Innovations in Breast Cancer Prevention: Vaccines, Genetics, and Technology in Combating Triple-Negative Breast Cancer

ABSTRACT:

Breast cancer is a condition characterized by uncontrolled cell growth in breast tissue, with triple-negative breast cancer (TNBC) being an especially aggressive and difficult-to-treat subtype. Genetic mutations in BRCA1, BRCA2, PALB2, and other genes significantly increase the risk of developing TNBC. Currently, no FDA-approved vaccine exists to prevent breast cancer, but recent research is exploring immunization strategies that could reduce the impact of TNBC, particularly in high-risk individuals. Vaccines targeting tumor-specific antigens, such as α-lactalbumin, show promise in clinical trials by training the immune system to recognize and destroy cancer cells before tumor formation.

In addition to vaccine development, advancements in AI-driven imaging and genetic testing are revolutionizing breast cancer diagnosis, treatment planning, and risk analysis. These technologies enable more precise, personalized care and improve early detection. Looking ahead, combining vaccines with immunotherapies and targeted treatments may offer a new approach to breast cancer prevention and management. Continued research and clinical trials will be critical to bringing these innovations from labs to the clinic, ultimately aiming to reduce breast cancer and help individuals all over the globe.

INTRODUCTION:

Breast cancer is a disease that occurs when mutated cells in the breast grow uncontrollably. Normally, cells in the body grow, divide, and die in a controlled way. But in breast cancer, this

process doesn't work properly – cells keep growing and form a lump or mass called a tumor. These tumors can be benign or malignant. Malignant tumors can spread to nearby tissues or even to other parts of the body through the lymph or blood system. Breast cancer is commonly scanned for by using mammograms, breast ultrasounds, and MRIs. Mammograms use x-rays to create photographs of the breast while ultrasounds utilize sound waves. MRIs use magnetic fields along with radio waves to produce detailed images of the breast tissue.

Triple-negative breast cancer (TNBC) is a rare and aggressive form of breast cancer. TNBC differs from other types of invasive breast cancer in that it tends to grow and spread faster, it has fewer treatment options, and tends to have a worse outlook. TNBC doesn't have the estrogen or progesterone receptors along with the absence of HER2 protein – "About 34%-39% of primary TNBCs show a low expression of human epidermal growth factor receptor 2 (HER2-low), which is a target for new anti-HER2 drugs" ("Triple-Negative Breast Cancer"). In Figure 1, it illustrates how hormone levels can impact a cancer diagnosis.

