CDMRP
DEPARTMENT OF WAR
CONGRESSIONALLY DIRECTED
MEDICAL RESEARCH PROGRAMS

Breast Cancer Research Program

Accelerating Progress Toward a World Without Breast Cancer

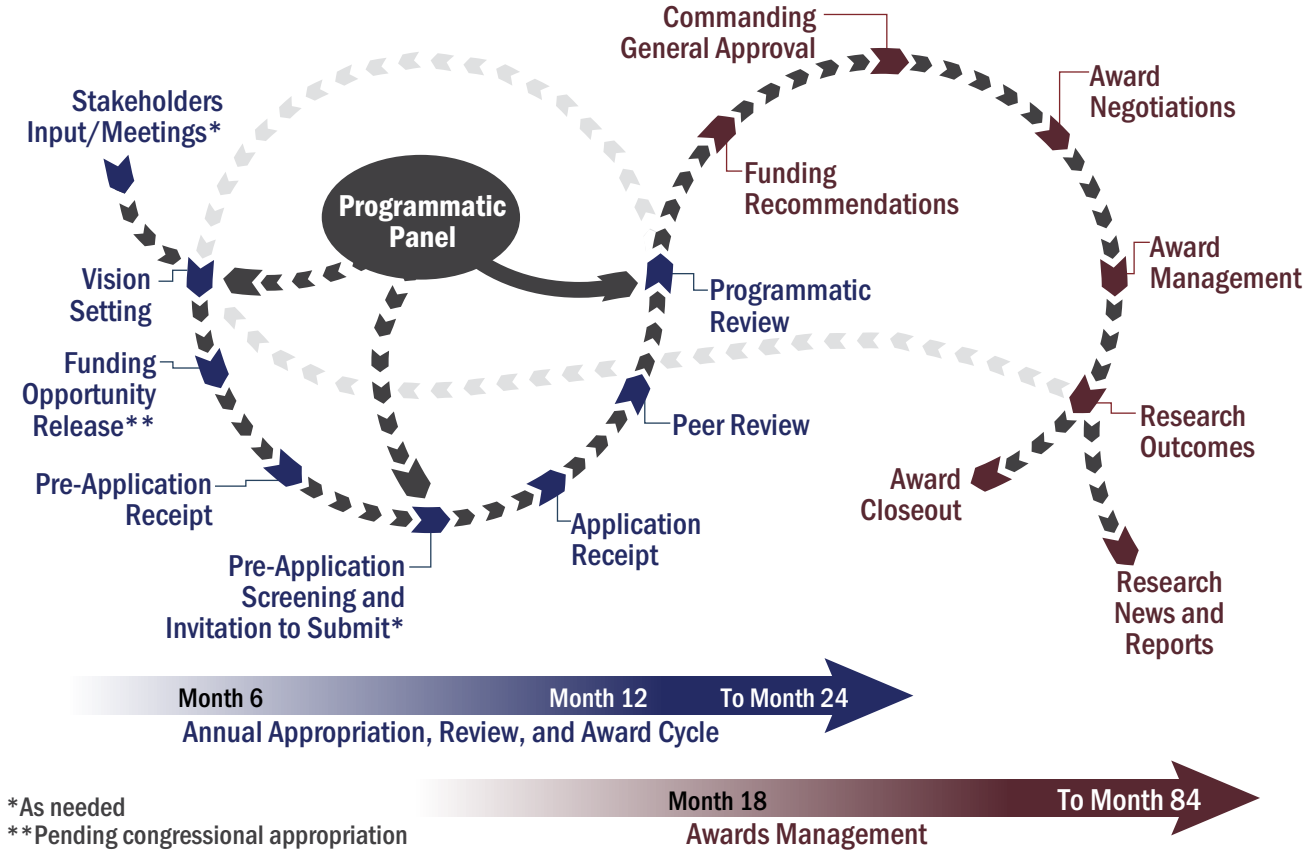
For more information, please visit
cdmrp.health.mil/bcrp

CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

Congress established the Congressionally Directed Medical Research Programs in response to a grassroots effort in 1992 led by the breast cancer advocacy community. That effort resulted in a congressional appropriation of funds for breast cancer research and initiated a unique partnership among the public, Congress and the military. Since then, Congress appropriated funding for additional targeted research programs. The CDMRP managed over $20.322 billion in congressional special interest funds from inception through fiscal year 2025. Congress provides general intent for each program and specifies funding as part of the annual Department of Defense appropriations bill.

APPLICATION REVIEW PROCESS

The CDMRP uses a two-tier research application review process. This process involves dynamic interaction between scientists, clinicians, consumers from advocacy communities, members of the military, and other specialists, as applicable. The first tier of evaluation is a scientific peer review of applications measured against established criteria determining scientific merit. The second tier is a programmatic review where applications with higher scientific or technical merit are evaluated for potential impact, adherence to the intent of the award mechanism, relevance to program goals and portfolio composition.



CDMRP Two-Tier Review Process

Photo provided

"The BCRP brings together the combined power of dedicated scientists, clinicians, advocates and the military to challenge the status quo, think outside the box, break down silos and encourage researchers to pursue projects that will make meaningful breakthroughs toward the goal of ending breast cancer. The BCRP has a documented history of funding research that has an actual impact on patients' lives. As someone who has been personally affected by breast cancer, I find it incredibly empowering to be able to bring the consumer voice to the table."

