



RESEARCH ARTICLE

Inflammatory Breast Cancer: What's in a Name?

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ABSTRACT

One of the most unique and highly aggressive types of cancer is known to be Inflammatory Breast Cancer. IBC is a distinct locally advanced breast cancer with a highly virulent course and extremely low 5- and 10-year survival rates. Although Inflammatory Breast Cancer only accounts for 1-3% of breast cancers it is estimated to account for 10% of breast cancer deaths annually in the United States. The accuracy of diagnosis and classification of this unique cancer is a major concern within patient and medical communities. This in turn has led to a strong advocacy movement. Historically, Inflammatory Breast Cancer was thought to be many different diseases but 100 years ago was defined as a unified disease. Over the past three decades several molecular studies have identified unique gene and protein signatures that make Inflammatory Breast Cancer a truly distinct entity. Despite this, the potential for inaccurate diagnosis and misclassification in cases of Inflammatory Breast Cancer is increased by many factors including its physical presentation.

Keywords: Inflammatory breast cancer, metastasis, tumor emboli, dermal lymphatics, stem cells, advocacy, miRNA

Introduction

Inflammatory Breast Cancer (IBC) is an unusual and highly aggressive form of epithelial breast cancer¹⁻³. This breast cancer subtype is characterized by rapid progression and poor prognosis: the disease is mainly diagnosed at stage IIIB-C or IV with a 5- and 10-year disease-free survival rates of 38% and 18%, respectively³⁻⁵. Overall survival of IBC patients is significantly less than non-IBC patients when diagnosed with distant metastases⁶. Younger women with a mean age around 46 years are especially affected by IBC⁷. The term “inflammatory” is due to the clinical presentation of this disease with several skin changes resembling inflammation⁸. This term is misleading because the inflammatory appearance may not be due to a true primary immune response. The presentation and prognosis derive from the fact that IBC patients do not have a solid tumor. Instead, they present with intralymphatic tumor emboli that form sheets and cords in the dermal lymphatics of the breast⁴⁻⁵.

Classification and naming systems are essential to the fields of science and medicine. In Western culture, to put a name to something is to make it exist⁹. In the case of a disease, it is the trigger that leads to a series of actions which can result in the saving of a life, or death. Once a diagnosis is decided, the code for that diagnosis is entered into the patient's record and in the United States, provided to the patient's insurer. Pathology reports, medical records, and death certificates all replicate this crucial piece of statistical information. Without it, there would be no official record of the existence of the disease. While IBC accounts for 1-5% of cases of annually diagnosed breast cancer, it comprises 10% of deaths from breast cancer annually and is classified as a rare disease⁸. In the case of IBC, difficulty in diagnosis leads to an underreporting of the incidence of the disease, resulting in significance consequences for patients. This review considers the discovery of the disease, diagnostic issues, progress in treatment and the patient advocate perspective. A patient advocate is defined as a “person with a lived experience either as a patient with cancer/cancer survivor or an informal caregiver/carer of a person with cancer who is advancing something larger for themselves and their community.” It excludes paid professionals who are nurses or case managers¹⁰. Younger women, African American women, and Arab American women have higher rates of diagnosis compared to other types of breast cancer¹¹. The process of classification and naming results in the creation of a community, initially of sufferers, and eventually a community of survivors. And in the case of inflammatory breast cancer, patient advocates have become the public face of a private disease. Because of its high mortality rate and lack of clinician experience with IBC, patient advocates play a crucial role in advancing knowledge of the disease.

The “Discovery” of Inflammatory Breast Cancer

The foundational article pertaining to IBC was published in 1924 by Burton J. Lee, M.D. and Norman E. Tannenbaum, M.D., “Inflammatory Carcinoma of the Breast,” though there is visual evidence of the disease dating back to ancient history. Lee and Tannenbaum

presented their findings of “mammary carcinoma” to several surgical societies, yet their audiences did not believe the condition to be cancerous, merely inflammatory. Their literature review cites previous research in which similar IBC symptoms were described but by a variety of terms, starting in 1814, with the observations of Charles Bell “a purple color is on the skin over the tumor.” “Mastitis carcinomatosa” was used by R. von Volkman in 1875, “carcinoma mastitoides” by F. A. Shumann in 1911, whom, according to Lee and Tannenbaum, included 11 cases from the literature, and “acute mammary carcinoma” by G.E. Learnmouth in 1916¹².