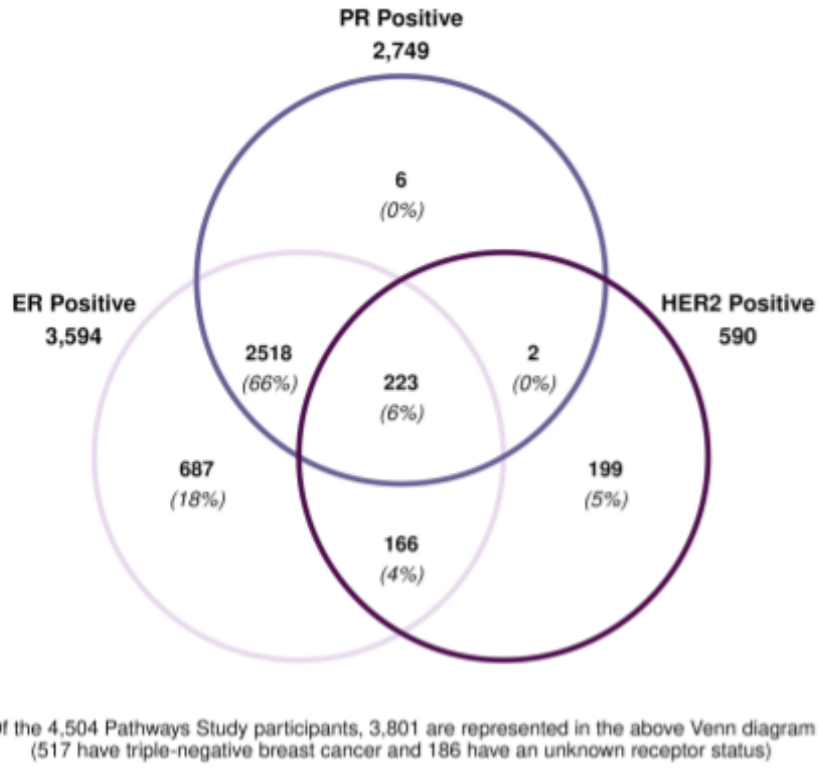

Figure 1: Hormone receptor and HER2 status in breast cancer.

This cancer is more difficult to remove, which is why chemotherapy and radiation therapy is mostly used among the individuals who have this form of breast cancer. Individuals who have these mutated genes – BRAC1, BRAC2 and PALB2 – have an increased risk of developing TNBC. People who have BRCA1 have a higher risk of developing TNBC, in a study conducted by Roswell Park, they share the statistic – "By age 70, women BRCA1 carriers have a slightly higher risk of developing breast cancer than BRCA2 carriers. Also, BRCA1 mutations are more often linked to triple negative breast cancer, which is more aggressive and harder to treat than other types of breast cancer. On the other hand, males with the BRCA1 gene mutation have a 1% lifetime risk of developing male breast cancer, while those that have BRCA2 gene mutation have a 6% risk of developing male breast cancer" ("What's the Difference"). In Figure 2, the data shows cancer diagnoses across the United States among males and females, including all races and ethnicities.

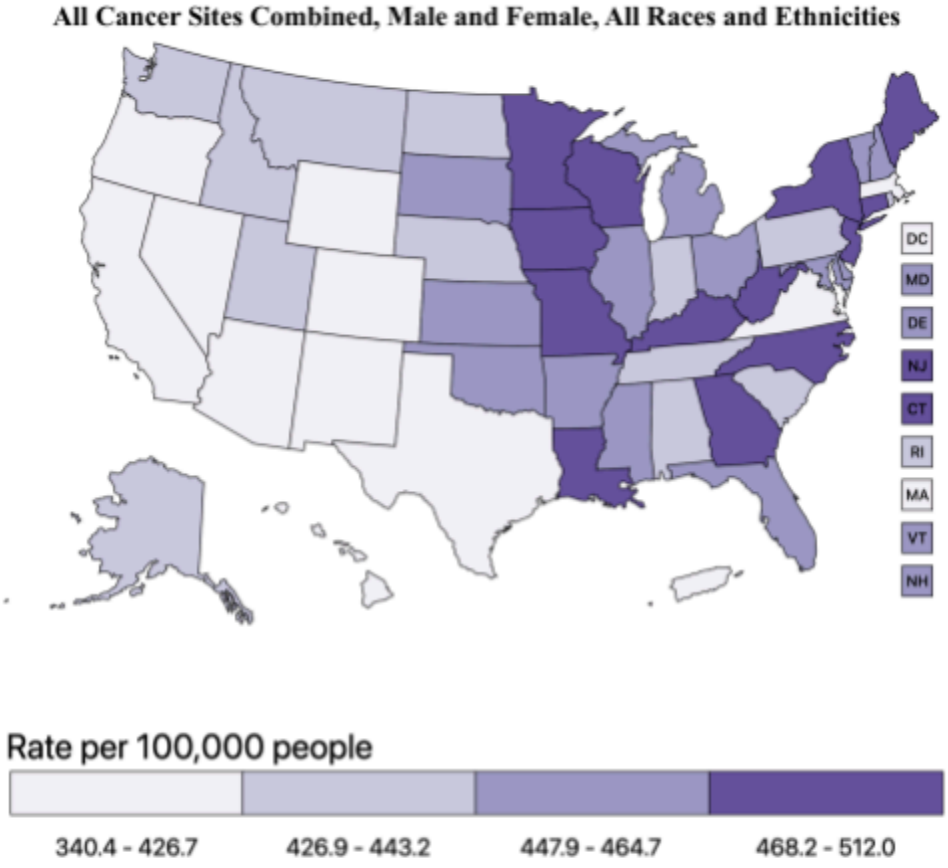

Figure 2: Cancer diagnoses including males and females, with all races and ethnicities across the United States.

