Ambry Genetics
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RESEARCH FOR YOUR PRACTICE

Genetic Testing for Triple Negative Breast Cancer

ARE WE CASTING A WIDE ENOUGH NET?

A collaboration between Ambry Genetics, Mayo Clinic and the Triple Negative Breast Cancer Consortium (TNBCC) published in *Journal of the National Cancer Institute*[1], identified genes beyond *BRCA1* associated with an increased risk of triple negative breast cancer (TNBC).

WHY THIS MATTERS TO YOU

Currently, guidelines recommend *BRCA1/2* genetic testing for women with TNBC diagnosed ≤60y; however, our study supports consideration of multigene panel testing, including genes beyond *BRCA1/2*, for all women with a diagnosis of TNBC, regardless of age of onset or family history of cancer.

BACKGROUND

- TNBC is associated with advanced disease stage and higher grade tumors at diagnosis[2], increased recurrence risks, and poor 5-year survival rates compared to other breast cancers[3].
- TNBC accounts for an estimated 15% of breast cancer in the Caucasian population and 35% in the African American population[4].
- NCCN® guidelines currently recommend *BRCA1/2* testing for women with TNBC diagnosed ≤ age 60. Recommendations for testing other cancer predisposition genes have not yet been established.
- In this study, researchers assessed 10,901 women with TNBC from two separate cohorts undergoing multigene panel testing (MGPT) to better understand gene-specific risks for this cancer type.

10,901
Women with TNBC assessed

POINTS FOR YOUR PRACTICE

- It is critical to identify germline mutations in genes associated with TNBC to better guide medical management.
- The majority of genes found to be associated with an increased risk of TNBC have NCCN® guidelines for increased screening and/or surgical intervention.
- Multigene panel testing, such as BreastNext, should be considered for all women with TNBC to identify pathogenic mutations in genes beyond *BRCA1/2*.

SIGNIFICANT FINDINGS

- 14% of women of any age with TNBC were found to have a germline pathogenic variant via MGPT
- Germline pathogenic variants in *BARD1*, *BRCA1*, *BRCA2*, *PALB2*, and *RAD51D* were associated with a high risk of TNBC (OR >5.0)
- *BRIP1*, *RAD51C*, and *TP53* were associated with moderate risk (OR >2.0) of TNBC
  - *RAD51C* was associated with a high risk (OR >5.0) of TNBC among African Americans, but only a moderate risk (OR >2.0) among Caucasians

Gene-Specific Risks of TNBC Among Caucasian Women

TNBC associated genes	Ambry TNBC Cohort		TNBCC TNBC Cohort	
	OR	p-value	OR	p-value
BARD1	5.92	2.20×10^{-9}	4.35	7.60×10^{-4}
BRCA1	16.27	$<2.2 \times 10^{-16}$	26.90	$<2.2 \times 10^{-16}$
BRCA2	5.42	$<2.2 \times 10^{-16}$	6.33	$<2.2 \times 10^{-16}$
BRIP1	2.28	5.55×10^{-3}	2.46	0.02
MSH6	2.38	0.04	2.07	0.39
NF1	2.13	0.05	N/A	N/A
PALB2	14.41	$<2.2 \times 10^{-16}$	7.63	7.05×10^{-9}
*RAD51C**	2.64	3.09×10^{-3}	2.88	0.01
*RAD51D***	6.97	3.10×10^{-4}	11.62	3.23×10^{-5}
TP53	2.75	0.02	1.49	0.65
TP53<=40y	8.49	2.19×10^{-4}	5.92	0.05

** RAD51C was associated with a higher risk of TNBC among African American women*

*** Novel association identified between RAD51D and TNBC risk*

Learn more about our research here.

REFERENCES

1. Couch et al. Triple Negative Breast Cancer Risk Genes Identified by Multigene Hereditary Cancer Panel. JNCI. 2018

2. Boyle P. Triple-negative breast cancer: epidemiological considerations and recommendations. Ann Oncol 2012;23 Suppl 6:vi7-12.

3. Buys SS, Sandbach JF, Gammon A, *et al.* A study of over 35,000 women with breast cancer tested with a 25-gene panel of hereditary cancer genes. Cancer 2017;123(10):1721-1730.

4. Plasilova ML, Hayse B, Killelea BK, *et al.* Features of triple-negative breast cancer: Analysis of 38,813 cases from the national cancer database. Medicine (Baltimore) 2016;95(35):e4614.