NATIONAL BREAST CANCER COALITION

ARTEMIS PROJECT

ANNUAL MEETINGS
MARCH 2-5, 2023

NATIONAL BREAST CANCER COALITION • ARTEMIS REPORT

I. INTRODUCTION

The National Breast Cancer Coalition (NBCC) was formed in 1991 to end breast cancer through the power of grassroots action and advocacy. Since that time, NBCC has built a strong coalition of advocates and organizations that support its mission. Launched in 2010 to support the NBCC's mission-oriented research goals, the Artemis Project®, under NBCC leadership, brings together leading researchers and trained advocates who set priorities and design and implement research plans that focus on two areas:

- **Primary Prevention:** How do we stop women and men from getting breast cancer?
- **Prevention of Metastasis:** How do we stop them from dying of breast cancer?

Artemis Project reports from previous annual meetings, found at www.stopbreastcancer.org/artemis, lay out the history of the Artemis Project. This report provides a summary of discussions and recommendations made at the 2023 annual Artemis meeting. This meeting had 24 participants, including advocate and scientific expertise ranging from immunology, biomedical engineering and genetics to molecular biology, radiation oncology and clinical oncology

2023 ANNUAL MEETING PARTICIPANTS

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II. BACKGROUND

The Artemis meeting began Thursday evening, March 2. Thursday was set aside for introductions, an NBCC update, Artemis' background and general scientific discussion. As is tradition, participants began by identifying and discussing current key, burning breast cancer questions. The meeting then moved to the session on "Primary Prevention," which was held from Friday, March 3, 2022, to noon on Saturday, March 4, followed by the session on "Prevention of Metastasis," which concluded after lunch on Sunday, March 5.

III. ARTEMIS PROJECT MEETING SUMMARY OF PREVENTION MEETING

March 2-4, 2023

BACKGROUND PRESENTATIONS

Review of Vaccine Landscape

Michelle Tregear, Danny Douek, Kim Lyerly

NBCC advocates have been tracking breast cancer vaccine trials since 2012. The majority have been vaccines for treatment or for secondary prevention. A 2021 review described 44 ongoing breast cancer vaccine trials, by subtype, disease stage, phase of the trial and vaccine platform, but not outcomes. In 2020, there were two new Phase 1 breast cancer prevention clinical trials. One, an alpha-lactalbumin vaccine for women with triple-negative breast cancer (TNBC) from the Cleveland Clinic, and the other from the University of Pennsylvania for women with BRCA1/BRCA2 mutations, including one arm for women previously treated for breast cancer and another arm for healthy women with or without a prior prophylactic mastectomy.

mRNA Immunization

Danny Douek

Douek presented a history of mRNA vaccine technology and an analysis of mRNA benefits and drawbacks leading up to the COVID-19 vaccine. He highlighted a 2005 study by Kariko, which found that RNA by itself looks like a virus. Other beneficial biological aspects of mRNA immunization include that its 10-day protein expression is well suited for maturing a B cell response; the vaccine components rapidly degrade; and it only requires an injection into the cytoplasm. While virus vectors are limited in terms of how many times they can be given due to the elicited reaction, there is no anti-vector immunity to mRNA. Additionally, no bioreactor is required with mRNA immunization since it is chemically synthesized, and multiple vaccine components can be included. Finally, Douek emphasized that the iterative design cycle is beneficial for rapidly trying a lot of different approaches. However, he also noted that protein expression and the immunogenicity for CD8 T cells need improvement. In addition, in considering mRNA vaccines in cancer, we still need to overcome the fact that the tumor microenvironment is immunosuppressive.

The 2023 Vaccine Landscape

Kim Lyerly

Lyerly described how COVID vaccine development allowed for robust clinical comparison of vaccine technologies. He questioned what conclusions can be drawn in vaccine delivery research from smaller clinical studies and smaller datasets. The COVID vaccine studies involved hundreds to thousands of patients and the analysis of immune responses for various vaccine strategies that could be directly compared. He noted that a leading vaccine vector, a recombinant adenoviral vaccine, did not mount as strong of an antibody response as two mRNA vaccines in humans. This was not expected by the vaccine community and highlighted that mRNA could be effective and safe, and in the case of COVID, superior to what was considered the best vaccine platform, recombinant viral vectors. In addition, the cellular-based vaccines did not perform well clinically. He also questioned the definition of success for vaccines. For example, does 90 percent protective mean 9 of 10 did not get infected or that they did not get sick from

infection? He showed COVID vaccine research with a huge range of antibody responses, but with much less variability in the protectability of outcome, so defining what should be a marker of vaccine success can be challenging.