Tracy Solak, Young Survival Coalition, FY24-FY25 Programmatic Panel Member

BREAST CANCER RESEARCH PROGRAM

VISION: A world without breast cancer

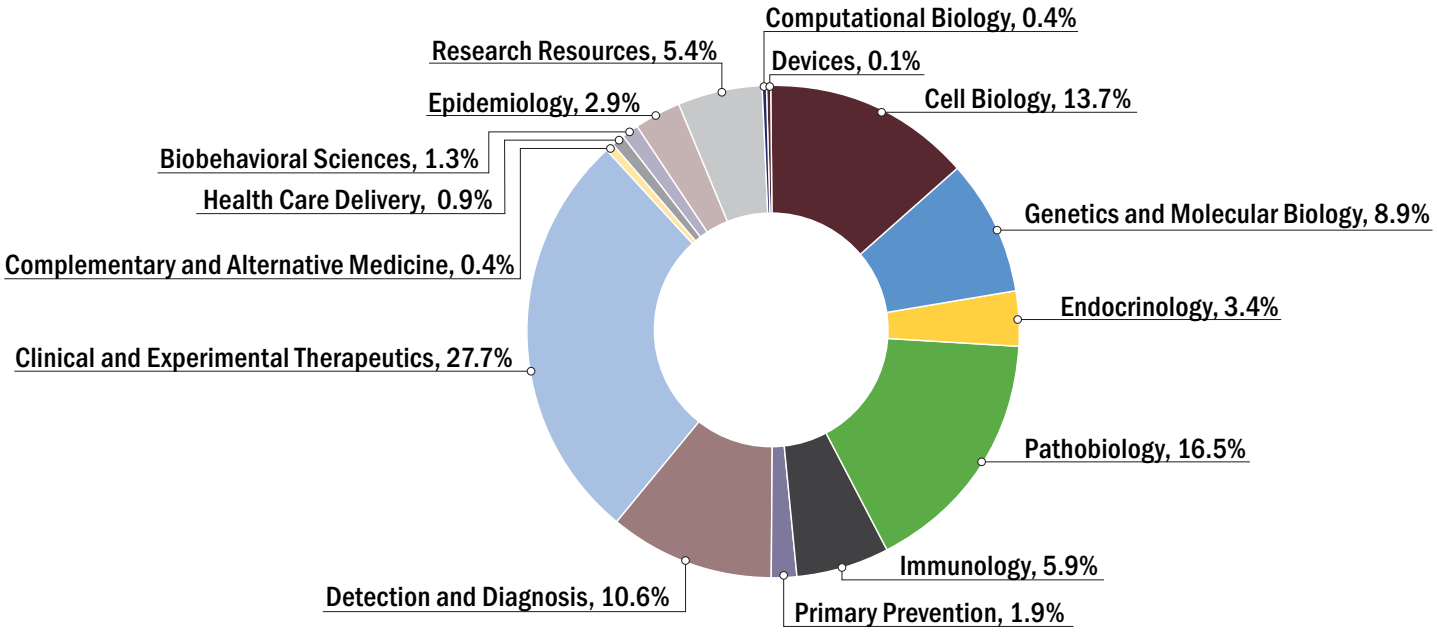
MISSION: To end breast cancer for Service Members and their Families, Veterans, and the general public by funding innovative, high-impact research through a partnership of scientists and consumers

ABOUT THE PROGRAM

The Breast Cancer Research Program plays a leading role in the fight against breast cancer through innovative approaches and focusing on research that will bring an end to the disease. The program originated in 1992 as a result of the dedicated efforts of breast cancer advocates. Their continued efforts, in concert with the program's accomplishments, resulted in $4.521 billion in congressional appropriations through FY25. The BCRP enables researchers to propose their best innovative ideas that address the urgency to end breast cancer. The program challenges scientists to pursue high-risk, high-reward research; explore new paradigms that could lead to critical discoveries; and make an unprecedented impact on breast cancer. The BCRP also promotes synergistic collaborations across disciplines and integrates scientists and consumers in unique and meaningful research partnerships.

From FY92 to FY24, the BCRP funded 7,428 awards. In order to achieve its mission to end breast cancer, the BCRP invested in many different areas of scientific research as depicted in the chart below, with the largest investment in clinical and experimental therapeutics.

FY92-FY24 Investment by Scientific Classification System Code



FY93-FY24 Metrics

PUBLICATIONS
>19,800

PATENTS, PATENT APPLICATIONS AND INVENTION DISCLOSURES
>1,400

CLINICAL TRIALS
226

THE BREAST CANCER LANDSCAPE

The BCRP outlined topics most pertinent to the program's mission of ending breast cancer in the *Breast Cancer Landscape*.[1] Key points include:

INCIDENCE AND MORTALITY:

- Worldwide, breast cancer accounts for nearly a quarter of all cancers in women.
- In 2050, with no major changes in prevention or treatment, more than an estimated one million women will die from breast cancer worldwide.

RISK FACTORS:

- Evidence attributes the majority of breast cancers to not only one factor, but to various physical, hormonal, environmental and genetic factors.
- Most risk factors are not modifiable.

RECURRENCE AND METASTASIS:

- An estimated 10% to 30% of women diagnosed with invasive breast cancer will experience a recurrence.
- Treatments to permanently eradicate metastasis do not exist. There is no cure once metastatic disease occurs.

TREATMENTS:

- Although breast cancers are highly heterogenous, the majority of women with breast cancer receive the same treatment, as though all breast cancers respond the same within a given subtype.
- Standard adjuvant therapies make only a small impact, between 5% to 10%, on disease-specific survival.
- The cost of treating breast cancer continues to rise, and financial burden from expenses linked to treatment is high among patients.

