WELCOME

Save the date: Dec 2020 IBC Virtual Education Meeting

MD Anderson is honored to host the 7th International IBC Consortium Meeting which is held every 2 years to bring together IBC researchers and clinicians internationally for scientific discussions about IBC and foster networking for collaborative research. Due to the majority of academic institutions still restricting business travel, the organizing committee recently decided to postpone the planned in-person conference scheduled in December 2020 until next year. In its place, we have decided to host a virtual educational meeting on Saturday December 5th, through Zoom focusing on clinical topics with high level summaries of new clinical and translational data. The agenda is currently being finalized and will be available on our website shortly. Patients and advocates are welcome to attend this educational meeting, and we encourage sharing with outside medical teams as well. Registration will be live by November and will be publicized through our social media and current email lists.

How we use your Boot Walk donations to make a difference

A big thank you to all members that participated, fundraised, and supported the ‘IBC Wranglers’ Boot Walk team and our mission to end IBC. In the past 4 years, team IBC Wranglers has raised a total of $328,859.33, and the funds have been used to support over 60 research patients with their hotel and parking expenses, to study IBC aggressive biology and brain metastasis; to establish the world’s first IBC mouse model with human immune cells; to explore molecular target for the treatment of IBC; to support a PhD student to examine the link between risk factors and IBC biology, and to develop blood-based assay identifying biomarkers for the prediction of patients’ response to immunotherapy.

Funds raised last year have been allocated to IBC Clinical and Laboratory Research leaders to support advancements in IBC, and the funds have been utilized as follows -

Patients diagnosed with aggressive cancer have drastically increased physical and emotional challenges as well as financial hardship. We allocated $30,180 from the Boot Walk funds to assist patients participating in IBC clinical trials (2016-0177, 2016-0537, and 2016-0890). During the previous year, the IBC program supported 30 patients with hotel and parking expenses (approx. $15,000) for their follow up visits to MD Anderson Cancer Center (IBC Clinical Research)

Finding new and effective treatments for IBC requires a better understanding of the drivers of IBC aggressive biology. We previously demonstrated that NDRG1 is crucial in driving tumor progression and brain metastasis in IBC mouse models. We performed proteomics array screening in IBC cells and identified NDRG1-pathway mediators that can be therapeutically exploited. We also conducted immunohistochemical staining of IBC patient tumors and demonstrated that NDRG1 is independently correlated with worse clinical outcomes. Thus, the fund helped establish the potential importance of NDRG1 as a target for therapy and a prognosis marker in IBC. This work was presented at the San Antonio Breast Cancer Symposium (SABCS) and Annual Postdoc Symposium at MD Anderson, and two manuscripts related to this project are in preparation for submission to peer-reviewed journals (Dr. Debeb lab).

With Boot Walk funding support, we established the world’s first IBC mouse model with human immune cells. Using this mouse model, we showed that panitumumab, an antibody that specifically reduces the activity of EGFR protein,
increases the number of immune cells that can kill cancer cells and reduces IBC tumor growth. We also showed that the effect of panitumumab on immune cells made immunotherapy (immune checkpoint inhibitor, ICI) more effective in IBC. These exciting results have led us to prepare for a clinical trial to test panitumumab plus an ICI in patients with IBC. We are now applying for an extramural grant (an NIH R01 grant submitted in June 2020) and negotiating with Amgen and Merck for drug supplies. We just received Amgen’s commitment to supporting this trial. Our ultimate goal is to improve IBC patients’ survival by establishing immune checkpoint inhibitors combined with EGFR-targeted therapy. The generated data helped us receive the Emerson Collective Cancer Research Fund to investigate how panitumumab mediates IBC tumor surrounding microenvironment. These findings were orally presented at the 2019 AACR Annual Meeting and the 5th Annual Immuno-Oncology Young Investigators’ Forum. The poster presentation at the 41st Annual San Antonio Breast Cancer Symposium was awarded the 7th Annual Zeta Tau Alpha Houston Alumnae Association Fellowship in Inflammatory Breast Cancer Research. (Dr. Ueno- Dr. Wang lab)