The following notable characteristics of the disease found by Lee and Tannenbaum in the 28 cases they examined demonstrate why this is a foundational article for IBC. The findings include “the overlaying skin may be red and brawny, and this blush may extend far beyond the normal limits of the mammary gland.” The skin is hot, and the nipple is retracted. As the disease progressed, they describe the skin changing color to deep red or reddish purple and to the touch as “brawny and infiltrated¹².” In their cases, the inflammatory symptoms appeared between 4-5 weeks to 3 months after the first sign of any other related symptoms. The average patient age in the group was 44.6 years old, with 35% younger than 39 (the youngest was 24 and the oldest 62).

The authors also include a list of other conditions which may be confused for “inflammatory carcinoma” and the reasons why these other causes must be ruled out to establish a true diagnosis. When abscess of the breast was suspected, no elevated temperature or white blood cell count should exclude this. Erysipelas would result in an increased leucocyte count. Some doctors though exposure to “X-radiation” caused the inflammation. With radiation, however, the erythema appears typically 10-14 days post exposure and the skin changes correspond specifically to the areas treated verses the progressive and persistent symptoms in carcinoma. Tuberculosis of the breast should not be confused with carcinoma because the onset is slower, there would likely be other symptoms of tuberculosis present, and it is a chronic disease. In a true case of ulcerating carcinoma of the breast, it is the result of “a secondary invasion and destruction of the skin by a tumor” whereas inflammatory carcinoma is rarely ulcerating, except in the terminal stage, which is still unusual. In true cases of cancer *en cuirasse*, these usually occur in women over age 50 and develop over years. In Paget's disease of the nipple, the disease presents as a granular surface, includes yellow discharge resembling chronic eczema, and it typically only on the areola. It is also unilateral. The last condition described is gumma of the breast, a rubbery tumor which develops in tertiary syphilis. This cause can be ruled in or out using a Wasserman test¹².

The treatments Lee and Tannenbaum recommend in 1924 excluded surgery. Their study found that when surgery was used, the disease reappeared almost immediately, and extensively, and led rapidly to death. They hypothesized this was due to the “diffuse invasion of the dermal lymphatics.” They recommended radiation at 2-4 day intervals every 6-8 weeks. Out of their 28 cases, 14

died, 3 were observed too recently to come to any conclusions about the efficacy of treatment. Of the 11 who survived, 4 were doing well at the time of publication, while 8 were in the final stages of the disease. Lee and Tannenbaum concluded that with radiation treatment only, a patient could gain 1 to 2 years of life, more than surgical treatment alone, and more than a combination of surgery and radiation. They also noted that inflammatory carcinoma showed no consistent pathological type, just as their bacteriologic and biochemical analyses revealed nothing consistent or unique in all the cases studied¹². Just as they observed in the early twentieth century, inflammatory carcinoma was difficult to diagnose due to a similar presentation to other diseases, and no unique bacteriological or biochemical results, the same confusion persists today.

Diagnostic Problems

The largest problem cancer patients face in general, is incorrect diagnosis, leading to delays in correct diagnosis, and appropriate treatment. This is particularly acute in the case of IBC, with its rapid onset and high mortality rate. It has been described as “an oncologic emergency, and making the diagnosis promptly can be the difference between curable and incurable disease.”¹³ Much of this may be attributed to lack of clinician education about the symptoms of IBC. While much has changed since the publication of the foundational article on IBC in 1924, difficulties in diagnosing IBC have not; clinical definitions can be confusing, and the standard breast cancer screening tool, the mammogram, is not useful.

The staging definitions are defined by the American Joint Committee on Cancer (AJCC) issued by the National Cancer Institute and uses TNM classification: T=size and invasiveness of primary tumor (the higher the number, the more invasive), N=presence or absence of tumor in regional nodes, M=presence or absence of distant metastases¹⁴. The most important factor used in the AJCC diagnosis of IBC is erythema “diffuse erythema and edema involving 1/3 or more of skin of the breast” as stated in the 2017 8th edition of AJCC staging manual. In many cases, erythema may or may not be present – “many experts who treat large numbers of patients with IBC agree that this requirement should be removed from the staging system”¹³.

Researchers found the “lack of objective pathobiological diagnostic criteria means there is no gold standard against which to test assertions about clinical symptoms”¹³. The major screening tool for breast cancer is mammography. IBC patients typically have normal, or no mass detected mammography results. Ultrasonography is recommended as a follow up, followed by an MRI, then a punch biopsy.