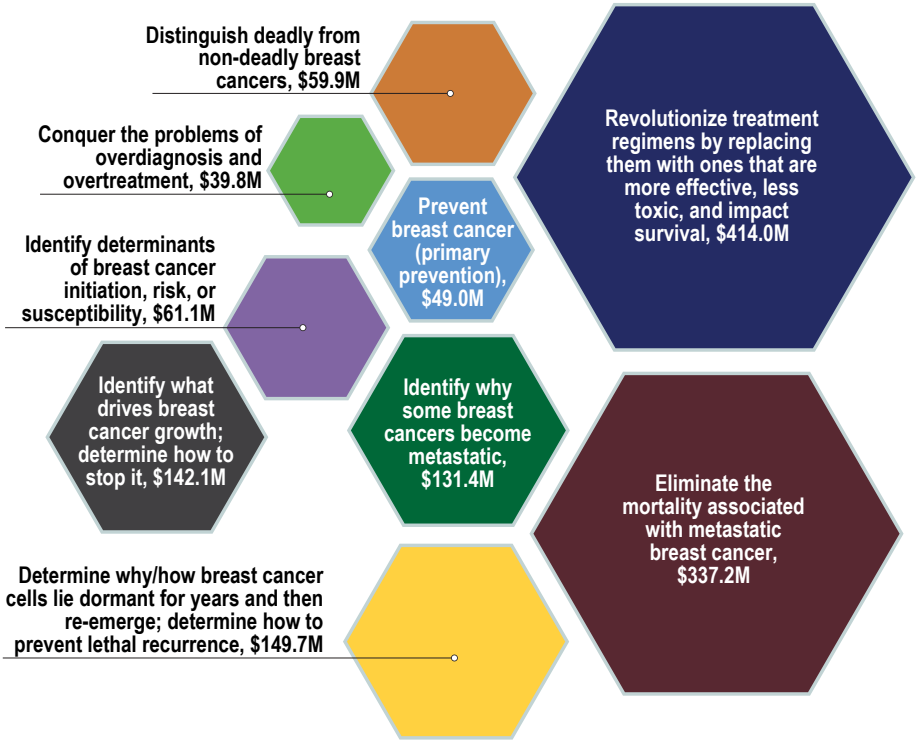
[1] Available at cdmrp.health.mil/bcrp

OVERARCHING CHALLENGES

Each project, with consideration of the current breast cancer landscape and the BCRP's mission to end breast cancer, must address at least one of the following BCRP overarching challenges. The chart below shows the program's investments in each overarching challenge from FY13 to FY24.

- Prevent breast cancer (primary prevention)
- Identify determinants of breast cancer initiation, risk, or susceptibility
- Distinguish deadly from non-deadly breast cancers
- Conquer the problems of overdiagnosis and overtreatment
- Identify what drives breast cancer growth; determine how to stop it
- Identify why some breast cancers become metastatic
- Determine why/how breast cancer cells lie dormant for years and then re-emerge; determine how to prevent lethal recurrence
- Revolutionize treatment regimens by replacing them with ones that are more effective, less toxic, and impact survival
- Eliminate the mortality associated with metastatic breast cancer

FY13-FY24 Portfolio Investment by Overarching Challenge



RELEVANCE TO MILITARY HEALTH

- Breast cancer is the most common non-skin cancer in women and is the **deadliest cancer in females under 40**.[2,3]
- The incidence rate of breast cancer is **higher in female Service Members 40 to 59 years of age** than in the general population.[4]
- The incidence rate for active-duty females is **seven times higher** than the average rates of 15 other cancer types across all Service Members.[5]
- On average, the Military Health System provided care for **67,739 women** and **507 men** for invasive breast cancer annually between 2015 and 2024, including an average of **420 active-duty military members** each year.[6]

IMPACT IN THE MILITARY HEALTH SYSTEM

Military Health Service providers filled more than **132,900 prescriptions** between 2007 and 2024 for four FDA-approved drugs developed in part by BCRP-funded research: abemaciclib, palbociclib, ribociclib and trastuzumab.[7]

[2] https://gis.cdc.gov/Cancer/USCS/#/AtAGlance/
[3] https://seer.cancer.gov/statfacts/html/aya.html
[4] https://pubmed.ncbi.nlm.nih.gov/37725334/
[5] https://www.health.mil/Reference-Center/Reports/2016/01/01/Medical-Surveillance-Monthly-Report-Volume-23-Number-7
[6] Source: Defense Medical Surveillance System of the Defense Health Agency
[7] Source: Defense Health Agency Pharmacy Operations Division

STRATEGIC PARTNERSHIPS: Scientists and Consumers Working Together to End Breast Cancer

Photo provided

"The BCRP is a phenomenal program that fosters advances in science with direct benefit to patients. The panel of subject matter experts carefully reviews the proposals and makes recommendations with priority of helping patients through their cancer journey. This thoughtful and efficient process unifies the recommendations of advocates, scientists, clinicians and the military to help end breast cancer."

U.S. Navy Cmdr. Diego Vicente, M.D., FY22-FY25 Programmatic Panel Member

Photo provided

After being diagnosed and treated for my breast cancer, I used to think there were few ways for regular people like me to influence the science and research being done working towards an end to breast cancer. Thanks to my BCRP participation, I view the end of breast cancer as a possibility now. I've seen the power of constituent voices—real people impacted by breast cancer—in moving the needle. Continuing to fund this research provides hope to those afflicted, honors those we have lost, and drives progress toward a future without breast cancer."

Meridith L. Rothstein, Delaware Breast Cancer Coalition, FY23-FY24 Consumer Peer Reviewer

Photo provided

"The BCRP has been a critical catalyst for our research into harnessing the immune system to treat breast cancer. The BCRP provided transformative support that allowed us to take our ideas from the laboratory to a successful clinical trial. The discoveries made by the BCRP investigators, including our own group, have substantively moved the needle closer to ending breast cancer by funding innovative approaches that have revolutionized how we think about and treat breast cancer."

Stephen Shiao, M.D., Ph.D., Cedars-Sinai, BCRP-Funded Investigator

RESEARCH HIGHLIGHTS

Developing Antibody-Drug Conjugates for Breast Cancer Eradication


Photos provided

Brad St. Croix, Ph.D., and Martin Schnermann, Ph.D.,
National Cancer Institute

Antibody-drug conjugates, ADCs, pair cell targeting capabilities of antibodies with the potency of a cytotoxic drug payload to locate and destroy tumor cells.[8] While FDA-approved ADCs for breast cancer are available, barriers to their therapeutic index remain, including challenges with off-target effects and dose-limiting toxicity related to the payload and drug delivery. To overcome these barriers and develop an ADC effective across breast cancer subtypes, St. Croix and Schnermann are investigating a new ADC that targets CD276, a surface protein broadly expressed in tumors. Because both breast cancer cells and cancer-associated stromal cells overexpress CD276, also called B7-H3, this approach enables simultaneous targeting of the tumor and its supporting microenvironment.

