The 2016 ASCO Annual Meeting was held June 3rd – 7th, 2016 in Chicago, Illinois. The annual event serves as a “meeting of the minds,” an opportunity for practitioners and scientists across disciplines to share developments in treatments, therapies, and ground breaking research. The conference is the largest of its kind in the oncology field, with an average turnout exceeding 30,000. The 5 day event provides a collaborative forum in which oncology professionals can also share and update clinical trial results. The Morgan Welch Inflammatory Breast Cancer Research Program and Clinic continued its participation in the event this year.

Abstracts/Posters presented at the 2016 ASCO Annual Meeting:

**Phase II study of panitumumab, nab-paclitaxel, and carboplatin followed by FEC neoadjuvant chemotherapy for patients with primary HER2-negative inflammatory breast cancer**


EGFR overexpression is an independent poor prognostic factor in patients with inflammatory breast cancer (IBC). The IBC animal model indicated that EGFR-targeted therapy inhibited IBC tumor progression via reversing EMT and suppression of CSC phenotype. It was hypothesized that the combination of an anti-EGFR monoclonal antibody to neoadjuvant chemotherapy for IBC produce higher pathological complete response (pCR; including breast and axilla) rates compared with our historic rates (triple-negative [TN], 12%; HR+/HER2-, 7%) of 527 patients. Comparing changes in gene expression before and after treatment with panitumumab, candidate gene expression changes that might predict the pCR were identified. The validation of these candidates is ongoing, but preliminary data showed that our novel NAC regimen was well tolerated and produced unprecedentedly high pCR rates in primary TN-IBC.
Open-label phase Ib study of entinostat (E), and lapatinib (L) alone, and in combination with trastuzumab (T) in patients (pts) with HER2+ metastatic (mHER2+) breast cancer after progression on trastuzumab


Maximum tolerated dose (MTD) was defined for Group 2 - Entinostat, lapatinib and trastuzumab combination. Entinostat 12mg every other week + lapatinib 1000mg daily + trastuzumab 8mg/kg to 6mg/kg q3 weekly was safe and well tolerated. Dose limiting toxicities included grade 3 and 4 hematologic toxicities, grade 3 diarrhea and grade 4 hypokalemia. Prolonged disease control from this regimen was observed. There was a trend toward longer progression-free survival for patients with IBC and previous lapatinib treatment, but the difference was not significant. Available data on CTC and signaling molecule markers do not show a relationship to outcome, but statistical power is limited. Phase II study in combination with a HER2 targeted agent should be explored as a therapeutic option for metastatic trastuzumab-resistant HER2-positive breast cancer. A hypothesis-oriented predictive biomarker development strategy: matched tissue and blood collection, preclinical data based marker testing plan is needed.

Recent Awards and Grants

We congratulate the following individuals who have been recognized for their significant accomplishments in IBC research:

Dr. Geoffrey Bartholomeusz, Associate Professor (Experimental Therapeutics) received the 2016 AVON 39 – The Walk to End Cancer award for his collaborative research with Drs. Bedrich Eckhardt, Naoto T Ueno, Savitri Krishnamurthy and Ms. Vidhu Sharma for “Developing ex-vivo tumor models of inflammatory breast cancer for drug testing.”

Angie Marie Torres-Adorno, PhD Candidate, Breast Medical Oncology, was selected for the 2016 AACR Translational Cancer Research for Basic Scientists Workshop in Boston, based on her research projects aimed at treating aggressive types of breast cancer including IBC and TNBC. Mentor – Dr. Naoto T. Ueno.

Dr. Sangeetha Reddy, Clinical Research Fellow (Cancer Medicine - Fellowship Program) was named winner of the “2016 Young Investigator Award” from ASCO, for her research proposal on “Immune and molecular determinants of response to neoadjuvant chemotherapy in IBC”. In her research study, she will assess the influence of genomic factors on the IBC immune microenvironment, thereby revealing genomic and immune targets for developing treatment combinations with neoadjuvant chemotherapy and immune targeted therapy. Mentors – Drs. Jennifer Wargo and Naoto T. Ueno.

Dr. Bisrat Debeb, Assistant Professor (Radiation Oncology) received a 3 year Susan G. Komen grant for his research on early brain metastasis initiation and colonization from breast cancer using IBC cancer brain metastasis mouse models developed in our laboratory.

During MD Anderson’s Education Week (May 23-27), Jay Paul Reddy, MD, PhD, Clinical Postdoctoral Fellow, Radiation Oncology, received the Susan Papizan Dolan Fellowship in Breast Oncology. Mentor – Dr. Wendy Woodward.

Dr. Bisrat Debeb, Assistant Professor (Radiation Oncology) was named the recipient of a travel award for the 2016 NCI CRCHD PACHE Investigators Workshop in Rockville, Maryland for his abstract “LCN2 in inflammatory breast
Dr. Chandra Bartholomeusz, Assistant Professor (Breast Medical Oncology) was awarded the Institutional Research Grant for “Overcoming MEK-inhibitor resistance in TNBC by targeting Mcl-1, anti-apoptotic protein.” Her research using IBC cell lines holds promise in identifying therapeutic targets for IBC.