TNBC/IBC has an aggressive disease progression, associated with poor patient outcomes. The Boot walk funds immensely helped support my lab research focused on exploring and demonstrating the importance of the ‘MAPK signaling pathway in TNBC/IBC.’ This pathway is activated in TNBC/IBC disease and is associated with aggressive disease progression and metastatic spread. Based on this finding, we believe that the MAPK pathway is potentially an excellent molecular target for the medical treatment of IBC. We plan to expand our research in this area further to discover new IBC targeted therapy options. We have presented this work at the MD Anderson Breast Medical Oncology Department and the Division of Cancer Medicine Grand Rounds (DOCM) Meetings and published a manuscript in Scientific Reports. (Dr. Bartholomeusz lab)

With our Boot Walk support, we funded a PhD student who is dedicated to IBC research. She is examining the link between risk factors and IBC biology. She presented her initial findings at the San Antonio Breast Cancer Symposium (SABCS) last winter and connected her work in animals to our clinical database. She demonstrated how the patient data that classic appearing IBC is more aggressive than borderline IBC and has submitted that work to SABCS. She is now extracting epidemiology information from those classic cases to inform her molecular studies and better understand why people get IBC. (Dr. Woodward lab)

The Boot Walk funds were used to develop blood-based assays to identify biomarkers that could predict how breast cancer, and in particular IBC, patients respond to immune-based therapies. The biomarkers we investigated involved T-lymphocytes, the predominant immune cells affected by immune-based therapies, including checkpoint inhibitor therapies. Dr. Hui Gao developed the T-cell clonality assay to determine factors associated with response to anti-PD-1 therapy (pembrolizumab). She performed blood-based analyses to identify different T-cell clones (repertoire) and T-cell phenotypes to evaluate their association with progression-free survival (PFS) in patients with metastatic IBC (mIBC) or mTNBC. Our studies suggested that T-cell reactivity at baseline and a lower percentage of CD4+ T cells with the CTLA4/Tim3/2B4 phenotype were favorable prognostic factors for patients receiving pembrolizumab. This proof-of-concept provided promising data that T-cell clonality and phenotyping of T-cell exhaustion markers can help identify potential responders and be applied to ongoing and future trials with immune-based therapies. (Dr. Reuben lab)

We developed a methodology designed to harness the benefits of utilizing PDX models. We developed a unique patient-derived xenograft derived ex vivo (PDXEx) model from the cellular milieu released from a PDX tumor harvested from a mouse. The gene expression profiles of our PDXEx models demonstrated a highly significant correlation to the gene expression profiles of the host PDX, indicating the clinical relevance of this model system in identifying and testing new targeted therapies for the treatment of IBC. Immunohistochemistry analysis showed a high expression of membrane-bound human aspartate β-hydroxylase (ASPH). ASPH is a membrane protein that contributes to the aggressive behavior, metastatic potential, and chemo-resistance of many tumors, including breast cancer. The expression of ASPH is very low or negligible in adult tissues, where it usually is localized only to internal compartments. However, upon cellular transformation, ASPH is re-expressed and translocates to the tumor cell surface. It plays a role in mediating metastasis, aggressive behavior, therapeutic resistance, tumor recurrence, and
reduced survival of patients. Through a collaborative study, we tested a range of IBC cells with ASPH inhibitors. We showed that although targeting ASPH did not affect cell proliferation, and it had a significant impact on inhibiting colony formation assay. We predict that small molecule inhibitors generated against ASPH could be moved into clinical trials for chemo-resistant metastatic TNBC. (Dr. Geoffrey Bartholomeusz lab)

New Research Technology in IBC Translational Lab

Breast Medical Oncology Research has been awarded institutional support to purchase a VICTOR Nivo Multimode Microplate Reader recently. This is the fourth consecutive submission approved to support our team's research. The plate reader will supplement current capability in absorbance, luminescence, fluorescence intensity, time-resolved fluorescence, and fluorescence polarization. It is designed for low-throughput routine assays. This Equipment can help us further enhance the quality of basic research to support our lab teams and allow broad usage for a variety of ongoing research initiatives, including grants (R01, CPRIT, BCRF, DoD, and pharma) applications to advance IBC research.