Preliminary data showed that the CD276-targeted ADC could extend survival in mouse models of metastatic breast cancer, leading to an FY20 Breakthrough Award Level 1 – Partnering Principal Investigator Option to further optimize the molecule. The team re-engineered the CD276 ADC to improve stability, reduce off-target binding and enhance the drug-to-antibody ratio for more efficient tumor targeting. After multiple design iterations, the optimized CD276 ADC demonstrated striking results in a patient-derived breast cancer model: complete and durable tumor eradication at doses 10 to 40 times lower than earlier versions. Importantly, the ADC accumulated selectively in the tumors and surrounding microenvironment, with minimal uptake in non-target tissues.

One key factor that enhanced the ADC's performance was the addition of extra purification steps, which improved drug purity but are not typically included in standard production. BrickBio, which licensed the CD276 antibody used to create the ADC, is now applying its proprietary site-specific drug labeling technology to generate a more uniformly labeled ADC—streamlining manufacturing and bypassing the need for extensive purification. The company aims to advance this innovative therapy into clinical testing. Building on these findings, and with support from an FY24 Expansion Award, the research team plans to evaluate their ADC in models of brain-metastatic breast cancer. Because the brain exhibited the lowest levels of ADC accumulation, the PIs will re-engineer their approach to enhance delivery across the blood-brain barrier, while continuing to minimize nonspecific binding and toxicity. Altogether, their work highlights the therapeutic promise of CD276-directed ADCs and their potential to address difficult-to-treat forms of breast cancer, including those that metastasize to the brain.

Publication:

Yang Feng, et al., "Engineering CD276/B7-H3-Targeted Antibody-Drug Conjugates With Enhanced Cancer-Eradicating Capability," *Cell Reports* 42, no. 12 (2023): 113503, https://doi.org/10.1016/j.celrep.2023.113503.

[8] National Cancer Institute Dictionary of Cancer Terms (https://www.cancer.gov/publications/dictionaries/cancer-terms/def/antibody-drug-conjugate).

Using Machine Learning to Predict Breast Cancer Recurrence and Inform Treatment Decisions

Photos provided

Dezheng Huo, Ph.D., and Alexander Pearson, M.D., Ph.D.,
The University of Chicago

Hormone receptor positive, HR+, breast cancer is a highly variable subtype of breast cancer. This variability can lead to challenges in diagnosis and treatment. Clinicians can use gene expression analysis to predict a patient's risk of disease recurrence and response to different treatment options. Oncotype DX®, or ODX, is one molecular test clinicians use to tailor therapeutic decisions for patients with early-stage HR+/human epidermal growth factor receptor 2 negative, HER2-, breast cancer. The ODX uses genomic data from the cancer cells to predict disease recurrence and inform decisions related to treatment. While ODX serves as a valuable tool for diagnosis and treatment, the test costs, processing time and accessibility in low-resource settings represent potential challenges in some cases.[9,10]

To meet the need for a low-cost, rapid test for breast cancer management in resource-limited environments, Huo and Pearson saw a potential to overcome these challenges through mathematical modeling. With support from a FY21 Breakthrough Award Level 2 – Partnering Principal Investigator Option, the team developed a machine learning model for the prediction of ODX scores by integrating clinical indicators such as age, tumor size, progesterone receptor status, tumor grade and cancer growth rates.

Huo and Pearson trained and validated their model using multiple datasets with large patient groups reflective of the general population. They tested the model's ability to predict ODX scores and correlate with survival outcomes. The team discovered that adding quantitative pathology data to previous models improved the concordance between the model prediction and true ODX scores. Their model consistently and accurately predicted ODX scores in two validation environments across demographics, indicating a potential generalizability to populations worldwide. Importantly, the model can accurately predict individuals with low risk of recurrence even if their analysis contained a limited number of data points. This clinical risk prediction model may assist oncologists by identifying low-risk patients who do not need adjuvant chemotherapy. In areas without access to genomic testing, clinicians could employ this tool to tailor treatment plans and reduce treatment burden on patients and families.

Publication:
Asim Dhungana, et al., "Development and Validation of a Clinical Breast Cancer Tool for Accurate Prediction of Recurrence," *NPJ Breast Cancer* 10, no. 46 (2024), https://doi.org/10.1038/s41523-024-00651-5.

[9] Angela Mariotto, et al., "Expected Monetary Impact of Oncotype DX Score-Concordant Systemic Breast Cancer Therapy Based on the TAILORx Trial," *Journal of the National Cancer Institute* 112, no. 2 (2020): 154-160, https://doi.org/10.1093/jnci/djz068.

[10] Katya Losk, et al., "Factors Associated With Delays in Chemotherapy Initiation Among Patients With Breast Cancer at a Comprehensive Cancer Center," *Journal of the National Comprehensive Cancer Network* 14, no. 12 (2016): 1519-1526, https://doi.org/10.6004/jnccn.2016.0163.

Using Patient-Derived Tumor Models to Help Predict, Prevent and Treat Early Metastatic Recurrence of Breast Cancer



Photos provided

Bryan Welm, Ph.D., Alana Welm, Ph.D., and Christos Vaklavas, M.D., The University of Utah

Approximately 20% to 30% of all breast cancer patients develop metastatic disease,[11] and predicting a patient's risk of recurrence remains a challenge. Researchers have developed a novel tool, called patient-derived xenograft models, to study individual breast cancer patients' tumors in the laboratory. By placing a piece of the patient's tumor into an animal, scientists can study the tumor's growth and progression to metastatic disease. Bryan Welm and Alana Welm generated preliminary data confirming these models not only mimic a patient's primary tumor disease but often metastasize to the same tissues observed in patients. This suggests that information generated from the patient-derived xenograft models may demonstrate clinical utility.

