Ambry Genetics

RESEARCH FOR YOUR PRACTICE

Redefining Inherited Breast Cancer Risks

From our collaboration with Dr. Fergus Couch (Mayo Clinic), Huntsman Cancer Institute, and the University of California – Irvine, the published study in JAMA Oncology dives deep to uncover these risks.

WHY THIS MATTERS TO YOU

A challenge for healthcare providers when it comes to recommending the next steps for patients after genetic testing is ascertaining actual breast cancer risk. This collaborative study, the largest of its kind to date, adds a critical piece of the puzzle to clarify breast cancer risks associated with many genes.

The more insight we offer healthcare providers about the significance of certain genetic mutations, the better they can guide and treat their patients.

BACKGROUND

- Breast cancer is the most common cancer in women, with up to 10% of women diagnosed having a hereditary cause (germline mutation).
- Multigene panel testing identifies a substantial portion of germline mutations for those with a personal and/or family history of breast cancer.[1-3]
- Associations between germline mutations in genes beyond *BRCA1/BRCA2* were studied and updated breast cancer risks were estimated in a case-control analysis of patients with breast cancer and Exome Aggregation Consortium (ExAC) reference controls.

65,057

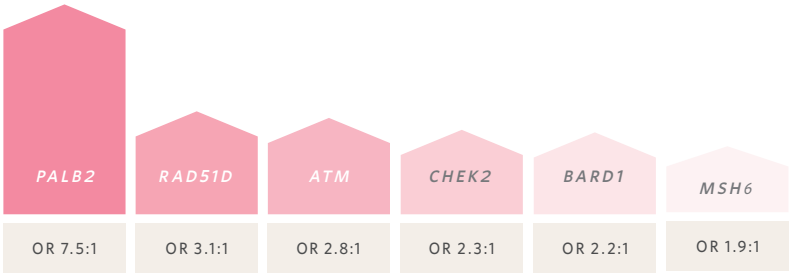
Women with breast cancer studied

POINTS FOR YOUR PRACTICE

- All studied genes with defined breast cancer risks are found on several of Ambry's cancer panels, including BreastNext, OvaNext, and CancerNext.
- Findings from this study support *PALB2* as a high risk breast cancer gene and support current NCCN® guidelines recommending high risk breast cancer management of women with *PALB2* mutations.[4]
- *ATM*, *BARD1*, *CHEK2*, and *RAD51D* were established as moderate risk breast cancer genes, allowing clinicians to be more confident counseling their patients regarding cancer risks and management recommendations.
- Future studies are needed on other mutation types to further evaluate the contribution of genes in this study that did not show a significantly increased risk for breast cancer.

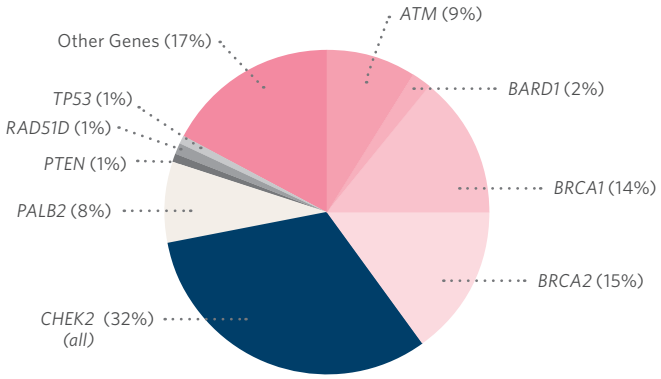
SIGNIFICANT FINDINGS

- 83% of the positive findings were in genes that demonstrated moderate or high risk for breast cancer, increasing the likelihood of an impact on clinical management
- Results confirmed or newly identified increased odds ratios (OR), or the likelihood of developing breast cancer, for several genes (see top figure to the right)
- Risk estimates were established for additional genes associated with moderate breast cancer risk: *BARD1*, *RAD51D*, *MSH6*
- Identified genes that did not confer substantially increased breast cancer risk, requiring further study: *BRIP1*, *NBN*, *MRE11A*, *RAD50*, *RAD51C*, *MLH1*, and *NF1*



The lifetime risk for a woman in the general population to develop breast cancer is ~12%

Mutation Frequency in Breast Cancer Patients



Learn more about our research here.

REFERENCES

1. Couch F, *et al.* Associations between cancer predisposition testing panel genes and breast cancer. JAMA Oncol. 2017. [Epub ahead of print.]
2. Easton DF, *et al.* Gene-panel sequencing and the prediction of breast-cancer risk. N Engl J Med. 2015 Jun 4;372(23):2243-57.
3. Kapoor NS, *et al.* Multigene panel testing detects equal rates of pathogenic *BRCA1/2* mutations and has a higher diagnostic yield compared to limited *BRCA1/2* analysis alone in patients at risk for hereditary breast cancer. Ann Surg Oncol. 2015 Oct;22(10):3282-8.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Genetic/Familial High-Risk Assessment: Breast and Ovarian. V2.2017. Available at nccn.org. Accessed February 7, 2017.
5. Antoniou AC, *et al.* Breast-cancer risk in families with mutations in *PALB2*. N Engl J Med. 2014 Aug 7;371(6):497-506.