To this day there is not a FDA approved vaccination for anyone to get that can remove or lessen the risk of developing breast cancer. With the rise of breast cancer diagnoses, a solution is urgent. This paper will explore the vaccines and technologies currently in development, as well as how genetic testing can aid in the early detection and personalized treatment of TNBC, ultimately helping to reduce its impact.

BREAST CANCER AND GENETIC MUTATION:

BRAC1 and BRAC2 are tumor suppressor genes, which, when they function normally keep tumors from forming. Altered or mutated copy of the BRAC1 and BRAC2 can cause a higher risk of breast cancer. Having these mutations can increase the risk of developing breast cancer; “For example, approximately 12% of women in the general population will develop breast cancer at sometime in their lives. But, for women with a BRCA1 or BRCA2 mutation, the risk of developing breast cancer increases to as much as 72%” (“What’s the Difference”). Although BRAC mutations are the most common among women, other gene mutations can also lead to inherited breast cancer, but they’re less common and have less of a risk of breast cancer than the BRAC’s mutations.

Mutations in several key genes can contribute to the development and aggressiveness of triple-negative breast cancer (TNBC). For example, mutations in the ATM gene reduce the cell’s ability to detect and repair DNA damage, leading to genetic instability that promotes tumor growth. Similarly, mutations in PALB2 disrupt important DNA repair pathways, causing DNA damage to accumulate and driving cancer progression; these mutations may also make tumors more sensitive to specific treatments like PARP inhibitors. The TP53 gene, which normally stops damaged cells from dividing or triggers their death, is often mutated in TNBC, allowing

damaged cells to multiply unchecked and making the cancer more aggressive and resistant to treatment. Mutations in CHEK2, another DNA repair gene, impair the cell's ability to pause and fix DNA damage, contributing further to tumor growth. Additionally, mutations in CDH1, which codes for a protein that helps cells stick together, can cause cancer cells to lose adhesion and spread more easily, increasing invasiveness. Finally, mutations in STK11, a gene that regulates cell growth and metabolism, can disrupt normal cell control and promote tumor progression. Together, these genetic changes create the aggressive and difficult-to-treat nature of TNBC. In Figure 3, it shares how common BRAC1 and BRAC2 genetic mutations are in breast cancer causes that are known to be caused by a mutation.