Recent Publications

**miR-141-Mediated Regulation of Brain Metastasis From Breast Cancer**


About 15% to 30% of patients with advanced breast cancer develop brain metastases of which triple-negative and human epidermal growth factor receptor 2 (HER2)–overexpressing cancers are disproportionately represented. Despite major advances in primary breast cancer and systemic malignancies, the prognosis for patients with brain metastases remains dismal, with median survival times ranging from five weeks without treatment to six months with multimodality treatment. Also, the incidence of brain metastases is increasing with the advent of effective targeted systemic therapies for breast cancer such as trastuzumab. Despite the substantial clinical need, the molecular basis for brain metastasis is still poorly understood.

Herein, we developed and characterized novel brain metastasis mouse models and investigated the potential role of miR-141 in brain metastatic colonization of breast cancer cells. The study suggests miR-141 is a regulator of brain metastasis from breast cancer and should be examined as a biomarker and potential target to prevent and treat brain metastases.

**Histone deacetylase inhibitor-induced cancer stem cells exhibit high pentose phosphate pathway metabolism**

Bisrat G. Debeb, Lara Lacerda, Richard Larson, Adam R. Wolfe1,5, Savitri Krishnamurthy, James M. Reuben, Naoto T. Ueno, Michael Gilcrease, Wendy A. Woodward

Through this study, it was demonstrated that histone deacetylase (HDAC) inhibitors can “reprogram” differentiated triple-negative breast cancer cells to become quiescent stem-like cancer cells. We hypothesized that the metabolic state of such cells differs from that of their differentiated progeny. In untreated cells, glucose uptake was higher in ALDH+ cells than in ALDH− cells (p = 0.01) but lactate production was not different; treating ALDH− or ALDH+ cells with VA or SAHA similarly increased glucose uptake without changing lactate production but upregulated G6PD, a rate-limiting enzyme in pentose phosphate pathway metabolism. NADPH production was higher in HDAC inhibitor-treated stem-like cells than in vehicle-treated cells (p < 0.05). Two G6PD inhibitors, 6-aminonicotinamide and dehydroepiandrosterone, decreased mammosphere formation efficiency and ALDH activity and 6-aminonicotinamide reduced the VA-induced increase in ALDH+ cells. Finally, patients expressing high G6PD mRNA had significantly worse overall survival (p < 0.001), and patients with high G6PD protein showed a similar trend towards worse disease-specific survival (p = 0.06). (G6PD) expression was evaluated in a tissue microarray from 94 patients with node-positive invasive breast carcinoma and in two publically available databases and correlated with overall survival. Energy metabolism in HDAC inhibitor-induced stem-like cancer cells differed sharply from that of differentiated cell types. HDAC inhibitor-induced dedifferentiation promoted metabolic reprogramming into the pentose phosphate pathway, which is targeted effectively by G6PD inhibition. These findings show a potential for a
future dual-therapy approach to targeting bulk differentiated cells with HDAC inhibitors and CSCs with G6PD inhibitors.

**Landscape of somatic mutations in 560 breast cancer whole-genome sequences.**


Whole-genome sequences of 560 breast cancers were analyzed to advance understanding of the driver mutations conferring clonal advantage and the mutational processes generating somatic mutations. It was found that 93 protein-coding cancer genes carried probable driver mutations. Some non-coding regions exhibited high mutation frequencies, but it was also found that most have distinctive structural features probably causing elevated mutation rates and do not contain driver mutations. Mutational signature analysis was extended onto genome rearrangements and showed twelve base substitution and six rearrangement signatures. Three rearrangement signatures, characterized by tandem duplications or deletions, appeared to be associated with defective homologous-recombination-based DNA repair: one with deficient BRCA1 function, another with deficient BRCA1 or BRCA2 function, the cause of the third is unknown. This analysis of all classes of somatic mutation across exons, introns and intergenic regions highlights the repertoire of cancer genes and mutational processes operating, and progresses towards a comprehensive account of the somatic genetic basis of breast cancer. This can pave the way for personalized breast cancer treatment, including IBC.

**News/Events**

We welcome James L. Murray III, MD to our IBC Program. He is an experienced breast medical oncologist with an extensive background in immuno-oncology and currently involved in many translational biomarker developments. His participation in the IBC Clinic will give our program the opportunity to provide timely medical oncologist consultations for our new patients with IBC.
IBC Multi-Team Clinic (IBC MTC): The IBC Multi-Team Clinic launched in August 2015 at our Nellie B. Connally Breast Center, continues to serve our patients. Our highly specialized multi-disciplinary physicians work together to create a personalized treatment plan. In just one appointment and one place, patients can meet their radiation, surgical and medical oncologists, and leave with a plan of action and peace of mind that comes from having the best physicians care for them, every step of the way.