Strategic Initiative: Rare Tumor Initiative to sequence IBC

The Rare Tumor Profiling Initiative is a high-priority strategic project for MD Anderson that provides a unique opportunity for investigators to obtain comprehensive data on 1,500 rare tumor samples, including whole-exome sequencing (WES) of tumor and germline, RNA sequencing of tumor, and high throughput multiplexed immunofluorescence based immunoprofiling of the tumor immune microenvironment. This effort is an attempt to help bring catalytic change in the landscape of rare tumor research.

The IBC Program participated in the project to obtain comprehensive profiling of IBC patient samples, which will help us identify potential diagnostic, prognostic, and predictive biomarkers that can be utilized to guide clinical management of patients with IBC. This project is co-led and implemented by IBC Pathology Leader Savitri Krishnamurthy, M.D., Xiaoping Wang, Ph.D., Larry Coffer II, M.S., Anita Wood, and Angela Alexander, Ph.D.

Dr. Krishnamurthy reviewed cases from the IBC registry including tissues that were procured in different clinical trials. She selected the baseline core needle biopsy specimens including fresh snap frozen cores and corresponding formalin fixed and paraffin embedded tissue block of the breast tumor and peripheral blood mononuclear cells from 20 patients who were enrolled in the protocol 2016-0177 (A randomized phase II study of neoadjuvant carboplatin/paclitaxel (CT) versus panitumumab/carboplatin/paclitaxel (PaCT) followed by anthracycline-containing regimen for newly diagnosed primary triple-negative inflammatory breast cancer). These samples were submitted to the Translational Molecular Pathology lab for QC and simultaneous RNA/DNA extraction. The QC report showed that only 1 out of 60 DNA and RNA samples failed to meet the needed yield for proceeding with sequencing. Other samples from this case were excluded, and all other remaining 57 samples (19 RNAs; 19 tumor DNAs; 19 germlines) were finally subjected for sequencing. We expect to receive the results of sequencing very soon.

In summary, we appreciate the opportunity provided by MD Anderson to participate and explore IBC as one of the rare tumor types. We hope that the results of the investigation will enlighten our understanding of IBC.
Summer 2020 CPRIT CURE Undergraduate Research Program

Dr. Bisrat Debeb’s laboratory had the opportunity to mentor Anh Nguyen and Nothando Mangena for 10 weeks, and due to COVID, the mentoring occurred all virtual. Dr. Debeb, Dr. Villodre, and Dr. Hu trained the students and showed how to use different databases and software to analyze gene and protein expression (Gene set enrichment analysis, Ingenuity Pathway Analysis, Oncomine, and cBioportal).

Anh Nguyen is from Vietnam and currently a senior at Concordia College in Moorhead, Minnesota, with a major in Biology and minors in Chemistry and Neuroscience. Her career goal is to become a cancer researcher and get involved in translational research. “It was great to be a part of the CPRIT/CURE program at the MD Anderson this summer. Although it is a virtual internship due to the COVID-19 pandemic, I truly enjoy the time participating in this program. I have learned how to obtain public datasets and analyze data as well as to enlarge my knowledge in cancer biology, especially breast cancer. The virtual internship was not the one I expected; however, I am thankful for all the great effort of the organizers of the CPRIT/CURE program to help me gain research experience and expand my horizons through various activities, such as enrichment lectures and journal clubs. The internship reinforces my interest in cancer research and is an essential step to help me achieve my career goal”.

