



# Focus on IBC

July 2009

## IBC Research Foundation Newsletter

### ASCO 2009

*By, Ginny Mason*  
Executive Director, ibcRF

Despite the heat and humidity of Orlando, Florida and worries about the H1N1 flu, approximately 30,000 people from around the world attended the American Society of Clinical Oncology (ASCO) Annual Meeting, May 29 to June 2, 2009. More than 4,000 abstracts were accepted to this year's Annual Meeting, with nearly 2,300 actually presented and more than 1,700 published online only. These abstracts represent the most cutting-edge breakthroughs in cancer care and were chosen on the basis of potential to improve patient outcomes. This year's meeting theme was "Personalizing Cancer Care."

The Inflammatory Breast Cancer Research Foundation had the opportunity, for the 5th time, to be a part of the ASCO Patient Advocacy Booth area. We were assigned one of the 20 sections, along with 19 other cancer non-profit groups. It has become quite a competitive process to be in this prime location at the meeting. Organizations securing spots are encouraged to send their volunteers to the educational and poster sessions, attend the daily advocate educational sessions, while keeping their booth staffed during all exhibit hours. Special thanks to Rita Kate VanOrsdal, Gayla Little, Becky Rosen, Harriet Beckham who (in addition to myself) did an outstanding job educating meeting attendees about inflammatory breast cancer. Stacks of brochures and bookmarks were given out and important contacts made. The new IBC Spanish Information Sheet had its debut at this meeting. Look for an announcement when the Spanish

### Essential Role for eIF4G1 Overexpression in Inflammatory Breast Cancer Pathogenesis

The Inflammatory Breast Cancer Research Foundation is excited to share the following research news from Dr. Robert Schneider, associate director for translational research at The Cancer Institute, co-director of breast cancer research, and the Albert B. Sabin Professor of Molecular Pathogenesis at NYU School of Medicine and Dr. Deborah Silvera, a postdoctoral research fellow. The study was also co-authored by Dr. Silvia Formenti, chair of the department of radiation oncology at NYU Langone Medical Center.

"Scientists from The Cancer Institute at New York University Langone Medical Center have identified a key gene---eIF4G1----that is overexpressed in the majority of cases of inflammatory breast cancer (IBC), allowing cells to form highly mobile clusters that are responsible for the rapid metastasis that makes IBC such an effective killer", reported a EurekaAlert press release June 14, 2009.

This finding could lead to new targeted approaches for the treatment of IBC. "Dr. Schneider and his colleagues found that the overexpression of the gene eIF4G1 reprograms how the IBC tumor cells make proteins. Other researchers have identified genes associated with IBC, but this is the first gene shown to orchestrate how IBC tumor cells form special structures---unique to this disease---known as 'tumor emboli'. These small clusters of highly mobile tumor cells are responsible for the rapid metastasis of IBC. Because these cell clumps are not stationary or fixed, they can quickly travel to other areas of the body."

Understanding the unique molecular expression signature(s) of IBC will help identify targets that can be exploited for treatments. Herceptin was developed to target the Her 2/neu protein or oncogene. Her 2/neu is overexpressed more frequently in IBC than other breast cancers and has been an important tool to control aggressive breast cancers. Targets like these should not be confused with genetic mutations that increase risk for breast cancer as in the case of hereditary mutations in either BRCA 1 or BRCA 2. Mutations in these genes can increase risk for developing breast cancer, but have not been associated with IBC.

Information Sheet is available for download and printing on the website.

This was not a particularly "big year" for breast cancer announcements in general. However, it was exciting to be a part of the plenary presentation describing high response rates to a new class of agents, the poly ADP-ribose polymerase (PARP) inhibitors. This enzyme plays a central role in DNA repair in cancer cells, so was considered a potentially good target. PARP is upregulated in triple-negative breast cancer and BRCA-mutation-carrier patients. Results from a randomized Phase II study in metastatic triple-negative breast cancer patients found that the agent BSI-201 significantly improved survival. The two arms compared gemcitabine (Gemzar) and carboplatin with or without intravenous BSI-201. Overall survival for the BSI-201 group was 9.2 months, while 5.7 for the other group. A second Phase II study used olaparib as a single agent in patients with a BRCA1 or BRCA2 mutation and advanced breast cancer. This was a small (27 pts) single-arm study testing two different doses of the agent. Those receiving the higher of the two doses had significant tumor shrinkage. Phase III trials with more patients will give a clearer picture of the utility of these agents. A recent New England Journal of Medicine article, "Inhibition of Poly (ADP-Ribose) Polymerase in Tumors from BRCA Mutation Carriers" is available at [the New England Journal of Medicine](#) website.