With support from a FY13 Breakthrough Award – Funding Level 3 – Clinical Trial, Bryan Welm and his team conducted an observational study of 80 patients with newly diagnosed, nonmetastatic, estrogen receptor negative or ER-low breast cancer to evaluate whether patient-derived xenografts can serve as accurate predictors of recurrence. With a median follow-up of 2.6 years, the team observed that 13 of 80 patients developed a recurrence, nine of whom relapsed within the first year. Notably, the team found a strong association between successful growth of patient-derived xenografts in animal models and relapse in the first year. Disease relapse occurred in eight of 18 patients, or 44 percent, whose tumors grew in mice, compared to only one of 62 patients, or 1.6 percent, whose tumors did not grow in mice. In two of the patient-derived xenograft positive cases, the team examined genetic mutations within the tumor and performed drug profiling to predict response to available therapeutics. One of the patients received alpelisib as a monotherapy based on the profiling results, and at the time of the 2024 publication, the patient's tumor remained in remission.

Following promising findings from the initial study, with support from a FY21 Breakthrough Award – Funding Level 3 – Partnering PI Option, Alana Welm and Christos Vaklavas are conducting a clinical trial to identify possible therapies for patients at high risk of early recurrence based on their tumor growing as a patient-derived xenograft. The team will grow tumors in mice and as organoids, conduct drug sensitivity assays and return the results to clinicians to inform treatment decisions. If validated, the use of patient-derived xenografts could revolutionize cancer drug development, clinical trial design and patient care. This team's innovative approach could lead to a new paradigm of personalized oncology care, sparing patients from toxicities of ineffective drugs and improving survival.

Publication:

Christos Vaklavas, et al., "TOWARDS Study: Patient-Derived Xenograft Engraftment Predicts Poor Survival in Patients With Newly Diagnosed Triple-Negative Breast Cancer," *JCO Precision Oncology* 8 (2024): e2300724, https://doi.org/10.1200/PO.23.00724.

[11] Alessandra I. Riggio, et al., "The Lingering Mysteries of Metastatic Recurrence in Breast Cancer," *British Journal of Cancer* 124, no. 1 (2021): 13-26, https://doi.org/10.1038/s41416-020-01161-4.

Targeting Nanobioparticles to Treat Brain Metastases via Human Epidermal Growth Factor Receptor 3

Photo provided

Lali Medina-Kauwe, Ph.D., Cedars-Sinai Medical Center

Patients diagnosed with brain metastatic breast cancer often receive a poor prognosis, demonstrating an urgent need for effective treatments.[12] A tightly joined layer of cells, called the blood-brain barrier, restricts the entry of therapeutic materials to the brain, significantly limiting the treatment options for breast cancer patients with brain metastases. Cells lining the blood-brain barrier and various tumor types, including some brain metastatic breast cancers, express human epidermal growth factor receptor 3 on the cell surface. Because the blood-brain barrier and certain cancer cells contain high levels of HER3, Medina-Kauwe explored whether HER3 could serve as a potential point of entry to the brain and target for treating the metastases.

With support from a FY14 Breakthrough Award – Funding Level 2 and a FY18 Expansion Award, Medina-Kauwe sought to use nanobioparticles targeting HER3 to deliver therapeutics directly to brain metastases from breast cancer. The team engineered the nanobioparticle by copying parts of the HER3 binding protein, neuregulin, and adding an additional component allowing encapsulation of therapeutic cargo. These components allow the nanobioparticle to cross the blood-brain barrier, accumulate specifically into HER3-positive cancer cells and deliver the encapsulated therapeutic cargo. Upon uptake, the team demonstrated that the nanobioparticles released the loaded cargo for targeted tumor cell death. Additionally, mouse model studies established that the nanobioparticles targeted the HER3-positive breast cancer cells, delivering their cargo and causing tumor shrinkage. Notably, the studies suggested an improved therapeutic profile compared to current therapies and agents using traditional methods to cross the blood-brain barrier.

This novel HER3-targeting nanobioparticle approach may revolutionize treatment for patients with brain metastatic breast cancer. The nanobioparticle's ability to cross the blood-brain barrier for targeted delivery of therapeutic cargo provides an approach to treatment which may limit off-target effects. With additional support from a FY21 Breakthrough Award – Funding Level 2, Medina-Kauwe's research continues through the investigation of bioparticles with a modified design intended to improve these agents under development for treatment of HER3-expressing brain-localized and brain-metastatic breast tumors.

Publication:

Felix Alonso-Valenteen, et al., "Systemic HER3 Ligand-Mimicking Nanobioparticles Enter the Brain and Reduce Intracranial Tumour Growth," *Nature Nanotechnology* 20, no. 5 (2025): 683-696, https://doi.org/10.1038/s41565-025-01867-7.

[12] Naoki Niikura, et al., "Brain Metastases in Breast Cancer," *Japanese Journal of Clinical Oncology* 44, no. 12 (2014): 1133-1140, https://doi.org/10.1093/jjco/hyu156.

IN THE CLINICAL PIPELINE

The BCRP has invested in the discovery and development of multiple therapies and diagnostic tools, many of which have continued to advance through the clinical pipeline. The BCRP is also currently funding several projects with clinical trials underway or in preparation.