Unlike other types of breast cancer, there is usually no palpable tumor with IBC. Instead, clusters of tumor cells (tumor emboli) grow, often in the dermal lymphatics. Instead of seeing a lump in the breast, a woman will see swollen, warm to the touch skin changes, *peau d'orange* skin texture and perhaps an inverted nipple. This is often misdiagnosed as an infection. It can also be more difficult for a patient to see skin color changes on darker skin

tones. Inflammatory Breast Cancer is classified as a rare cancer by the National Cancer Institute, because it occurs in fewer than 15/1000,000 people annually in the United States. Because it is often misdiagnosed, it is difficult to know the true number of actual cases as it is diagnosed by clinical presentation and not identification via a pathology report¹⁵. Rare cancers, because they are not seen often by many health care providers, are more difficult to correctly diagnose, have fewer clinical trials of which they are the focus, and have fewer specialist clinicians to treat them¹⁴. Risk factors for IBC are high body mass index, African American and/or Hispanic heritage, and low educational attainment¹⁶, which is why IBC is an NIH-designated cancer health disparity¹⁷. In a study of SEER (Surveillance, Epidemiology, and End Results, NCI) done on non-Hispanic white, Hispanic white, black and Asian/Pacific Islander women diagnosed with IBC between 1990-2004, black women had significantly poorer survival than non-Hispanic white women, while Asian/Pacific Islander women had higher survival rates than non-Hispanic white women¹⁸. Nonwhite patients are diagnosed at a younger age than white patients (57.8 years verses 61.8 years). Relative 20-year survival rates for IBC patients (using cohort analysis and period analysis, stratified by race) is 22.1% for white patients, and 16.2 for black patients. The 10-year survival rate is 30.7% for white patients and 18.4% for black patients, while the 5-year survival rate is 42.5% for white and 29.9% for black patients¹⁵. These statistics demonstrate, in part, the importance of the social determinants of health on morbidity and mortality outcomes, and the need for more public health education on IBC. In 2008, an International Expert Panel was convened at the First International Conference on Inflammatory Breast Cancer, and established IBC management guidelines. If a patient responds to induction chemotherapy, then a modified radical mastectomy is recommended. Immediate reconstruction is not advised due to the necessity of high doses of postoperative radiation, and possible recurrence¹⁹.

Who is your doctor?

Most generalists will never see a case of IBC. Most women's first contact with the healthcare system is often a primary care provider, including OBGYNs, internists, emergency physicians, and family practitioners. This can be problematic for patients because IBC requires a “high degree of suspicion”²⁰ meaning that the clinician must be familiar with the symptoms of IBC to begin with in order to utilize the correct diagnostic tools. One study¹⁷ revealed that the majority of primary care providers (physicians, PAs, nurse practitioners) surveyed were generally aware of unique IBC symptoms but would be unlikely to consider it when presented with patients with mastitis or skin changes. Most would prescribe antibiotics, a return visit and refer for a mammogram. They reported unfamiliarity with IBC epidemiology, or that IBC is more common among younger, premenopausal women, and believed mammograms were the most appropriate diagnostic test for IBC.

Barriers to Inflammatory Breast Cancer Care

The most obvious barrier to any type of medical care in

the United States is lack of access, which correlates to lack of insurance. The Affordable Care Act of 2010 mandates private insurers, Medicaid, Medicare and Tricare cover the cost of mammograms²¹. As previously indicated, mammograms alone are not useful in diagnosing IBC. A patient must also live within a reasonable distance from a diagnostic facility and have transportation to the facility, as well as childcare if needed. All of these factors are barriers for many patients, even those with private insurance. The recommendation is that once a patient is diagnosed with IBC, she should be referred to a specialized IBC clinic²² (which is typically only found in an academic medical center). This excludes many patients who do not reside in or near a major metropolitan area with an academic medical center with an IBC specialty clinic. As an alternative, a community healthcare provider can remotely connect with an IBC specialist, or an IBC clinic can provide telemedicine for rural residents²². Additional barriers include low health literacy levels and a lack of trust in health care system. Providers also found it difficult to give patients all the necessary information about a rare and complex disease in the 20 minutes they are allotted to spend with each patient. Providers surveyed indicated an interest in “peer coaching from women who have been treated for IBC¹⁷.”

Globally, research demonstrates that IBC is a larger portion of breast cancers in low-income countries than in high income countries. Patients in low-income countries face additional barriers such as low access to screening, diagnosis in latter stages of the disease (IBC is always stage-III at diagnosis, and stage IV in ~30% of cases²³), and low availability of multidisciplinary services²⁴.

The Role of the Patient Advocate in IBC

In 1998, the position of patient advocate was approved by the National Cancer Institute Intramural Council and today has an Office of Advocacy Relations. The National Cancer Institute published recommendations about advocacy, defining a research advocate as “someone who brings a nonscientific viewpoint to the research process, and communicates a collective patient perspective. A collective patient perspective is created when a person has knowledge of multiple disease experiences and conveys this collective perspective rather than his or her own exclusive experience²⁵. They are the patient voice in cancer research; as one stated “We have a PhD in experience – that offers a valuable opportunity to share in and guide the work being done²⁶.”