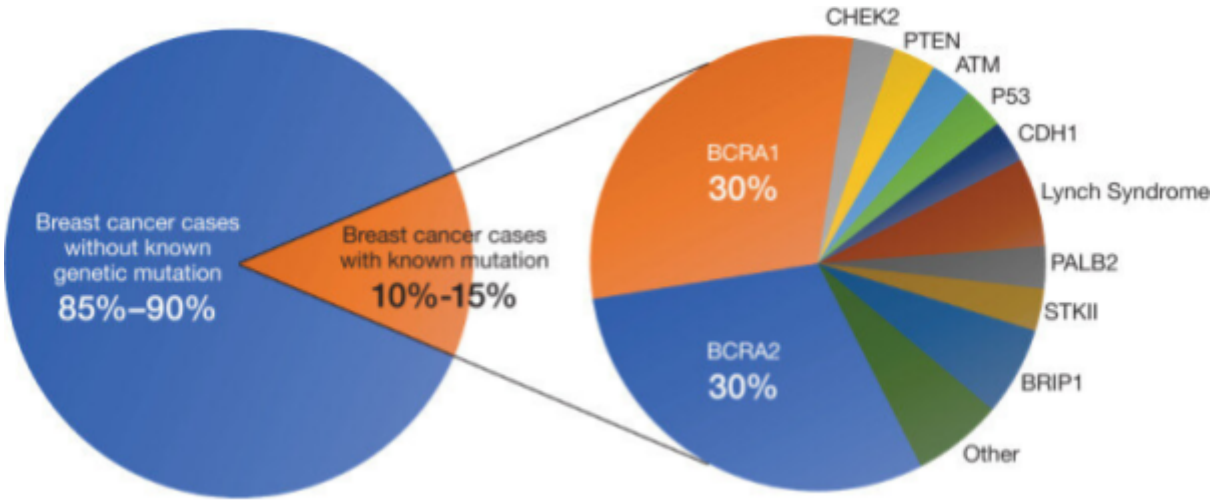

Figure 3: The image shows that 10-15% of breast cancer cases are hereditary, primarily involving BRCA 1 and 2 mutations, with rarer cases linked to PTEN and TP53 mutations.

Having any of these mutations can cause a risk for cancer, getting genetic testing is the best way to look for these problems – Genetic testing can be done to look for inherited mutations, especially the BRAC's genes along with the less common ones.

IMMUNIZATION AND VACCINES:

Immunization for breast cancer is a goal that many scientists hope to reach some day. 13% of the female population will be diagnosed with an aggressive type of breast cancer – one of which

could be triple-negative breast cancer. Vaccines work by imitating an infection, the presence of a disease-causing organism in the body to engage the body's natural defenses. For vaccines to work there needs to be an active ingredient for the body to fight so it can learn how to defend itself when the real disease compromises the body. The active ingredient in all vaccines is an antigen, the name for any substance that causes the immune system to begin producing antibodies. In a vaccine, the antigen could either be: weakened or killed bacteria or viruses, bits of their exterior surface or genetic material, or a bacterial toxin treated to make it non-toxic. White blood cells, also known as leukocytes, are a vital part of the body's immune system. They circulate in the blood and lymph, they are crucial for fighting off infections and other diseases. They act as the body's defense, responding to injury and illness by attacking foreign invaders like bacteria, viruses, and fungi. White blood cells are created in the bone marrow but dispersed throughout the body in low numbers, ready to begin multiplying and attacking microbes and substances not native to the body. A vaccine provides acquired immunity against a disease. It works by stimulating the body’s immune system to recognize and fight off a specific pathogen, like a virus or bacteria, without causing the full effects of the disease. There are many different ways to get immunized from a disease. These are 4 ways to get immunity:

1. Passive: which is provided by antibodies produced by another human being or animal.
2. Active: comes from being exposed to a disease-causing organism.
3. Natural: comes from being infected by the disease-causing organisms, whether the infection is symptomatic or not.
4. Vaccine-induced: comes from being exposed to killed or weakened bacteria or viruses (or even just important pieces of them) through vaccinations.

Along with these methods to gain immunity there are two different types of vaccines – live-attenuated vaccines and non-live vaccines. Live-attenuated vaccines contain living bacteria or viruses, these vaccines can provide protection with only two doses (the measles, mumps and rubella vaccines are live-attenuated vaccinations). While non-live vaccines typically require three or more doses to provide protection, the effectiveness of these vaccines can fade over time so getting a booster is crucial to stay protected (the COVID-19, rabies and typhoid vaccines are non-live vaccinations).

To develop a breast cancer vaccine, researchers must identify a specific target – such as a protein or genetic mutation that is present only in cancer cells and absent in healthy ones. Because breast cancer arises from the body's own cells rather than an external pathogen, the immune system does not recognize it as a threat. Therefore, the vaccine must train the immune system to detect and respond to this unique target as if it were a harmful invader.