Lyerly expressed that in order for vaccines to work in preventing cancer, there are necessary sequences of activity—a vaccine could fail due to the tumor microenvironment, which may be hostile to the immune response that is generated by a vaccine, or the vaccine may fail because the general immune response isn't sufficient to eliminate cancer. Participants pointed out that from the time an individual develops cancer, there is already a systemic change in the immune system that persists. Participants asked what, in the context of a prevention vaccine for which there is no tumor to suppress, the ideal type of immunity is that we want to generate. Another issue discussed included vaccine delivery methods and whether intranasal, intramucosal or intradermal administration had been tried in cancer vaccines.

Seed Grant Update: Prevention Vaccine Project Update

Keith Knutson

Knutson described the Artemis prevention vaccine, which targets nonmutated self-antigens (overexpressed tumor-associated antigens) and has a prime-boost strategy. Details and history of the vaccine development process and design of the Phase I trial are described in prior Artemis Annual Reports.

Knutson brought the group up to date on the National Cancer Institute (NCI) PREVENT process and reported that a bid had been accepted for production of the modified vaccinia virus Ankara (MVA) portion of the vaccine. NCI has committed to support the Artemis vaccine through a Phase 2 clinical trial. Discussion continued focused on the Phase I trial, and Knutson explained that the Mayo Clinic will partner with other institutions to increase patient diversity. For example, there are plans to work with Emory for the Phase 1 trial.

Participants asked whether there would be an immune response threshold for the initial 12 patients in the safety lead-in cohort, since they will all have advanced cancer and likely suppressed immune systems. Knutson responded that for the safety lead-in cohorts, we will just be looking at safety. Further group discussion revolved around the endpoints and population for the trials.

Microchimerism in Alloimmunity and Autoimmunity: Multifaceted and Protean

J. Lee Nelson

Nelson presented a definition of microchimerism and the various tools available to detect microchimerism. Microchimerism occurs in healthy individuals and in a number of different diseases, including autoimmune diseases such as neonatal lupus and rheumatoid arthritis, cancers such as breast cancer, infectious diseases like malaria and neurobiology among people with epilepsy or brain tumors.

Nelson described a study in which maternal heart cells were found in male babies who had died of neonatal lupus, an autoimmune disease that can develop in utero, even though the mother didn't necessarily have lupus. This shows that microchimerism can be present as differentiated cell types in tissues. She also described a few cancer studies, most of which showed a potential protective effect of microchimerism. Most studies of breast cancer described reduced risk among women who had births, perhaps related to human leukocyte antigen (HLA)-disparate cells from the fetus providing protection. Other studies showed a potentially detrimental effect, such as fetal vascular endothelial cells found in the mother contributing to melanoma growth.

Nelson concluded with several factors contributing to whether microchimerism can have beneficial effects or detrimental effects: the source of microchimerism, the age of the recipient when microchimerism was acquired, the time elapsed since microchimerism acquisition; the potential interaction with other microchimerism sources; and the specific HLA of microchimerism, the recipient and the HLA relationship. In the setting of cord blood transplantation for cancer where risk of leukemia relapse is reduced, she suggested that the maternal microchimerism that is present in cord blood could function in an instructive role as "licensing to kill."

The cells age with the recipient. It is unclear how these cells are maintained over decades at really small levels, so it might be related to dormancy. If these cells can be anything, could they sometimes be the origin of cancer? For example, chronically immunosuppressed transplant patients have skin cancers (squamous cell) show up everywhere on their bodies. For the purposes of Artemis, in direct contrast to skin cancer, breast cancer among transplant patients is very rare, and we don't know why.

Participants discussed the possible protective effect of microchimerism and breast cancer and whether that effect was also seen among postmenopausal women. Nelson responded that a similar protective effect was not seen among older women and commented that there could be something about fetal cells as they age and/or about changes to a woman's immune system as she ages.