Today, patient advocates work for many types of cancer, though the patient advocates who work in IBC have a unique role. They are really partners in research, beginning at the preclinical stage. They are essential (and now required by granting agencies) to assist in formulating the research questions and identify patient concerns. In the clinical trial phase, advocates evaluate the whether the inclusion/exclusion criteria are acceptable to patients²⁶. Advocates may also serve on research teams; they may present at conferences and serve as panelists in workshops. Some may also serve on national advisory boards²⁷.

Being an advocate may present challenges. Some advocates may lack scientific knowledge. Much of the research material is highly technical and requires knowledge of medical and scientific terms not familiar to most lay people. Patient advocates, however, are highly motivated to acquire this language, first as a patient undergoing treatment, then as an advocate, playing an active, participatory role in research. In IBC, one of the potential challenges is relying on the same set of patient advocates; there are not a large number of IBC survivors, so the advocates may be over relied upon.

Patient advocates attend conferences, take notes, then make the information public, via their personal network, and/or through social media. It is important to note that while social media has made access to support from other cancer survivors much more readily available, without proper moderation, a few individuals may promote unproven medical treatments or ask for financial support²⁸.

Inflammatory Breast Cancer has an international consortium so it can be expensive to travel to some conferences. Additionally, there is the cost of hotels, transportation and food. Often the cost of patient advocate travel is underwritten by nonprofits involved in cancer advocacy, education, and research. In addition to cost and the high degree of scientific literacy required to be a research advocate, there is also a lack of diversity. If one lives near a major city with an academic research center, there are more opportunities to be involved than for an individual living in a rural location. While the cost of some travel to conferences is underwritten, advocates who work must take time off from employment, and if they have children, they must arrange for childcare. For IBC in particular, in order to survive the devastating disease, a patient's best chance is to be treated (after being correctly diagnosed, and in a timely manner – two barriers) by an IBC specialist found at one of six IBC treatment centers in the United States (Baylor College of Medicine, Houston, Texas; Dan L. Duncan Comprehensive Cancer Center, Houston, Texas; Dana-Farber Cancer Institute Inflammatory Breast Cancer Program, Boston, Massachusetts; Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, Illinois; University of Michigan Comprehensive Cancer Center, Ann Arbor, Michigan; University of Texas MD Anderson Cancer Center, Houston, Texas). There is a research center at University of Delaware, Newark, Delaware. Internationally, there are three IBC research and treatment centers: *Institut Paoli Calmettes*, Marseille, France, *Instituto Nacional de Cancerologia (INCAN)* Mexico City, Mexico and the University of Antwerp, Antwerp, Belgium²⁹. Treatment at these centers is available to those with appropriate insurance coverage. Patients may also enroll in a clinical trial if one for their condition is actively recruiting. There are links to clinical trials on the webpages of the Inflammatory Breast Cancer International Consortium²⁹ and of IBC Network Foundation³⁰.

The Patient's Voice

Valerie Fraser's story captures the experiences of many IBC advocates. Fraser woke up on New Year's Day in

2007, with swelling in her left breast. It did not go away in a few days, it just got worse her gynecologist and radiologist diagnosed an infection. The masses on the ultrasound, they believed, were abscesses. Her local breast clinic could not see her for an appointment for 2 months. Not satisfied with this delay, she asked the receptionist if she could send her ultrasound to the director so he could assess if she could wait two months. She sent in her ultrasound had an appointment the next day, and a biopsy the following week. Three weeks after she first noticed symptoms, she was diagnosed with stage IIIb IBC and ductal carcinoma grade 2. Fraser then began to research as much as she could on IBC, discovering that only 40% of IBC patients were alive 5 years post diagnosis and treatment²⁸.

Valerie's previous experience of her father's bladder cancer and her mother's breast cancer gave her both the confidence and the impetus to follow up and push for treatment, as well as do her own extensive research. In 2013, she was part of the formation of the Inflammatory Breast Cancer International Consortium, for which she is the Secretary and Director of Research, Advocacy and Board Governance. In 2023, she stated "As an educated and trained scientific career research advocate, I continue to work with many leading cancer institutions and organizations, consult on grant projects, clinical trial advisory and working groups and serve on scientific peer panel reviews and steering committees bring both the patient and research advocate perspective²⁸."