Nothando Mangena is an international student from Zimbabwe in Southern Africa. She is currently a rising junior at Carleton College in Minnesota. “I was blessed to get the opportunity to intern at MD Anderson through the CPRIT CURE Program. Under Dr. Debeb’s members’ guidance and support, I learned how to use different analysis tools, and I was able to analyze the role of MAPK14 in breast cancer. I am grateful to the lab members for not only teaching me but supporting me and creating a conducive environment to learn. As well as the CPRIT CURE program organizers for making sure the program continued despite the COVID-19 pandemic”.

Recent Awards and Grants

Chandra Bartholomeusz, MD, Ph.D., Associate Professor, Department of Breast Medical Oncology – Research, was awarded an Institutional Research Grant entitled, The Role of Early Growth Response 1 (EGR1) in metastasis of TNBC.

Xiaoping “Maggie” Wang, Ph.D., Assistant Professor, was awarded the Emerson Collective Cancer Research Fund, the title of the award “Enhancing EGFR-targeted therapy by blocking immunosuppression in the tumor microenvironment in inflammatory breast cancer.”

Naoto Ueno, MD, Ph.D., Professor, Jangsoo Lee, Ph.D., Assistant Professor, and Toshiaki Iwase, MD, Ph.D., Postdoctoral Fellow each were invited to submit a level 3 grant for IBC with the Department of Defense

Takashi Semba, MD, Postdoctoral Fellow, received the MD Anderson Institutional Award titled “Susan Papizan Dolan Fellowship in Breast Oncology.”
Recent Publications


**2020 Annual AACR Meeting Abstracts Presented**

“**Mechanism of MEK inhibitor resistance in triple-negative breast cancer**” presented by Maria Gagliardi, Moises Tacam, Lakesla Iles, Yuan Qi, Lajos Pusztai, Debu Tripathy, Geoffrey Bartholomeusz, Chandra Bartholomeusz

“**Potential of 6-mercaptopurine and 5-azacitidine in halting progression of poor prognosis residual disease in triple negative breast cancer**” presented by Balraj Singh, Vanessa N. Sarli, Anthony Lucci.

**News/Events**

Team IBC Wranglers will participate in the annual Boot Walk once again. This year it is all virtual. To learn more about joining the effort, please read below.

As you are already aware, cancer affects so many people we love and care. Cancer did not pause for the pandemic, and neither will we. COVID-19 has changed our way of living, our managing of routine challenges, and has led to canceling so many important moments in our lives. Our cancer research is still ongoing during this pandemic. Unfortunately, the research funding is diminishing.

Despite the pandemic and its challenges, the 5th MD Anderson’s Boot Walk to End Cancer® event is not canceled and is scheduled for Saturday, Nov 7, 2020. However, this year we will not be walking side-by-side on MD Anderson’s campus as in prior years, we will put on our boots to join 5,000 cancer fighters around the globe and walk the 1.2 miles WHEREEVER WE ARE, ON ANY DAY AND AT ANY TIME (Now till Dec 31, 2020). We will remain strong when we come together as a community committed to ending cancer.
We are extremely passionate about the people we help and the research we do. This year, our patients and our research need your support even more, and our goal is to raise $100,000. We plan to use these funds to continue to support more patients with travel expenses while on clinical trials, and to expand more clinical and research collaborations in the community through the IBC Connect program to increase IBC community outreach, awareness and improvement of early and accurate diagnoses, thus being able to provide the best standardized treatment for IBC in the community.

We would be honored to have your support for team IBC Wranglers. Supporting this event is easy:

1. Join team IBC Wranglers, walk 1.2 miles anywhere you are, on any day and at any time.
   - Registration is free. [http://mdacc.convio.net/goto/IBCWranglers](http://mdacc.convio.net/goto/IBCWranglers)
   - Click on ‘JOIN THIS TEAM’ and go through the registration steps.
2. If you would like to donate (tax deductible) to team IBC Wranglers:
   - Please click this link: [http://mdacc.convio.net/goto/supportIBCProgram](http://mdacc.convio.net/goto/supportIBCProgram)
   - If you are sending a check: PAY TO: MD Anderson Cancer Center, Memo: BWH20 IBC Wranglers, and mail the check to: MD Anderson Boot Walk, P.O. Box, 4470, Houston, TX 77210
3. We would love to see your pictures of your walk alone or with family and friends. Please email your pictures to ibcp@mdanderson.org.