Clonal Hematopoiesis of Indeterminate Potential

Discussion led by Frank Calzone

Participants discussed the evolution of genetic mutation over time and its relationship to microchimerism, as well as its effect on heterogeneity. While mutations underlie aging, it has not been proven that they clonally underlie cancer. Calzone described field defects, in which a genetic change in a cell can take over in a tissue that turns over frequently. For example, a person has a BRCA1 mutation, but then there is a transformational event that causes cancer. What happens to a micrometastasis that finds itself in such an environment? Could circulating DNA be used to look at field defects in a different way, and how does microchimerism fit into these ideas?

Participants wondered whether the mutations are there and not generating an immune response because the mutations are engendering tolerance. A suggestion was raised to map out what the T cell will recognize and where the mutations would be later in life, then to select against the ones compatible with the immune system. We will need to break tolerance for primary prevention. And since the immune system can compartmentalize by tissue, we may want to break tolerance in certain tissues.

WORKING GROUP TOPICS, DISCUSSIONS AND ACTION PLANS

After discussion and debate, participants agreed on five primary prevention topics for working group activity. The groups were chosen and convened to discuss each topic, presented to the large group for discussion, and met again for a final report. Working groups then outlined 12- to 18-month action plans for each topic area.

Nerve-Racking Prevention: Modulating Neuronal Signaling for Primary Prevention of Breast Cancer (Mind Control)

Mikala Egeblad, Silvia Formenti, Andrei Goga, Michelle Tregear, Shawn Zhang

The group discussed what is happening in breast cancer regarding interactions between the tumor and nerves. In normal breast tissue, nerves grow along the ducts. But during early cancer lesion development, nerves begin growing into the ducts through what appears to be a process of neurogenesis. Might these nerves stimulate tumors to grow faster? Could there be a Botox-like treatment to prevent breast cancer, perhaps injected into ductal carcinoma in situ (DCIS) or atypical ductal hyperplasia (ADH) to prevent malignant lesions from developing? What would happen if we removed nerve-based stimulation to disable the nerves from sending local signals?

Next Steps:

Three aims were described:

1. Define the types of nerves in the healthy breast and then in breast cancer and breast cancer precursors.
2. Adapt existing experimental models so that they can be used to interrogate what the nerve infiltration is doing in tumor initiation and metastasis.
3. Test approaches to eliminate nerve-tumor interactions in order to prevent invasive breast cancer.

The group identified knowledge gaps and identified needs as follows:

- **Human tissue with outcomes data:** 3D tissue clearing, RNAseq (bulk, single cell, spatial transcriptomics), approaches to measure the presence of neurotransmitters and MIBI-TOF (NT spatial localization).
- **Animal and culture models:** Models to test prevention and acceleration and to manipulate candidate drivers.
- **Approaches for denervation:** Pharmaceutical (beta blockers for sympathetic), local neurotoxic (Botox motor neurons and parasympathetic) and surgical approaches.

After the large-group discussion and input, a plan was developed.

License to Kill (Microchimerism)

Keith Knutson, Lee Nelson, Michele Rakoff, Alana Welm

Microchimerism is the presence of cells from one person in a genetically different individual (e.g., when women retain in their body a small number of fetal cells from their babies and/or the baby retains

some maternal cells). The key question identified by the group was whether or not microchimerism has a functional role in reducing breast cancer risk among parous women. Given that the frequency of microchimerism is less than 1 percent of cells, what is the likelihood that they could modulate the immune response to a developing cancer?

The group proposed the following potential mechanisms by which microchimerism could functionally result in reduced breast cancer risk:

- The "adjuvant" effect, whereby the immune system is just generally activated by the presence of microchimerism, and this contributes to tumor clearance.
- Microchimeric cells differentiate to immune cells and kill the cancer through a non-antigen-specific mechanism.
- Microchimeric cells express something that vaccinates against the tumors, like retroviruses or fetal antigens.
- Maternal cells recognize the tumor via HLA.
- mRNA transfer via exosomes from the microchimeric cells to the tumor cells.

During the large-group discussion, participants raised a number of questions around tolerance, previous experiments, male breast cancer and HLA sharing.

Key Question:

1. Generational memory can occur through microchimerism. Does microchimerism have a functional role in reducing breast cancer risk?

Next Steps:

The group listed a number of questions and tasks for both human and animal studies, including as follows:

1. Determine the frequency of microchimerism in the breast.
2. Determine risk association and transplant possibilities.
3. Determine sequencing needs.
4. Determine the need for various studies in hybrid mice.