CURRENT RESEARCH AND CLINICAL TRIALS:

As of 2025, there is no breast cancer vaccine available for people to use. There are various universities and clinics working on creating a vaccine for the market. A clinic that has been developing a vaccine is Cleveland Clinic based in Cleveland, Ohio. Cleveland Clinic is testing a vaccine to prevent triple-negative breast cancer.

This experimental vaccine targets α-lactalbumin, a protein typically produced only during lactation but found in most TNBC tumors, making it an ideal immune system target. By introducing this protein in a controlled way, the vaccine trains the body's T-cells to recognize and destroy TNBC cells without harming normal breast tissue. Developed over more than 20 years of

research, the vaccine has so far shown to be safe, with only mild side effects like redness or swelling at the injection site. Though it does not protect against all types of breast cancer, it may be particularly effective in preventing TNBC in women at high genetic risk, especially those with BRCA1, BRCA2, or PALB2 mutations. Below, in Figure 4, it shows how a vaccine can focus on the α-lactalbumin protein to kill the cancerous cells in the body.

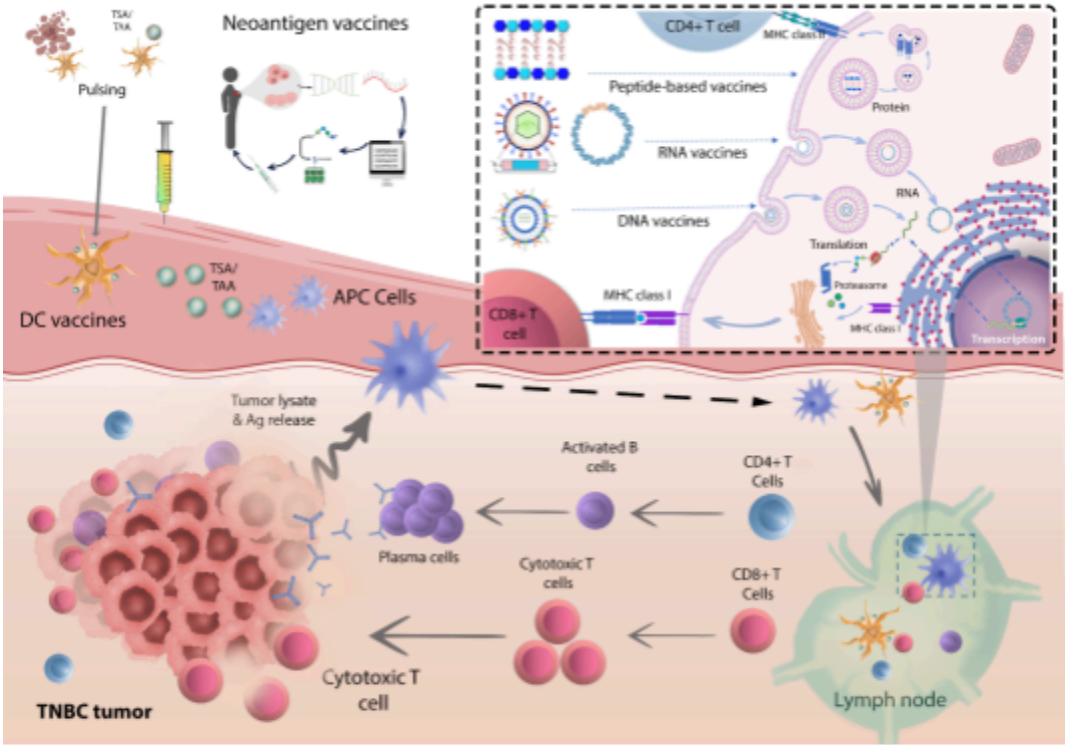

Figure 4: This image shows how personalized vaccines activate the immune system to target and kill triple-negative breast cancer cells by training T cells to recognize tumor markers.