**IBC DAY** – IBC Wranglers update: As we approached Breast Cancer Awareness Month and the Annual MD Anderson Boot Walk, Team IBC Wranglers advanced our fundraising efforts as a group on IBC Day, Sunday Oct 4th, 2020. Our team lead by our lab manager, Larry Coffer planned a walk around Hermann Park in Texas Medical Center, starting near the statue of Sam Houston, to help galvanize support for our Boot Walk team. It was exciting to see the team come together to complete one full loop around Hermann Park, and help raise funds to support our patients and our research. Thanks team!!

Every dollar you donate is important to the success of this effort. Thank you in advance for your participation and your contributions!

**IBC Online Activities for Patients**

The program usually participates in multiple October breast cancer awareness events including the High Tea and annual BC walk in Richmond TX. However, this year due to COVID-19, these in-person events are unable to be held, and other MD Anderson outreach events are extremely limited as well. Instead, our program has identified the following opportunities to increase education and awareness regarding IBC and increase outreach to our patients and stakeholders.
IBC LEARNING ACADEMY
October 23, 2020 to October 24, 2020

The IBC Network Foundation is hosting a virtual training program for advocates to learn about IBC, and the IBC program is honored to provide support by way of speakers and administrative leadership. This program, a 2-day rigorous course offered through Zoom will focus on what makes IBC unique from a biological and treatment perspective, so that patient advocates have a solid core knowledge base from which to launch their advocacy efforts. Patients will be introduced to the wide spectrum of advocacy projects such as research-advocacy (grant review or serving as advocates for grant applications), fundraising and patient-focused education and communication.

In addition to IBC program faculty presenters, several invited speakers from outside of MD Anderson, including pre-selected patients will participate by sharing their stories to further enlighten participants to the spectrum of IBC presentation. The course will be free to attend (with a small suggested Boot Walk donation), and the lectures will be recorded and posted on a website created by the IBC Network Foundation for future interested registrants to watch. For more information and to sign up, please visit http://www.IBCLearningAcademy.org. Any questions may be directed to Terry Arnold, Founder of the IBC Network Foundation at terry@theibcnetwork.org.

The program has initiated a monthly chat starting in October 2020 for informal networking and brainstorming for program members and interested patients/advocates. Drs Ueno and Alexander will be there consistently, and other program members are invited as well. The clickable link to join is in the box on the right.

IBC Program Presentations

Who are we – What are our roles in conducting clinical trials
Jie Willely, MSN, RN, Research Nurse Manager, and IBC Clinical Research team members
Department of Breast Medical Oncology

The prediction of Treatment Response to Neoadjuvant Immunotherapy for the Patients with Primary Triple Negative Breast Cancer
Toshiaki Iwase, M.D., Ph.D., Postdoctoral Fellow
Department of Breast Medical Oncology

Decorin, a novel negative modulator of E-cadherin in inflammatory breast cancer
Xiao Ding Hu, Ph.D., Postdoctoral Fellow
Department of Breast Medical Oncology - Research

Pathology related issues of Breast tissue evaluation following Neoadjuvant chemotherapy
Savithi Krishnamurthy, M.D., Professor
Pathology/Laboratory Medicine

Investigation of the role of SMAD4 germline mutation in inflammatory breast cancer
Takashi Semba, M.D., Postdoctoral Fellow
Department of Breast Medical Oncology - Research

Newsletter Committee

Hope Murphy Angela Alexander
Marcy Sanchez Swetha Bopparaju
Naoto Ueno Emily Schlee Villodre