Prevention of Lethal Breast Cancer: "COVID Vaccine" vs. "Measles Vaccine"

Joe Camardo, Sara Hurvitz, Chris Li, Tracy Edler Solak

There's a possibility that vaccinating people before diagnosis will reduce breast cancer incidence overall but not have a significant impact on mortality. The group looked to existing vaccine paradigms for guidance on the various strategies through which vaccines can be effective and determined that reducing mortality, in line with how the COVID vaccine functions, is more important to accomplish than aiming to reduce the incidence, like the measles vaccine. The group hypothesized that if we can effectively subtype the disease to identify the people who will die from breast cancer from those who will not die, then we would be able to address lethality in a vaccine 2.0 and not just reduce incidence.

Next Steps:

1. Conduct a study to address the barriers to researching this issue, particularly regarding the large sample size necessary to draw any actionable conclusions.
2. Find the deadliest forms of breast cancer and focus on preventing them; these include luminal B, triple-negative and other subtypes that make up about 50 percent of all breast cancer cases.

Participants concluded that a study of this type is needed because different subtypes of breast cancer will require different primary prevention strategies, but our ability to effectively subtype breast cancer remains limited. The group aims to bring together a diverse, multidisciplinary team to figure out how to assess these tumors and to run a large study that would result in enough information to move forward with a vaccine targeted at reducing mortality.

Mutant Me

Michele Atlan, Frank Calzone, Brandon DeKosky, Danny Douek, Steve Elledge, Cyrus Ghajar, Kim Lyerly

Oncogenic mutations can exist in normal epithelia without causing overt tumors. Studies looking at normal skin, eyelids and esophagus tissue among healthy individuals have found "fields" of mutated cells within the normal epithelia. Such studies have not yet been done for breast cancer to determine whether these fields of mutated cells are being "seen" by the immune system, and if not, is there an immune pressure shaping the mutations that emerge? If mutant cells are present in the normal breast epithelium and T cells are ignoring them potentially because they are missing an "alarm signal," could the group use a preventive local adjuvant (instead of a vaccine) to provide such a signal and eliminate these cells?

Next Steps:

1. Determine whether the normal human breast epithelium contains oncogenic mutations.
2. Perform more functional experiments in mice:
   - Begin collecting normal and BRCA carrier breast tissue and blood.
   - Perform sequencing on these samples.
   - Begin establishing the mouse models needed for the in vivo experiments.

The large group discussed whether the evidence of mutations in individual cells showed that they were translated and transcribed into epitopes, as well as whether the mutations were associated with rapidly proliferating cells that would invoke an inflammatory response to bring in T cells. Discussion occurred around the need to know more about the mutations that arise in normal breast tissue beyond what we already know from The Cancer Genome Atlas (TCGA) and other issues regarding consent.

Pregnancy and Breast Cancer Risk

David Bowen, Peter Fasching, Judi Hirshfield-Bartek, Simon Knott

A regression model predicted significant breast cancer risk reduction in North America if, on average, women had 6.5 children and breastfed each of them for two years. Is there a way to simulate this beneficial effect without pregnancy?

The overall idea was to profile women throughout pregnancy and breastfeeding to fully understand the changes that are induced during this process. The largest barrier to this research was anticipated to be recruiting participants. One approach considered creating interest by enrolling a large proportion of women at high risk for breast cancer, whose breast cancer status could then be followed over time. Another way to recruit participants would be to do a feasibility study among women who had gotten a mammogram within two years of pregnancy, because they might be more open to breast diagnostic testing. The group discussed the effects from the timing of pregnancy, racial differences in breast cancer and pregnancy, and how to analyze the data.

Next Steps:

1. Conduct a pilot study to provide information on the feasibility of a larger study in the U.S.
2. Ensure the pilot study monitors breast cancers (e.g., biopsy and incidence).

IV. SUMMARY OF PREVENTION OF METASTASIS MEETING

March 4-5, 2023

BACKGROUND PRESENTATIONS

Seed Grant Update: How Do Dormant Disseminated Tumor Cells Evade Immune Recognition?

Cyrus Ghajar

This project investigated whether 1) engineered T cells kill disseminated tumor cells (DTCs) expressing a model antigen and 2) if T cell recognition and killing depend on the proliferative status of a DTC. Ghajar found that DTCs persist in the bone marrow despite T cell-mediated clearance of primary orthotopic tumors. He saw DTCs and T cells localized to the same niche, indicating that dormant DTCs may actively evade tumor-specific T cells. He identified the potential barriers to surveilling dormant DTCs.