Participants in the trial include women who have previously had TNBC and completed treatment, women who underwent preventive double mastectomies due to genetic risk, and those who still had cancer after receiving chemotherapy, surgery, and immunotherapy. Most participants developed a strong T-cell immune response, indicating their bodies are primed to fight TNBC cells should they appear. Some also produced antibodies, although the T-cell response was more consistent.

The vaccine was most effective at its maximum tolerated dose, and a Phase 2 trial is planned to further evaluate its preventive potential in a larger group. If successful, this would mark the first vaccine developed to prevent a specific type of breast cancer, offering a much-needed option for high-risk women—particularly those with BRCA1 mutations, which are linked to 70–80% of TNBC cases. Since TNBC does not respond to hormone therapy or HER2-targeted treatments, this vaccine represents a promising new preventive strategy aimed at stopping cancer before it starts, acting similar to HPV and flu vaccines.

NEW TECHNOLOGY FOR BREAST CANCER:

Along with new vaccinations being developed, new technology is also helping medical professionals with diagnoses and treatment plans for patients. An Illinois-based startup called SimBioSys focuses on AI-based modeling to improve cancer diagnosis, surgery planning, and treatment outcomes. Their technology converts black-and-white MRI images into – “Spatially accurate, volumetric images of a patient’s breasts. It then illuminates different parts of the breast with distinct colors — the vascular system, or veins, may be red; tumors are shown in blue; surrounding tissue is gray” (“SimBioSys”). Surgeons can use these 3D visualizations to help guide surgeries and treatment plans and to better understand tumor location and structure before surgery. To process all this information, the model uses NVIDIA A100 Tensor Core Graphic Processing Units (GPUs) for high-performance training and deployment of AI medical models. Unlike conventional imaging methods that rely on static images and radiologist interpretation, this platform introduces a more consistent, data-driven approach to preoperative assessment. SimBioSys has also developed AI tools that convert prone-position MRI scans into supine models, replicating how the breast appears during surgery by accounting for gravity and tissue

dynamics. Additionally, the company is advancing a rapid recurrence risk prediction tool that combines 3D tumor characteristics with pathology data and patient demographics to deliver accurate, cost-effective risk assessments within hours. TumorSight Viz was approved by the FDA in December of 2023.

HOPE FOR THE FUTURE:

Advancements in medical technology continue to offer up promising improvements in cancer prevention and treatment. mRNA vaccine technology, which has proven to be effective during the COVID-19 pandemic, is rapidly evolving and holds potential for targeting various cancers by training the immune system to recognize tumor-specific antigens. AI-driven tools are increasingly being developed to predict tumor antigens more accurately, enabling personalized vaccines and therapies tailored to individual patients' tumors.

Early genetic screening is another critical area, especially for individuals with a family history of breast cancer linked to BRCA1 and BRCA2 mutations. Improved screening methods can identify high-risk patients sooner, allowing for earlier interventions and more effective preventive strategies. Looking ahead, the development of long-term prevention vaccines may transform cancer care by reducing the incidence of cancer before it develops. Additionally, combination therapies, integrating vaccines with immunotherapies, targeted treatments, and traditional methods, have the potential to become the new standard of care, enhancing treatment efficacy and patient outcomes. These future directions offer hope for more effective, personalized, and preventive approaches in cancer management.

CONCLUSION:

Breast cancer, especially the triple-negative subtype, continues to pose significant challenges in diagnosis, treatment, and prevention. The identification of key genetic mutations such as BRCA1, BRCA2, and PALB2 has greatly enhanced our understanding of the disease's underlying causes and risk factors, paving the way for more personalized approaches to patient care. Despite the absence of an FDA-approved vaccine for breast cancer, promising developments like the α-lactalbumin-targeted vaccine under clinical trials highlight the potential for immunization to become a vital tool in preventing triple-negative breast cancer, particularly for high-risk individuals. This emerging vaccine represents a groundbreaking shift in cancer prevention, aiming to train the immune system to recognize and destroy cancer cells before they can establish and spread.