*BCRP-funded** *Current phase supported by other sources* *Previous phase supported by other sources*

VACCINES AND IMMUNOTHERAPIES	Pre-IND**	Phase 1/2	Phase 3
STEMVAC: Mary "Nora" L. Disis, Natasha Hunter and Kari Wisinski *A multiantigen vaccine, STEMVAC, for adjuvant treatment of patients with moderate or extensive residual triple-negative breast cancer.*	■	■	
Mammaglobin-A cDNA Vaccine: William Gillanders *A mammaglobin-A DNA vaccine to induce antitumor immunity in breast cancer patients undergoing neoadjuvant endocrine therapy or chemotherapy.*		■	
Folate Receptor Alpha Vaccine: Keith Knutson, Edith Perez and Saranya Chumsri *A vaccine targeting the folate receptor alpha in patients with TNBC to prevent or delay recurrence.*		■	
HER2 Bi-Armed Activated T Cells, or HER2 BATs: Lawrence G. Lum *A therapy that induces the development of "memory" antigen-specific cytotoxic T cells directed at HER2 to treat patients with metastatic breast cancer.*	■	■	
TRC105: Ben Seon *A monoclonal antibody that targets endoglin to suppress the growth of both established and new breast tumors.*	■	■	
AVX901 HER2 Vaccine, also called VRP-HER2: H. Kim Lyerly *A vaccine composed of an alphaviral vector expressing the human HER2 gene to treat patients with HER2+ metastatic breast cancer.*	■	■	
Alpha-Lactalbumin Vaccine: G. Thomas Budd, Vincent Tuohy and Thaddeus Stappenbeck *A vaccine for TNBC patients recovering from current standard of care therapy or administered to healthy individuals to prevent the development of breast cancer.*		■	
Multivalent Th1 DNA Vaccine With HER2-Pulsed IL-12 Secreting DC1 Vaccine: Brian Czerniecki *Combining a multivalent Th1 epitope anti-oncodriver DNA vaccine and HER2-pulsed IL-12 secreting dendritic cell 1, or DC1, vaccine to improve complete pathologic response rates and prevent recurrence in HER2+ breast cancer.*		■	
Trastuzumab Emtansine/Pertuzumab with HER2 HLA-DR Vaccine Therapy: Keith Knutson and Saranya Chumsri *A multi-epitope HER2 vaccine administered during anti-HER2 maintenance therapy in patients with residual disease post-neoadjuvant chemotherapy to block disease recurrence and metastasis.*		■	
Radiotherapy-Mediated Immunomodulation: Stephen Shiao and Simon Knott *Using preoperative focal radiation combined with pembrolizumab to generate antitumor immune responses in patients diagnosed with early-stage operable TNBC or ER+ breast cancers.*		■	
Dendritic Cell Vaccines: Pawel Kalinski, Brian Czerniecki and Marco Davila *Dendritic cell vaccines against HER2/HER3 combined with pembrolizumab to treat patients with brain metastasis from TNBC or HER2+ breast cancer.* *Dendritic cell vaccine to treat patients with leptomeningeal disease from TNBC or HER2+ breast cancer.*	■	■	

* May also be supported by non-BCRP sources

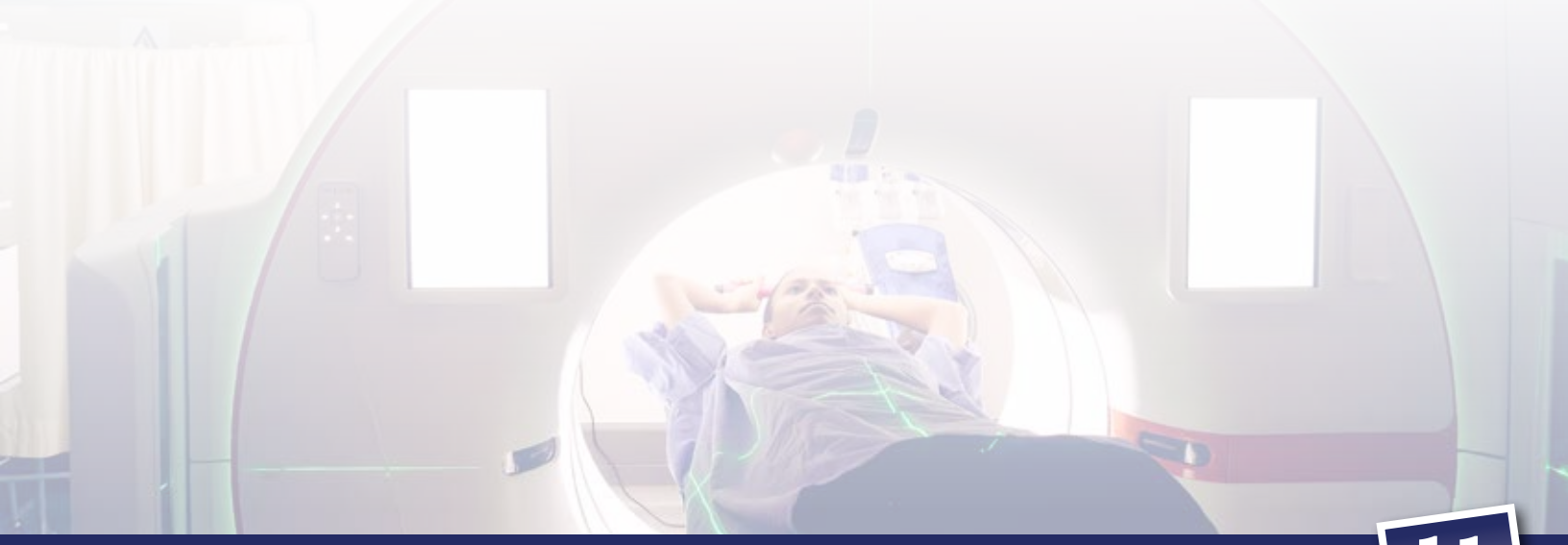
** Investigational New Drug, IND

IN THE CLINICAL PIPELINE (cont.)