Next Steps:

1. Thoroughly define the role of tissue-specificity.
2. Define human DTC antigens and neoantigens.

Human-omics Reveals Mechanisms Underlying Local and Distant Tumor Formation

Simon Knott

Acknowledging recent work by Swanton on epidermal growth factor receptor (EGFR) promotion of lung tumor formation by air pollution, Knott questioned if something analogous was happening in the breast and whether there were types of

mutations that interacted with environmental stimuli to induce a transformation to cancer. He discussed whether this concept could apply to early pregnancy versus later pregnancy protection and the accumulation of mutations over time.

Participants noted that while an environmental carcinogen might explain the first growth of one of the dormant cells, once a patient develops a metastasis, additional organs then develop metastasis. What is it about the leading metastasis that changes the balance of the body and all the dormant cells?

Knott then presented a study by Schultz's group on the genomic characterization of metastatic patterns from the prospective clinical sequencing of 25,000 patients, presented a paper by Chuck Perou on the AURORA US Metastasis Project and summarized what was found from bulk sequencing of both primary and metastatic tumors.

Participants cautioned that the AURORA study included very few bone metastases, which is a huge limitation for ER+ breast cancer. Advocates asked who owned the thousands of patients' primary-metastasis-matched pair samples from the AURORA study, as well as whether there might be sample leftovers available for further research or whether the bulk analysis used the entire sample.

WORKING GROUP DISCUSSIONS AND ACTION PLANS

Four prevention of metastases topics were identified for the breakout discussions.

Beating the Clock: Harnessing Circadian Rhythms to Prevent and Treat Metastasis

Michele Atlan, David Bowen, Mikala Egeblad, Judi Hirshfield-Bartek, Chris Li

Studies have shown that different hormones and biological processes peak at different times during the day and night, including cortisol, insulin and melatonin levels; neutrophil and lymphocyte activity; body temperature; and muscle strength. Studies have also shown that circadian rhythms were linked to cell dissemination and an increase in metastasis and that treatments are more effective at certain times of the day. The group identified several knowledge gaps, including the underlying biology that regulates circadian changes in cancer cell behavior and more detailed data on timing of treatments and cell shedding.

The group described an animal model and an observational human study to address the gaps.

Next Steps:

1. **Pre-clinical:** Use mouse models of DTCs/early metastatic disease to determine whether disrupting circadian rhythms can influence colonization and whether metastatic disease is more treatable at specific times.
2. **Clinical:** Conduct a small observational study of 50 patients with Stage 3 TNBC at diagnosis.

The large-group discussion included the possibility of utilizing epidemiological evidence from populations in occupations with disrupted work schedules or populations in the Nordic countries in winter versus summer months. The group also discussed a possible mismatch between the circadian rhythm of the tumor cells and the circadian rhythm of the body.

Memory T and B Cells

Brandon DeKosky, Silvia Formenti, Keith Knutson, Michele Rakoff, Shawn Zhang

The group's hypothesis was that immunological memory contributes to preventing metastatic emergence. What is driving immunological memory in patients, and what can we learn about how immune memory and tumor interactions provide protection?

The group identified a number of knowledge gaps, including the need to characterize immune memory and understand how it relates to recurrence, as well as how T cell responses are maintained in connection with pembrolizumab treatment to learn what type of immune memory can be boosted by intervention to prevent recurrence. The group also briefly alluded to measuring response to tumor associated antigens.

Next Steps:

1. Develop a sampling plan for study populations receiving the standard of care therapy during primary tumor and initial treatment (all patients), as well as during recurrence (50 percent of patients).
2. Measure and understand tumor-specific T cell receptors (TCRs):

During the large-group discussion, participants asked how difficult it might be to find the T cell specificity and whether there might be common ones across patients, whether it would be possible to enumerate the number of antigen-specific T cells to address whether the rarity of T cells

and their target is correlated with recurrence or lack of recurrence, whether the mutations in the tumor correlate with patients who don't undergo pathological complete response (identifying mutations associated with immune escape and tolerance) and what effect radiation therapy might have. Participants noted that it will be important to decouple driver mutations from the mutations that could be immunogenic and that lineage deconstruction would be helpful using DNA.