In addition to vaccine research, advancements in technology, including AI imaging and improved genetic screening techniques, are transforming breast cancer management. These innovations not only enhance early detection and surgical planning but also support the development of personalized treatment plans tailored to each patients' unique tumor profile. Looking forward, the integration of vaccines with immunotherapies and other targeted treatments holds great promise for improving outcomes and reducing recurrence rates. Continued research, investment, and clinical trials will be essential to making these hopeful strategies widely available, ultimately aiming to reduce the incidence and mortality of breast cancer and improve the quality of life for patients worldwide.

REFERENCES:

"Breast Cancer Basics | Breast Cancer." *CDC*, 5 November 2024, https://www.cdc.gov/breast-cancer/about/index.html. Accessed 21 August 2025.

"Breast cancer patients with genetic mutations. Approximately 10–15% of..." *ResearchGate*, https://www.researchgate.net/figure/Breast-cancer-patients-with-genetic-mutations-Approximately-10-15-of-breast-cancer_fig1_343226639. Accessed 21 August 2025.

"Breast Cancer Risk Factors You Can't Change." *American Cancer Society*, 16 December 2021, https://www.cancer.org/cancer/types/breast-cancer/risk-and-prevention/breast-cancer-risk-factors-you-cannot-change.html. Accessed 21 August 2025.

"Clinic Announces Updated Breast Cancer Vaccine Findings." *Cleveland Clinic Newsroom*, 8 November 2024, https://newsroom.clevelandclinic.org/2024/11/08/cleveland-clinic-announces-updated-findings-in-preventive-breast-cancer-vaccine-study. Accessed 21 August 2025.

"Definition of HER2 - NCI Dictionary of Cancer Terms - NCI." *National Cancer Institute*, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/her2. Accessed 21 August 2025.

"Explaining How Vaccines Work | Vaccines & Immunizations." *CDC*, 10 August 2024, https://www.cdc.gov/vaccines/basics/explaining-how-vaccines-work.html. Accessed 21 August 2025.

"Data Visualizations." The Pathways Study, [no date], https://thepathwaysstudy.org/data_visualizations.html. Accessed 21 August 2025.

"U.S. Cancer Statistics Data Visualizations Tool." *Centers for Disease Control and Prevention*, U.S. Department of Health and Human Services, 2 June 2025, https://gis.cdc.gov/Cancer/USCS/.

"Triple-Negative Breast Cancer: Current Understanding and Future Therapeutic Breakthrough Targeting Cancer Growth and Metastasis." *Frontiers in Pharmacology*, vol. 14, 2023, article 10024122, https://pmc.ncbi.nlm.nih.gov/articles/PMC10024122/.

"Triple-negative Breast Cancer | Details, Diagnosis, and Signs." *American Cancer Society*, https://www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/triple-negative.html. Accessed 21 August 2025.

"Update on Phase 1 Trial of Preventive Breast Cancer Vaccine." *Consult QD*, 4 January 2024, https://consultqd.clevelandclinic.org/update-on-phase-1-trial-of-preventive-breast-cancer-vaccine. Accessed 21 August 2025.

Hosseini, Mina, et al. "Cancer Vaccines for Triple-Negative Breast Cancer: A Systematic Review." *Vaccines*, vol. 11, no. 1, 2023, https://www.mdpi.com/2076-393X/11/1/146. Accessed 23 August 2025.

"What is the Difference Between BRCA1 and BRCA2?" *Roswell Park Comprehensive Cancer Center*, 18 June 2020, https://www.roswellpark.org/cancertalk/202006/what-difference-between-brca1-brca2. Accessed 21 August 2025.

Wolfberg, Elias. "SimBioSys Helps Surgeons Target Breast Cancers." *NVIDIA Blog*, 31 October 2024, https://blogs.nvidia.com/blog/simbiosys-3d-visualizations-breast-cancer-tumors/. Accessed 21 August 2025.