*BCRP-funded** *Current phase supported by other sources* *Previous phase supported by other sources*

VACCINES AND IMMUNOTHERAPIES	Pre-IND	Phase 1/2	Phase 3
HER2-Specific Helper T Cell Epitope Vaccine, also called H2NVAC: Keith Knutson and Amy Degnim *A HER2/neu subdominant-epitope-based vaccine to enhance HER2-specific CD4 T cell immunity in patients with ductal carcinoma in situ.*			
Anti-HLA-A2/NY-ESO-1 TCR-Transduced Autologous T Lymphocytes: Rongfu Wang *A2-ESO-1 TCR-T cells to treat patients with relapsed/refractory locally advanced or metastatic TNBC that overexpresses NY-ESO-1.*			
ESR1 Peptide Vaccine plus GM-CSF and Montanide ISA: Zachary Hartman *A vaccine that targets five neoepitopes of estrogen receptor alpha, or ESR1, in combination with GM-CSF and Montanide™ ISA to treat patients with ER+ breast cancer.*			
Dendritic Cell Vaccines in Combination With Trastuzumab or Nivolumab: Peter Forsyth and Gary Koski *Dendritic cell vaccines combined with trastuzumab or nivolumab to treat patients with breast cancer leptomeningeal disease.*			

DIAGNOSTICS AND IMAGING	Pre-IND	Phase 1/2	Phase 3
Targeted HER2 Radiotracer: Gary Ulaner *^{89}Zr-trastuzumab as an imaging agent for HER2+ breast cancer.*			
TrackDOI: Darren Roblyer *A new optical metabolic scanning technology, TrackDOI, to monitor breast cancer patient tumor response to neoadjuvant chemotherapy in real time.*			
^{124}I-PU-H71-PET: Gabriela Chiosis *Novel imaging agent, ^{124}I-PU-H71-PET, as a non-invasive probe for positive emission tomography imaging of tumors in patients with breast cancer and other malignancies.*			



IN THE CLINICAL PIPELINE (cont.)

*BCRP-funded** *Current phase supported by other sources* *Previous phase supported by other sources*

THERAPEUTICS	Pre-IND	Phase 1/2	Phase 3
Fatty Acid Synthase Inhibitor: Ruth Lupu and Tufia Haddad *Combining the fatty acid synthase inhibitor, TVB-2640, with paclitaxel and trastuzumab to treat patients with taxane-resistant metastatic HER2+ breast cancer.*			
Enzalutamide and Fulvestrant: Anthony Elias and Jennifer Richer *Combining enzalutamide with fulvestrant to limit signaling through androgen receptors expressed on advanced ER+ breast cancers resistant to anti-estrogen therapy.* *Preoperative fulvestrant with or without enzalutamide to reduce tumor growth prior to surgery in ER+ breast cancer patients with locally advanced disease.*			
Meclofenamate: Joan Massague *An FDA-approved nonsteroidal anti-inflammatory drug, meclofenamate, to prevent new brain metastases in patients with recurrent or progressive brain metastasis from a solid primary tumor.*			
Denosumab, XGEVA®: Josef Penninger, Judy Garber and Christian Singer *Prophylactic administration of denosumab to prevent the development of breast cancer in women with BRCA1 germline mutations.*			
Biomarker-Driven Targeted Therapy: Christina Curtis, George Sledge and Jennifer Caswell-Jin *Therapeutics targeting driver gene amplifications present in integrative clusters IC1, IC2 and IC6 to treat high-risk ER+, HER2- breast cancer.*			
Neoadjuvant Endocrine Therapy, or NET, With Radiotherapy: Silvia Formenti and Sandra Demaria *Treating HR+ breast cancer with a combination of focal radiotherapy and letrozole NET to enable a response to immunotherapies.*			
Functional Precision Oncology—Patient-Derived Breast Tumor Grafts: Christos Vaklavas and Alana Welm *Patient-derived breast tumor grafts to predict, prevent and inform treatment of recurrence in patients with HR-low, HER2- or TNBC.*			
Ruxolitinib: Yi Li *Ruxolitinib for prevention of breast cancer in patients with high-risk and precancerous breast conditions.*			
AOH1996: Robert Hickey and John Perry *A novel inhibitor, AOH1996, of the cancer-associated proliferating cell nuclear antigen protein, caPCNA, to treat refractory solid tumors including breast tumors.*			
Abemaciclib and Pembrolizumab: Sandra McAllister *Combining abemaciclib, a CDK4/6 inhibitor, with pembrolizumab, a PD-1 inhibitor, to treat HR+, HER2- breast cancer.*			
Ivermectin With Balstilimab: Peter Lee *Combining ivermectin with balstilimab, a PD-1 inhibitor, for the treatment of metastatic TNBC.*			
Zunsemetinib With Capecitabine: Sheila Stewart and Cynthia Ma *A MAPK-activated protein kinase 2 inhibitor, zunsemetinib, or ATI-450, combined with capecitabine to treat HR+, HER2- breast cancer patients with bone metastases.*			

IN THE CLINICAL PIPELINE (cont.)

*BCRP-funded** *Current phase supported by other sources* *Previous phase supported by other sources*

THERAPEUTICS	Pre-IND	Phase 1/2	Phase 3
MBQ-167: Jose Rodriguez-Orengo *MBQ-167, a dual Rac and Cdc42 inhibitor, to treat patients with advanced breast cancer where standard of care failed or proved intolerable.*			
ML-016: Mauro Ferrari *An injectable nanoparticle generator, iNPG-pDOX, for treatment of TNBC with lung and liver metastases.*			
Naxitamab and Sacituzumab Govitecan: Clinton Yam and Venkata Battula *Naxitamab in combination with sacituzumab govitecan to treat patients with metastatic TNBC that previously received at least one line of systemic therapy for metastatic disease.*			
Tetrathiomolybdate With Capecitabine: Linda Vahdat and Vivek Mittal *Tetrathiomolybdate in combination with capecitabine to treat patients with TNBC at high risk of recurrence.*			
NB004: Andrei Goga *An orally available PIM kinase inhibitor, NB004, to treat advanced breast cancers in patients where standard treatments are ineffective.*			
Neratinib and Trastuzumab Deruxtecan: Ron Bose and Cynthia Ma *A potent pan-HER2 inhibitor, neratinib, combined with an antibody-drug conjugate to target HER2, trastuzumab deruxtecan, to treat patients with tumors harboring alterations in HER2.*			
Tocilizumab With and Without Carboplatin: Harikrishna Nakshatri *Carboplatin as a single agent and carboplatin combined with the interleukin 6 receptor inhibitor, tocilizumab, to treat patients with metastatic triple-negative or ER-low breast cancer.*			
AT-0174: Jennifer Richer *A dual inhibitor of tryptophan-2,3-dioxygenase, AT-0174, to inhibit tryptophan metabolism in breast cancer to reduce tumor growth and alleviate antitumor immunity in patients with advanced disease.*			

PRODUCTS MAKING AN IMPACT

TREATMENTS

Trastuzumab, Herceptin® - ***Dennis Slamon***
This monoclonal antibody that targets the HER2 receptor revolutionized breast cancer treatment and the field of targeted therapeutics for HER2+ early-stage and metastatic breast cancers.