Jeannine Donahue had a bilateral mastectomy in 2007, right before she turned 27 years old. She recalled "I was told by my doctors that I was too young to have breast cancer and my symptoms of a swollen breast, pain and a rash were noting to be concerned about²⁸." Jeannine is currently the Breast Program Manager Weill Cornell Medicine.

Joshlyn Earls story provides the perspective of an African American IBC survivor. Due to social determinates of health, women of color have more adverse health outcomes with IBC. The erythema is less visible on darker skin, and they are less likely to get adequate breast screening^{31,17}. In November 2010, Joshlyn's chiropractor noticed some calcifications below her breast, when he examined her full body x-ray, so he referred her to an internist. She then had a mammogram three months later. She had another in March 2011, then a third in April that year, by which time she was in extreme pain. The results of the final mammogram were "cloudy." A few days later, she had an ultrasound which showed a solid mass. Two weeks later a needle biopsy revealed high-grade infiltrating ductal carcinoma. Seven months later, she received the diagnosis of IBC. She clarified "my surgeon explained the difference between a pathological diagnosis and a clinical diagnosis, for which I feel every surgeon should take the extra 5 minutes to explain to a patient so that they understand what they actually have, not just say 'breast cancer²⁸."

Being a cancer patient is exhausting, time consuming, and expensive. Even with insurance, there are co-pays, deductibles, arguments over covering Tier 4 drugs, lost

work time and lost family time, all of which takes a toll on the body, mental health, and psyche, in addition to the disease's toll. Depending on the type of job one has, and the type of cancer, it may not be possible to continue to be employed while undergoing cancer treatment. Hourly employees are unlikely to be able to take a medical leave of absence. For these reasons, and Joshlyn's own experience, she became an advocate. She stated "While doing my research I realized there was a need for an organization for women who were not only dealing with IBC, but the financial burden that comes with the diagnosis, which is why I went from a patient to an advocate, because of the lack of treatment I received and the lack of knowledge regarding IBC in the world. I knew to save my life and to help educate black and brown women I had to fight²⁸."

Joshlyn is the founder and CEO of Fighting 4 the Tatas Breast Cancer Organization³². In this role, she is a consumer reviewer for Department of Defense grants. She stated "Having the responsibility as a peer reviewer to speak for the entire breast cancer community on the impact of these applications was very scary and exciting all at the same time. I was given the opportunity to work side by side with scientist trying to figure out ways to improve the prognosis and prevent the metastasis of breast cancer the fact that I am a fighter my opinion was highly considered and valued. My high point was when a scientist actually changed a score because of an explanation of mine of the impact the application could have in the breast cancer community. From that point on, I was looked at differently and everyone involved in the consumer review understood that not only was I a breast cancer fighter but I was also a breast cancer advocate³³." Joshlyn's sense of pride, accomplishment and control is evident in her description of her role in the grant review process. Many patients refer to the loss of control or having to surrender control to a disease that takes over their lives. Being a patient advocate helps women make sense of their own experiences, grants them professional recognition by the medical and scientific community, and empowers them to focus on helping others³⁴.

Peggy Stephens was also misdiagnosed. She went to her doctor when she noticed something was wrong with her breast. Her doctor diagnosed mastitis, though she had not breastfed in more than two years. Peggy recounts a familiar scenario: "the doctor looked me in the face, [the doctor] who had minimal information and experience with IBC, dismissed me when asked what she knew about IBC, and said 'I know you don't have it.'" Peggy did her own research and after seven weeks finally had an ultrasound guided biopsy, then a skin biopsy (skin punch biopsy is recommended over fine needle) which confirmed what she thought, and her own doctor dismissed. She recalls "Once diagnosed and with only a minimal chance of survival, I started the fight of my life²⁸." Peggy is the president of the Inflammatory Breast Cancer Foundation³⁵ and started the first "IBC Get Together" in Michigan.

Heather Pirowski was diagnosed with Stage IIIb IBC in 2020. Nine months after her first mammogram (at age 43) came back clean, she started to notice that her left

breast had increased in size and was getting red. She didn't feel any lumps; the only sign women are ever taught to look for in breast self-exams. Her experience with breast cancer happened during COVID-19, so she experienced even more delays. Only because she sought a second opinion from a breast cancer oncologist (via virtual appointment), did she hear a clinician mention IBC. Heather states "It infuriates me know that doctors within the breast cancer field continue to overlook, misdiagnose, and dismiss IBC. I was a textbook case: inflamed breast, thickening of and cancer in the skin, chemotherapy not working...IBC is on the same level as brain metastasis. No one wants to touch it because it's aggressive and the prognosis is grim. IBC patient advocates are in limited number because this aggressive disease takes too many of us quickly²⁸." Heather is a board member of the Hoosier Breast Cancer Advocates³⁶ and vice president of advocacy with the Catherine Peachey Fund³⁷, which supports breast cancer research in her home state of Indiana.

