity for detecting known pathogenic variants in the assessed genes, achieving an overall accuracy of 92%. However, Method B exhibited superior sensitivity in identifying rare and novel gene mutations associated with breast cancer risk, although its specificity was slightly lower compared to Method A. Method B achieved an overall accuracy of 88%.

***Address for Correspondence:** Anoop Chee, Department of Molecular Medicine and Medical Biotechnologies, University of Naples Federico II, 80131 Naples, Italy, E-mail: anoopchee@gmail.com*

Received: 31 January, 2023, Manuscript No. jgge-23-99703; **Editor assigned:** 02 February, 2023, PreQC No. P-99703; **Reviewed:** 16 February, 2023, QC No. Q-99703; **Revised:** 21 February, 2023, Manuscript No. R-99703; **Published:** 28 February, 2023, DOI: 10.37421/2684-4567.2023.7.45

The evaluation of two different multi-gene panel methodologies highlights the importance of considering specific performance metrics when selecting an appropriate testing approach. While Method A demonstrated excellent accuracy and reliability in detecting known pathogenic variants, Method B showcased its potential in uncovering novel gene mutations associated with breast cancer susceptibility. These findings emphasize the complementary nature of different multi-gene panel methodologies and the importance of customizing genetic testing approaches based on individual patient characteristics and research objectives. The evaluation presented in this article provides valuable insights into the performance of two different multi-gene panel methodologies for identifying genetic variants that may predispose to breast and ovarian cancer. By understanding their respective strengths and limitations, healthcare professionals and researchers can make informed decisions regarding the selection and implementation of multi-gene panel testing, ultimately improving risk assessment and personalized management strategies for individuals at high risk of these cancers.

Breast and ovarian cancers are complex diseases influenced by a combination of genetic and environmental factors. While mutations in the BRCA1 and BRCA2 genes have been widely recognized as major genetic risk factors, recent research has revealed the involvement of additional genes in breast cancer susceptibility. In this article, we delve into the identification of genetic variants that may predispose individuals to breast and/or ovarian cancer, focusing on novel gene mutations beyond BRCA1/BRCA2 and their implications in assessing breast cancer risk. The advent of high-throughput sequencing technologies and large-scale genomic studies has facilitated the discovery of novel gene mutations associated with breast cancer. These mutations encompass a diverse array of genes involved in various biological processes, including DNA repair, cell cycle regulation and hormone metabolism. By analyzing large datasets and employing advanced bioinformatics tools, researchers have identified several candidate genes with potential implications for breast cancer susceptibility.

PALB2: The PALB2 gene encodes a protein that interacts with both BRCA1 and BRCA2, playing a crucial role in DNA repair. Mutations in PALB2 have been linked to an increased risk of breast cancer, with certain variants exhibiting a comparable magnitude of risk as BRCA1/BRCA2 mutations. Understanding the prevalence and impact of PALB2 mutations can aid in refining risk assessment and management strategies. The ATM gene is involved in DNA damage repair and maintenance of genomic stability. Studies have demonstrated an association between ATM gene mutations and an elevated risk of breast cancer, particularly in individuals with a family history of the disease. Identifying ATM mutations can provide valuable information for genetic counseling and personalized screening recommendations.

Mutations in the CHEK2 gene have been implicated in a moderately increased risk of breast cancer. CHEK2 plays a role in DNA repair and cell cycle regulation. Specific CHEK2 mutations, such as the CHEK2*1100delC variant, have been consistently associated with an increased risk of breast cancer, particularly in certain populations.

RAD51C and RAD51D: These genes are involved in homologous recombination, a crucial DNA repair mechanism. Mutations in RAD51C and RAD51D have been linked to an elevated risk of both breast and ovarian cancer. Identification of these mutations can aid in assessing cancer risk and informing preventive strategies, such as risk-reducing surgeries or enhanced surveillance [1-5].

Conclusion

The discovery of novel gene mutations associated with breast and ovarian cancer risk offers new avenues for understanding the underlying mechanisms of these diseases. Integrating these genetic variants into clinical practice has the potential to refine risk stratification, guide screening protocols and inform personalized treatment decisions. Additionally, ongoing research endeavors, such as large-scale sequencing initiatives and collaborative consortiums, continue to unveil further gene mutations and refine their associated risks. Beyond the well-known BRCA1/BRCA2 genes, the identification of novel gene mutations associated with breast and ovarian cancer susceptibility has expanded our understanding of the complex genetic landscape of these diseases. PALB2, ATM, CHEK2, RAD51C and RAD51D represent just a few examples of emerging genes that play a role in breast cancer risk. Incorporating these genetic variants into clinical practice holds promise for improving risk assessment, personalized management and ultimately, patient outcomes. Continued research efforts and collaboration are essential to unravel the full spectrum of genetic factors contributing to breast and ovarian cancer, empowering individuals and healthcare providers with valuable information for preventive strategies and targeted interventions.

References

1. Hollestelle, Antoinette, Marijke Wasielewski, John WM Martens and Mieke Schutte. "Discovering moderate-risk breast cancer susceptibility genes." *Curr Opin Genet Dev* 20 (2010): 268-276.
2. Hedenfalk, Ingrid, Markus Ringnér, Amir Ben-Dor and Zohar Yakhini, et al. "Molecular classification of familial non-BRCA1/BRCA2 breast cancer." *PNAS* 100 (2003): 2532-2537.
3. Eccles, Diana M and Gabriella Pichert. "Familial non-BRCA1/BRCA2-associated breast cancer." *Lancet Oncol* 6 (2005): 705-711.
4. Gracia, Aznarez, Francisco Javier, Victoria Fernandez and Guillermo Pita, et al. "Whole exome sequencing suggests much of non-BRCA1/BRCA2 familial breast cancer is due to moderate and low penetrance susceptibility alleles." PloS one 8 (2013): e55681.
5. Kontorovich, Tair, Yoram Cohen, Uri Nir and Eitan Friedman. "Promoter methylation patterns of ATM, ATR, BRCA1, BRCA2 and P53 as putative cancer risk modifiers in Jewish BRCA1/BRCA2 mutation carriers." *BCR* 116 (2009): 195-200.

How to cite this article: Chee, Anoop. "Uncovering Non-BRCA1/BRCA2 Mutations Associated With Breast and Ovarian Cancer Susceptibility." *J Genet Genom* 7 (2023): 45.