ATLAS Clinical Trial - ***Richard Peto***
The ATLAS trial indicated reduced risk of recurrence or death from breast cancer in women who took tamoxifen for 10 years versus 5 years, changing clinical practice for premenopausal women with ER+ breast cancer.

Prone Radiotherapy - ***Silvia Formenti***
Treating ductal carcinoma in situ patients in the prone position with an accelerated, hypofractionated, whole breast radiation therapy reduced unnecessary exposure to the heart and lungs.

Palbociclib, Ibrance® - ***Dennis Slamon***
This small-molecule cyclin-dependent kinase, or CDK, inhibitor received FDA approval for treatment of HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant.

Ribociclib, Kisqali® - ***Dennis Slamon***
This small-molecule CDK inhibitor received FDA approval for treatment of HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant. The drug also received approval for use in combination with an aromatase inhibitor for adjuvant treatment of some patients with high-risk early-stage HR+, HER2- breast cancer.

Abemaciclib, Verzenio® - ***Dennis Slamon***
This small-molecule CDK inhibitor received FDA approval for treatment of HR+, HER2- advanced or metastatic breast cancer as a monotherapy or in combination with an aromatase inhibitor or fulvestrant. The drug also received approval for use in combination with endocrine therapy for adjuvant treatment of some patients with high-risk early-stage HR+, HER2- breast cancer.

DIAGNOSTICS AND PROGNOSTICS

Sentinel Lymph Node Biopsy - ***Douglas Reintgen and Kathryn Verbanac***
This technique enables clinicians to determine both tumor staging and the extent to which more extensive lymph node surgery is necessary.

Molecular Breast Imaging - ***Carrie Hruska***
This FDA-approved, commercially available nuclear medicine technique uses high-resolution, dual-head gamma cameras to detect the functional uptake of a radiotracer in the breast.

Digital Mammography and Breast Tomosynthesis - ***Laurie Fajardo and Daniel Kopans***
This FDA-approved, commercially available three-dimensional digital mammography tool improved sensitivity for detection of breast cancer in women with dense breast tissue.

Breast Cancer Index® - ***Dennis Sgroi***
A commercialized test that evaluates the likelihood of recurrence and benefit from extended endocrine therapy.

MetaSite Breast™ - ***John Condeelis and Allison Harney***
A publicly available test, certified as meeting federal quality standards under the Clinical Laboratory Improvement Amendments, measures “Tumor Microenvironment of Metastasis” biomarker levels to predict the metastatic potential of the primary tumor.

MenaCalc™ - ***John Condeelis and Jeanine Pignatelli***
A clinically validated test for use in cancer treatment decision-making and as an independent prognostic factor and predictor of metastasis.

RISK ASSESSMENT

BRCA2 617delT Mutation - *David Goldgar and Susan Neuhausen*
One of the founder BRCA1/2 mutations that occurs in Ashkenazi Jews, a population with increased likelihood of BRCA1/2 mutations; now part of a commercialized test for this risk group.

OncoVue® - *Eldon Jupe*
This commercially available genetic-based breast cancer risk test enables clinicians to identify high-risk patients and individualize breast cancer screening and monitoring.

PTEN - *Michael Wigler*
A test is commercially available to confirm PTEN gene mutations for clinical and prenatal diagnoses and identification of at-risk family members.

PALB2 Mutations - *Bing Xia*
Mutations in the PALB2 gene increase breast cancer susceptibility twofold; a commercialized PALB2 genetic test is available for those with familial breast cancer.

BROCA Cancer Risk Panel - *Tomas Walsh and Mary-Claire King*
A comprehensive test that enables assessment of all known breast cancer genes and mutation types in a single assay.

PATIENT RESOURCES AND REGISTRIES

Dyson Family Risk Assessment Program - *Mary Daly*
This program provides counseling and risk analysis to individuals with a family history of breast or ovarian cancer.

Carolina Mammography Registry - *Bonnie Yankaskas*
This population-based mammography registry became a member site of the National Cancer Institute Breast Cancer Surveillance Consortium, a national registry that provides a resource for researchers to study mammography screening on a national level.

BreastCancerTrials.org - *Laura Esserman*
This online resource informs patients about breast cancer clinical trials and matches them with appropriate trials.

RESEARCH RESOURCES

Novel Models for Breast Tumor Growth and Metastasis - *Alana Welm*
Publicly available, patient-centric tumor graft mouse models that replicate the diversity of human breast cancer and enhance the study of tumor growth, metastasis, drug efficacy and prognosis.

Three-Dimensional Culture Systems - *Mina Bissell*
Three-dimensional culture models currently utilized across academic laboratories and by drug companies as screening assays to test for therapeutic response.

nCounter® Myeloid Innate Immunity Panel - *Lisa Coussens*
Commercially available research tool with utility for basic and translational immuno-oncology research.

Monoclonal Antibodies - *Janet Mertz*
Commercialized monoclonal antibodies that bind to estrogen-related receptor alpha, ERR-alpha, for studying breast cancer biology.

For more information, please visit
https://cdmrp.health.mil
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