Past Research Paving the Way

Up until 1999, IBC was an underrepresented form of breast cancer in terms of research focus. Its distinction as a distinct entity has been argued for the better part of a half-century. A detailed review of the literature over the span of 80 years starting from 1924 suggests that the infrequency of IBC coupled with its misdiagnosis, as 'mastitis' could be the main contributing factors of IBC being an understudied entity for such a long period of time³⁸⁻⁴¹. Most early investigations included individual or a small number of IBC samples incidentally, along with conventional breast cancers. These studies attempted to relate IBC to conventional breast cancers and most molecular studies focused on expression of genes and proteins associated with breast cancer such as hormonal receptor status, epidermal growth factor receptor (EGFR) and Her2 levels, oncogene and tumor suppressor expression⁴²⁻⁴³. Although not entirely informative for IBC, these studies helped to highlight that the unique phenotypic characteristics of the disease were due to a distinctive molecular profile from conventional breast cancers. Of note, EGFR overexpression is often associated with IBC, prevalent in about 30% of cases and indicative of poor outcome⁴⁴.

In 1999, van Golen and Merajver hypothesized that a limited number of genetic alterations give rise to IBC and that the disease is metastatic almost upon its inception⁴⁵. In this study, using a modified differential display technique, expression of transcripts from a primary IBC cell line (SUM149) with immortalized human mammary epithelial cells and lymphocytes from the patient that the SUM149 was derived from were compared. Seventeen differentially expressed genes were identified including two transcripts whose expression was found to be highly significant: Lost in Inflammatory Breast Cancer (LIBC, now designated as Wisp3) and RhoC GTPase. Expression of LIBC was lost in 80% of inflammatory tumors and 21% of non-inflammatory tumors and is a candidate tumor suppressor. Overexpression of RhoC GTPase was observed in 90% of inflammatory tumors, whereas only 38% of non-inflammatory tumors, and has been demonstrated to act as a driver of invasion and

metastasis⁴⁵⁻⁴⁶. The results of this study were confirmed by Vermeulen and colleagues 5 years later by tissue microarray analysis⁴⁷.

Soon after several studies over a 20-year period identified a number of unique molecular characteristics of IBC such as overexpression of E-cadherin, caveolin-1 and -2, which is opposite of what is normally observed in conventional breast cancer progression (reviewed in^{7, 43}). The Translational Research Group (TCRG) in Antwerp Belgium attempted to create a set of definitive diagnosis criteria that would allow for more accurate diagnosis of IBC. Van Laere et. al. first presented the integration of three Affymetrix expression datasets collected through the international IBC consortium allowing them to interrogate the molecular profile of IBC using the largest series of IBC samples ever reported². An IBC-unique 75-gene signature was identified. The study suggests that IBC is transcriptionally heterogeneous and the molecular profile of IBC, bearing molecular traits of aggressive breast tumor biology, shows attenuation of transforming growth factor beta (TGFβ) signaling. Our laboratory developed a novel method for culturing IBC emboli *in vitro*⁴⁸. Using this novel culture system, we along with the TCRG described low expression of TGFβ in IBC cell lines and patients, which promotes cohesive invasion of IBC cells^{2, 48}.

IBC Emboli Contain a Large Stem Cell Population

Because of the resemblance of IBC intralymphatic emboli to the embryonal blastocyst and their resistance to traditional chemotherapy/radiotherapy, Barsky and colleagues investigated the presence of stem cell markers on IBC⁴⁹. Using MARY-X spheroids, they identified embryonal stem cell markers including stellar, rex-1, nestin, H19 and potent transcriptional factors oct-4, nanog and sox-2 expressed. Most importantly, cells making up the MARY-X spheroids expressed CD44 (+)/CD24 (-/low), ALDH1, and CD133. Mammary cancer stem cells show a number of mechanistic pathways that contribute to expansion, maintenance and invasion. Specifically, two signal transduction pathways: NF-κB pathway and RAS/MAPK pathway are involved, indicating that these pathways play an important role in the molecular biology of mammary cancer stem cells⁵⁰. Interestingly, Van Laere et. al. documented that IBC samples are characterized by more frequent activation of the NF-κB, RAS/MAPK pathway and that RAS/MAPK activation is responsible for NF-κB activation in IBC, with 74% of human IBC samples containing a genetic signature indicative of a high stem cell composition, as opposed to 44% of non-IBC samples⁵¹.