Trans-Differentiation in Metastasis

Frank Calzone, Steve Elledge, Andrei Goga, Kim Lyerly, Tracy Edler Solak, Alana Welm

Trans-differentiation is the idea that one cell type can change states into another cell type. The group discussed whether a change in differentiation or cell state might be required for a disseminated cancer cell to establish and/or grow in a metastatic site. The group considered a broad definition of trans-differentiation to include any sort of adaptation that would give the disseminated cancer cell an advantage to grow in a new site, including changes in its metabolic or immune state.

Key Questions:

1. Which cells have the propensity to adapt to metastatic tissue?
2. Can plastic cells be forced to take on a nonmetastatic cell state that prevents them from being able to grow at the metastatic site?

Next Steps:

1. To address the first question, utilize a barcoded library of tumor cells, injecting them into mice, and use RNAseq to identify subsets of cells that change their cell state upon reaching the metastatic tissue.
2. To address the second question, pre-treat breast cancer cells with known agents that affect cell differentiation or the epigenetic state to determine whether treatment with any of these things alters the cells in a way that makes them incompatible with adapting to the metastatic sites.

During the large-group discussion, participants raised the issue of cross-talk and how the primary tumor communicates with and conditions the recipient tissue for metastasis. It was noted that the ability of cells to form a patient-derived xenograft (PDX) is correlated with clinical outcome—those that grow are the ones that recur and are not the ones correlated with pathological complete response. Participants also asked whether DTC reversion from dormant to dividing is immune mediated or metabolic.

We Go Both Ways

Joe Camardo, Danny Douek, Peter Fasching, Cyrus Ghajar, Sara Hurvitz, Simon Knott, Lee Nelson, Michelle Tregear

Dissemination of tumor cells can happen very early in cancer, and so one potential goal is to not necessarily prevent dissemination, but rather to keep DTCs dormant indefinitely to prevent DTCs from turning into metastatic disease. How do anti-metastatic tissues affect DTCs and vice versa? For example, there are observational data from rapid autopsy specimens that have shown women with ER+/PR+ DTCs in their muscle tissue (Crist et al., Nature Cell Biology 2022), which is not seen in normal muscle tissue.

What can we learn from tissues where metastases rarely, if ever, emerge?

Next Steps:

1. Define the burden of DTCs throughout the body and enumerate the niches that DTCs occupy.

Goal: Identify anti-metastatic organs and anti-metastatic niches (even within metastatic organs).

2. Recreate dormant and metastatic niches in culture and apply this idea to the anti-metastatic tissues and niches identified in Aim 1.

Goal: Create a screening platform and identify all the niche components that promote or inhibit DTC proliferation.

3. Convert niches that are permissive into niches that are nonpermissive and vice versa (strictly as proof of concept).

During the large-group discussion, participants discussed the heterogeneity of tumor cells, invasive lobular carcinomas, breast cancer being an age-dependent disease and a niche not necessarily being a singular thing. A niche may be permissive at one point in time, but not another, so it is critical to understand how everything comprising a niche may change over time.

V. CONCLUSION

More than a decade into its existence, the Artemis Project has fostered the establishment of numerous fruitful and long-lasting collaborations among diverse researchers and advocates who would have likely otherwise never crossed paths. The annual meetings continue to generate bold ideas and work plans on novel approaches for preventing breast cancer and preventing metastasis, many of which are brought to life through collaborative research efforts throughout the year.

Artemis continues to make progress on a preventive vaccine for breast cancer. In 2020, NBCC's proposal was accepted by the NCI's PREVENT program to advance the vaccine to a Phase 1 clinical trial with manufacturing support. Though progress has been slowed because of the COVID-19 pandemic, a clear path has been outlined for production for the Phase I safety trial and is poised to move forward now that the NCI PREVENT program has awarded a contract to manufacture the vaccine.

This year, in primary prevention, the distinct topics explored included risk prediction and reduction strategies, as well as systemic mechanisms such as determining and mitigating the role of neuronal signals in breast cancer. During the Artemis Meeting for the Prevention of Metastasis, determining the body's mechanisms to induce inhospitable tumor environments continued as a key theme, as well as ways to mobilize and destroy latent DTCs. The group also spent time discussing the state of the science and exploring how emerging technologies might be leveraged and incorporated into the goals of the Artemis Project: to prevent breast cancer and to end breast cancer deaths.

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