While not a new topic, more evidence was presented regarding the potential hazards of taking tamoxifen in combination with certain antidepressants. "Tumors were more than twice as likely to return after two years in women taking the antidepressants while on the cancer drug, compared with those taking tamoxifen alone," reported one source. The liver enzyme CYP2D6 breaks down tamoxifen into the active component that is used to reduce cancer recurrence. Some antidepressants (such as Paxil, Prozac and Zoloft) use the same enzyme, reducing the supply needed to adequately activate the tamoxifen. CURE magazine reports the FDA is considering changes to the tamoxifen label in light of this information. Studies have also studied variances in how patients metabolize tamoxifen based on individual, specific polymorphisms. While "not ready for prime time" it is clear that not everyone metabolizes

The Inflammatory Breast Cancer Research Foundation has been working with Dr. Schneider for the past few years as this research has taken shape, and we look forward to continued collaboration as Dr. Schneider and colleagues work on the next steps of this research.

The article, which will appear in Nature Cell Biology in July, is already available on-line at the Nature Cell Biology website. To read the full press release [click here](#).

## Clinical Trials of Interest to the IBC Community

*By, Ginny Mason*

*Executive Director, ibcRF*

Unfortunately very few adult cancer patients participate in clinical trials. In contrast, most pediatric cancer patients are enrolled in clinical trials. Why? There are a variety of reasons, but often it is as simple as patients asking about available trials when talking with their oncologist. Today's patients are often well informed, having "done their homework" before making treatment decisions. When discussing treatment options be sure to explore clinical trials. Often a clinical trial will provide the opportunity to receive state-of-the-art treatment before it is available to the general population. Should you be randomized to the standard treatment arm, you will still be receiving optimal care; usually provided by the skilled staff of a major cancer center.

While there are many clinical trials for breast cancer listed on [ClinicalTrials.gov](#), many of them exclude participation by those with inflammatory breast cancer. Fortunately, a quick run through the current listings brings up a number of trials that are either inflammatory breast cancer specific or at least include inflammatory breast cancer patients in the trial. This is good news for those dealing with this difficult disease. The following studies are Phase I or II. It is important to understand that these earlier stage trials involve dose finding and safety as the primary endpoints, although the Phase II studies are also examining efficacy or response to treatment.

One study currently recruiting participants is the DIGNITY Study (T for ThermoDox and Y for hyperthermia), ClinicalTrials.gov identifier: NCT00826085. This Phase I/II trial is sponsored by Celsion/Quintiles and is open at sites in FL, NY, OK and RI. The study is designed to evaluate the maximum tolerated dose, pharmacokinetics, safety, and efficacy of microwave hyperthermia and ThermoDox (Lyso-thermosensitive Liposomal Doxorubicin) in patients with breast cancer recurrence at the chest wall. Given the frequency of chest wall recurrence in inflammatory breast cancer, representatives from Celsion contacted the Inflammatory Breast Cancer Research Foundation with the trial information to alert the IBC community. To learn more about this study and the qualifying criteria [click here](#). A similar study

tamoxifen (or other drugs for that matter) at the same rate, and that can affect the benefit obtained from a given compound. Presenters suggested using other classes of drugs to treat depression in those patients taking tamoxifen to reduce the potential for problems.

During the conference Inflammatory Breast Cancer Research Foundation volunteers had the opportunity to meet and talk with at least three members of the Medical Advisory Board, connect with a variety of researchers, and network with other cancer advocates. Breakfast and dinner meetings provided opportunities to learn about new treatment options, clinical trials, and financial assistance programs offered by some of the pharmaceutical companies. The ASCO Annual Meeting can be an overwhelming experience, but it is also an amazing opportunity for Foundation volunteers to learn and to raise awareness of inflammatory breast cancer.

### Upcoming Events

**July 14 -**  
Working Matters: What You Need to Know; 12-1:30 pm; Teleconference from Living Beyond Breast Cancer [Click here.](#)

**July 15 -** FDA Oncologic Drugs Advisory Committee; Gaithersburg, MD [Click here.](#)

**July 16 -** Conference: Advancing Rare Diseases Research Through Networks and Collaboration, Bethesda, MD [Click here.](#)

**July 16 -** Teleconference: Understanding Peripheral Neuropathy; [Click here to register](#) or call 1-800-813-4673.

**July 20-22 -**Conference: caBIG Annual

Meeting: Solving Basic and Clinical Challenges in Cancer and Beyond; Washington, DC [Click here.](#)

**July 28-Aug. 2-** National Breast Cancer Coalition Fund Project LEAD Institute; La Jolla, CA [Click here.](#)

continues to recruit patients at Duke University.