Altered Signaling Pathways

In collaboration with the TCRG in Antwerp Belgium, we performed a comparative study between IBC and non-IBC patient samples to look at expression of several molecules involved in PI3K/Akt1 signaling axis⁵². A number of genes were upregulated in the IBC patient samples and when these were segregated by function it was found that PI3K/Akt1 signaling genes associated with cytoskeletal reorganization and motility were the

only genes significantly increased in IBC patients. A key driver of IBC metastasis, RhoC GTPase, was found to be a substrate for Akt1. Phosphorylation of RhoC GTPase by Akt1 was required for IBC cell invasion and is mediated by caveolin-1⁵³.

In the same comparative analysis it was also seen that the platelet derived growth factor receptor alpha (PDGFRa) was highly over-expressed in IBC compared to non-IBC⁵². It is very well documented that the canonical PDGFRa pathway involves PI3K/Akt activation⁵². Huang et al., reported that in comparison to RhoB GTPase null mice, RhoB GTPase heterozygous mice show punctate staining of PDGFRa in the cytoplasm towards the perinuclear region with relatively higher phosphorylated PDGFRa upon PDGF stimulation⁵⁵. Interestingly, we demonstrated that treatment of SUM149 IBC cells with farnesyl transferase inhibitors (FTIs) led to decreased RhoC GTPase-mediated invasion⁵⁶⁻⁵⁷. Therefore, it is plausible that increased PDGFRa expression and increased phosphorylation causes aberrant Akt1 activation and hence RhoC GTPase induced invasion and metastasis of IBC. Immunostaining of IBC cells suggests cytoplasmic localization of PDGFRa similar to glioblastoma and gastrointestinal stromal tumors (GIST)⁵⁸. Further, we reported that IBC patients that expressed high levels of cytoplasmic PDGFRa had a worse prognosis and shorter survival times than IBC patients that did not⁵⁸.

Ongoing Research

We recently began to study the potential mechanisms of IBC cutaneous metastases. Cutaneous metastases occur at a rate of >16% in IBC, like malignant melanoma, which also has a propensity to form cutaneous metastases⁵⁹⁻⁶⁰. IBC cutaneous metastasis is associated with chest wall recurrences, significantly decreasing the quality of life and survival⁶⁰. Various reports demonstrate a role for TGFβ in the etiology of melanoma cutaneous metastasis⁶¹⁻⁶². Transforming growth factor beta promotes tumor cell invasion and its expression can be induced in the stroma by radiation treatment⁶³⁻⁶⁸. As stated before in this review, expression of TGFβ in IBC patients, which may promote cohesive invasion of IBC cells^{2, 68}, while stimulation of IBC cells with TGFβ causes altered tumor cell behavior such as single cell invasion⁶⁹. IBC cells from emboli are able to invade in clusters via RhoC GTPase-dependent amoeboid movement and this invasion, by clusters of IBC cells, is disrupted by exposure to TGFβ⁶⁹.

Unpublished results from our laboratory demonstrate that SUM149 IBC cells stimulated with TGFβ undergo single cell invasion. When compared with cells that did not

undergo invasion, a number of distinct molecular differences were observed. Invaded cells expressed stem cell-like markers along with activated RhoC GTPase and Akt1. In contrast, noninvaded cells did not show any of these molecular markers. We refer to the invaded cells with stem cell-like properties as tumor initiating cells or "TICs", while referring to the noninvaded cells as "emboli cells". The invaded TICs also did not express E-cadherin, which is a stark contrast to the emboli cells. Most importantly, we identified microRNA-10b (miR-10b) in the TGFβ-stimulated TICs.

Our preliminary data suggests that miR-10b expression in the invaded TIC cells leads to decreased levels of the homeobox protein HOXD10 and increased expression of RhoC GTPase. Yang et. al. demonstrated that low HOXD10 acts as a tumor suppressor by inhibiting RhoC GTPase expression and affecting the Akt and MAPK pathways⁷⁰. Expression of miR-10b has been linked to progression of several cancers and can regulate the expression of genes that are involved in metastasis⁷¹⁻⁷³. For example, miR-10b can increase tumor cell motility by regulating fucosyltransferase 8 (FUT8), consequently activating the AKT signaling pathway and negatively regulating E-cadherin⁷⁴. In addition, core fucosylation of PDGFRa and EGFR by FUT8 is essential for receptor signaling⁷⁵. Preliminary data show that downregulation of miR-10b results in the IBC TICs losing their invasive and stem cell-like properties and becoming more emboli cell-like. These results are similar to data that was previously reported, loss of the metastatic capabilities of MBA-MB-231 cells through inhibition of their stem cell-like properties⁷⁶. This is a very promising research path since miR-10b could be a viable keystone therapeutic target that would affect multiple pathways driving IBC metastasis.