MD Anderson Boot Walk: "IBC Wranglers" Team Updates: We want to remind you that MD Anderson will be holding its first ever employee fundraising event, the MD Anderson Boot Walk to End Cancer, on November 12th. What better way to show your continued support to our IBC patients, survivors, and their families. We'd like to thank those who have already signed up. You can find helpful tips on fundraising and outreach on the events Facebook page, https://www.facebook.com/MDAndersonBootWalk/. An App is also now available to track your progress, link also available on the Facebook page. If you haven't had a chance to register yet, please check out the following link, www.mdanderson.org/bootwalk. After choosing to join a team, please make sure you enter “IBC Wranglers” to join our Program's team. You will then receive an email link to your customizable fundraising page and can begin reaching out for support. You can also make a personal donation directly to our team, without registering as a walker.

To date, we have raised $1,350. We appreciate everyone's hard work so far. Keep in mind that you'll be able to continue fundraising on behalf of our program until December 2016.

IBC 10th Anniversary: Wednesday, September 21st, 2016, our IBC Program will be hosting an IBC Advocate Luncheon, to kick off the celebration of the Program's 10th Anniversary celebration.

Guest Speakers Series

Dr. Zachary T. Schafer, PhD, Coleman Foundation Associate Professor of Cancer Biology (University of Notre Dame) presented “Bim-El sequestration: A mechanism for mediating anoikis evasion in inflammatory breast cancer cells?”

Dr. Schafer’s research interest is in the area of cancer cell survival during metastasis, especially understanding how breast cancer cells avoid anoikis, a programmed cell death process induced when epithelial cells are detached from their extracellular matrix (ECM).
Quarterly Oral Presentations

**Targeting cancer evolution in IBC**
Balraj Singh, PhD  
Associate Professor, Surgical Oncology

**An update on radiosensitivity and metastasis of IBC**
Omar Rahal, PhD  
Postdoctoral Fellow, Experimental Radiation Oncology

**Characterization of tumor infiltrating lymphocytes**
Evan Cohen, PhD  
Postdoctoral Fellow, Hematopathology

**Novel targets for cancer stem-like cells in triple negative breast cancer**
V. Lokesh Battula, PhD  
Assistant Professor, Leukemia Department

**The histone deacetylase inhibitor entinostat enhances the efficacy of the MEK inhibitor pimasertib against aggressive types of breast degradation**
Angie Marie-Torres, Graduate Research Assistant  
PhD Candidate, Breast Medical Oncology

**Identification of EPHA2 as a novel synergistic target in combination with eicosapentaenoic acid against aggressive types of breast cancer**
Angie Marie-Torres, Graduate Research Assistant  
PhD Candidate, Breast Medical Oncology

**Differences in MIPS imaging of IBC vs. non-IBC**
H. T Carisa Le-Petross, MD  
Professor, Diagnostic Radiology

Current Clinical Trials Open for New Patient Enrollment

**2006-1072** IBC Registry

**2013-0007** Phase II study of Denosumab to define the role of bone related biomarkers in patients with breast cancer and bone metastasis

**2013-0139** Phase IB trial of two folate binding protein peptide vaccine (E39 and J65) in breast and ovarian cancer patients

**2013-0436** Combination immunotherapy with Herceptin and HER2 vaccine E75 in low and intermediate HER2 expressing breast cancer patients to prevent recurrence

**2014-0464** A phase II study of BIBF-1120 (Nintedanib) for patients with HER2 normal metastatic inflammatory breast cancer

**2014-0533** A phase II study of anti-PD1 (MK-3475) therapy in patients with metastatic inflammatory breast cancer who have perceived prior chemotherapy with clinical response

**2014-0034** A phase II study using Talimogene Laherparepvec (T-VEC) as a single agent for IBC or non-IBC patients with inoperable local recurrence
Current Lab Studies

PA15-0499  Tissue biomarker study of T-DM1 and/or Pertuzumab resistant or refractory breast cancer
NI0000-A-U002

PA12-0097  Prognostic utility of CTCs assessed by AdnaGen technology and clinical outcome of patients with stage III breast cancer


PA12-0860  Assessing feasibility of sentinel lymph node increase dissection in IBC

PA14-0772  Derivation of patient derived xenograft tumor models from isolated CTC from breast cancer patients (IBC/TNBC)

PA14-0778  Gene profiles in androgen receptor-positive CTC in patients with metastatic breast cancer

In Remembrance

It's been 10 years since Morgan Welch's story inspired the establishment of the Morgan Welch Inflammatory Breast Cancer Research program and Clinic in 2006. May 18th was her birthday and she would have been 34 years old. Morgan and her story continue to provide strength and inspiration to our Program, our colleagues, our patients and our friends. Please join us in honoring Morgan's memory by telling at least one person about IBC. By doing so, let us save a life and help another individual celebrate a future birthday. We are motivated each day to fulfill our vision to be the world's premier center for the treatment and prevention of IBC through multidisciplinary and collaborative research.

If you are interested in learning more about our clinical trials, or lab studies, please email the Morgan Welch Inflammatory Breast Cancer Research Program and Clinic directly at ibcp@mdanderson.org. We are happy to provide general information and eligibility guidelines for our clinical trials and lab studies.