Another trial of interest comes from Cylene Pharmaceuticals. This Phase I study of oral CX-4945 is designed to test the safety, tolerability and highest safe dose level of this CK2 inhibitor in patients with advanced solid tumor cancers including inflammatory breast cancer. The ClinicalTrials.gov identifier for this trial is: NCT00891280. Currently there are three U.S. sites recruiting for this trial in AZ, CO and TX. To read more about this trial and the inclusion/exclusion criteria [click here.](#)

There are a number of trials evaluating the use of vaccines alone or in combination with other agents in the treatment of breast cancer. A new study, just starting recruitment, is a randomized, double-blind, controlled Phase II study of Stimuvax (L-BLP25 or BLP25 Liposome Vaccine) in combination with hormonal treatment versus hormonal treatment alone for first-line therapy of post-menopausal women with estrogen receptor (ER) positive and/or progesterone receptor (PgR) positive, inoperable locally advanced, recurrent or metastatic breast cancer. In conversation with the study sponsor, EMD Serono, representatives admitted that while this study permits inflammatory breast cancer patients, the very narrow criteria will limit participation. However, most vaccine studies are designed for Her 2/neu positive patients and this one is for the Her 2/neu negative patient population. This trial has just started to recruit patients and with only one location open in NC. Additional sites are scheduled to open across the country over the next few months. For additional information [click here.](#)

The above trials are just a few of the clinical trials open to inflammatory breast cancer patients at this time. To see the entire list and view individual trial details, go to <http://clinicaltrials.gov> and enter "inflammatory breast cancer" in the search box, or use the link from the Inflammatory Breast Cancer Research Foundation website: [www.ibcresearch.org](http://www.ibcresearch.org).

*\*\* This article is intended for informational and educational purposes only and in no way should be taken to be the provision or practice of medical, nursing or professional health-care advice or services. The information should not be considered complete or exhaustive and should not be used for diagnostic or treatment purposes without first consulting with your physician or other health-care provider. The Inflammatory Breast Cancer Research Foundation accepts no responsibility for the misuse of information contained within this website, email response or within the Email discussion messages. Clinical trial information is provided as a courtesy only and does not imply endorsement or recommendation by the Inflammatory Breast Cancer Research Foundation.*

Quick Links for  
IBC Patients  
and Caregivers



[Previous Newsletters](#)

[ibcRF BioBank](#)

[Donate to ibcRF](#)

1-877-STOP-IBC  
1-877-786-7422

[www.ibcresearch.org](http://www.ibcresearch.org)  
email: [info@ibcresearch.org](mailto:info@ibcresearch.org)

## Reflections from Our Volunteers

*By, Gayla Little*



This was my fourth year to help at ASCO, and I think I am just hitting my stride. As coordinator for the Inflammatory Breast Cancer Research Foundation Response Team, it is necessary that I keep up-to-date on current and breaking research findings on IBC specifically and breast cancer in general. When we staff a booth at ASCO, we are allocated two cards, which allow us entry into the sessions constantly going on in the rest of the convention center. We take turns using these cards, depending on the sessions we want to attend.

Since we often get questions, both online and off, about the benefit of MRI; I was able to get to a session this year on just that subject. While I was disappointed in what I heard, it was important to find out that there is a huge rate of false positives when MRIs are used to detect breast cancer. While IBC patients may still want to use MRI to help with diagnosis, it is vital that we are aware of the limitations of this type of scan and ALWAYS confirm what is found on the MRI with a biopsy.

I am grateful to all of you who donate to the Inflammatory Breast Cancer Research Foundation, because your contributions make attending ASCO and other worthwhile conferences possible. We learn vital information that can be passed along through our Response Team as well as connecting with various researchers around the country. The Inflammatory Breast Cancer Research Foundation is devoted to information based on RESEARCH and not wishful thinking. When we respond to emails, it is important that we respond with knowledge and not our gut reaction. So, thank you for making the gathering of information about IBC possible. Together, we are making advances toward ending this terrible disease.

## Addendum to July 2009 Newsletter Article

A message from Ginny Mason, RN, BSN  
Executive Director  
Inflammatory Breast Cancer Research Foundation

July 13, 2009

We have received a number of questions regarding the recent article that appeared in our July 2009 Newsletter titled ["Essential Role for eIF4G1 Overexpression in Inflammatory Breast Cancer Pathogenesis"](#) such as the following from an IBC survivor, followed by my response to her. As she suggested, we are sharing this publicly to aid in understanding.

*". . . I'm sure you will soon be publicizing this new research that shows that 80% of us that get IBC, share a common gene. Great news and the researchers say that it will certainly help develop new and specific drugs targeting that gene. However, for survivors like me, the real question is: If I have the gene, do I have a higher chance of recurrence? In other words, is it important for me to find out if I have the gene? I would write directly to the researchers to ask that question - even an opinion would be good, but I'm sure they would not write back to me. Can IBCRESEARCH ask this question and publicize the answer? My story is that I just passed five years of survival. I took my last Arimidex pill on Friday. Needless to say, stopping that pill has raised my anxiety level significantly. I had conventional treatment: Adriamycin, mastectomy, Taxol, radiation and my blood tests continue to be good. I appreciate any help you can give me and other survivors . . ."*

We appreciate your questions and know that this new research data has raised many questions for patients/survivors. A link to the EurekaAlert press release about Dr. Schneider's findings went out to our two email discussion lists and our next e-newsletter will also carry an article. Dr. Schneider, and colleagues, have been working on this research for a couple of years, moving from cell lines to mouse models, and then studying tissue samples from IBC patients. Our organization has been serving as collaborators on the study providing patient/advocate input. We are looking forward to further collaboration as Dr. Schneider and colleagues move forward in the development of a therapeutic that will target this substance associated with IBC.

One of the challenges in dealing with medical terms, especially in the field of cancer, is the word "gene." For most of us that word is associated with something that is passed along from parent to child and thought of as hereditary. Most breast cancer is not associated with any known genetic mutation (ie: hereditary.) Rather, most breast cancer is the result of mutations in the body's DNA that cannot be repaired and go awry.

In Dr. Schneider's paper (Essential role for eIF4G1 overexpression in the pathogenesis of inflammatory breast cancer: Nature Cell Biology July 2009) he doesn't use the term "gene" at all, he uses the term "translation initiation factor" for eIF4G1. This translational initiation factor is over-expressed in cases of IBC, as opposed to non-IBC cases. eIF4G1 plays a significant role along with E-cadherin, the surface component that causes IBC tumor cells to stick so tightly together forming tumor emboli. We've known for a long time that E-cadherin is over-expressed in IBC. Over-expression of eIF4G1 promotes formation of IBC tumor emboli by enhancing translation of IRES-containing p120 mRNAs, which promote IBC tumor cell survival and formation of tumor emboli. These tumor emboli help to make IBC difficult to treat and move to other sites in the body.

I realize the above is rather technical, but I hope it will give more explanation into what eIF4G1 is and

isn't. Regarding the question, "If I have the gene, do I have a higher chance of recurrence?" Chances are eIF4GI would be found in the tumor tissue. However, measuring that would not tell us anything about the chance of recurrence. It would just let someone know that the IBC tumor tissue was like 80% of other IBC tumor tissue. Testing your tissue (that's the only place this substance would be found) would not give you information to aid in your survival. However, studying this substance in tissue from the Inflammatory Breast Cancer Research Foundation BioBank, is the kind of thing that moves research forward. By studying human IBC tissue, researchers learn the things that set IBC apart from other breast cancers and help identify targets for treatment.

This new research is exciting as it may provide a new drugable target. Compounds will need to be developed then tried in cell lines and animal models, prove to be effective in those settings and, if worthy, move on to human clinical trials. It is a long process, but exciting to think that we might have a treatment option coming designed specifically to target one of the key components of IBC.

*Any communication from the Inflammatory Breast Cancer Research Foundation is intended for informational and educational purposes only and in no way should be taken to be the provision or practice of medical, nursing or professional health-care advice or services. The information should not be considered complete or exhaustive and should not be used for diagnostic or treatment purposes without first consulting with your physician or other health-care provider. The Inflammatory Breast Cancer Research Foundation accepts no responsibility for the misuse of information contained within its website, email response or within the Email discussion messages. Any physician referral is provided as a courtesy only and does not imply endorsement or recommendation by the Inflammatory Breast Cancer Research Foundation.*