Conclusion

IBC is a distinctive disease with relatively low incidence rate, yet it accounts for a disproportionate number of breast cancer deaths annually in the United States. Despite its dire prognosis, awareness of IBC by the general public and even health care providers remain low. Therefore, outcomes rely on many factors including early recognition of discreet symptoms that resemble benign conditions and having a doctor that can recognize the symptoms. Advocacy has improved IBCs visibility and awareness. Progress in both treatment and understanding the molecular basis of the disease has progressed over the past three decades and provide promise for the future.

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References

- Radunsky, G.S. and K.L. van Golen, *The current understanding of the molecular determinants of inflammatory breast cancer metastasis*. Clin Exp Metastasis, 2005. 22(8): p. 615-20.
- Van Laere, S.J., et al., *Uncovering the molecular secrets of Inflammatory Breast Cancer biology: An integrated analysis of three distinct Affymetrix gene expression data sets*. Clinical Cancer Research, 2013.
- Woodward, W.A., *Inflammatory breast cancer: unique biological and therapeutic considerations*. The Lancet Oncology, 2015. 16(15): p. e568-e576.
- Kleer, C.G., K.L. van Golen, and S.D. Merajver, *Molecular biology of breast cancer metastasis. Inflammatory breast cancer: clinical syndrome and molecular determinants*. Breast Cancer Res, 2000. 2(6): p. 423-429.
- Dawood, S. and V. Valero, *Clinical Aspects of Inflammatory Breast Cancer: Diagnosis, Criteria, Controversy*, in *Inflammatory Breast Cancer: An Update*, N.T. Ueno and M. Cristofanilli, Editors. 2012, Springer: New York, N.Y. p. 11-20.
- Fouad, T.M., et al., *Overall survival differences between patients with inflammatory and noninflammatory breast cancer presenting with distant metastasis at diagnosis*. Breast cancer research and treatment, 2015. 152(2): p. 407-416.
- Goldner, B., et al., *Incidence of Inflammatory Breast Cancer in Women, 1992–2009, United States*. Annals of surgical oncology, 2014. 21(4): p. 1267-1270.
- van Golen, K.L. and M. Cristofanilli, *The Third International Inflammatory Breast Cancer Meeting*. Breast Cancer Res, 2013. 15: p. 318-321.
- Rosenberg C, Golden, Janet, eds. *Framing Disease, Studies in Cultural History*. Health and Medicine in American Society. Rutgers University Press; 1992.
- Porter L, Goodman K, Mailman J, Garrett W. Patient Advocates and Researchers as Partners in Cancer Research: a Winning Combination. *American Society of Clinical Oncology Educational Book*. 2023:1-8.
- Il'yasova D. S-RS, Akushevich I, et al. What can we learn from the age-and race/ethnicity-specific rates of inflammatory breast carcinoma? *Breast Cancer Research and Treatment*. 2011;130(2):691-691.
- Lee BJ, Tannanbaum NE. Inflammatory carcinoma of the breast, a report of twenty-eight cases from the breast clinic of the Memorial Hospital. *Surgery, Gynecology and Obstetrics*. 1924;39:580-595.
- Le-Petross HT, Balema W, Woodward WA. Why Diagnosing Inflammatory Breast Cancer is Hard and How to Overcome the Challenges: a Narrative Review. *Chinese Clinical Oncology*. 2021;10(6)doi:10.21037/cco-21-116
- Institute NC. Cancer Staging. Accessed June 16, 2025. <https://www.cancer.gov/about-cancer/diagnosis-staging/staging>
- Abraham HG, Xia Y, Mukherjee B, Merajver SD. Incidence and Survival of Inflammatory Breast Cancer between 1973 and 2015 in the SEER Database. *Breast Cancer Research and Treatment*. 2020;185:229-238.
- Relation T, Li, Yaming, Fisher, James L., et al. Inflammatory breast cancer, trimodal treatment and mortality: does where you live matter? *Surgery*. 2022;171(3):687-692.
- Devi GR, Fish LJ, Bennion A, et al. Identification of barriers at the primary care provider level to improve inflammatory breast cancer diagnosis and management. *Preventive Medicine Reports*. 2023;36(102519):1-8.
- Schinkel JK, Zahm, S.J., Jatoi, I. et al. Racial/ethnic differences in breast cancer survival by inflammatory status and hormone receptor status: an analysis of the Surveillance, Epidemiology, and End Results data. *Cancer Causes Control*. 2014;25:959-968.
- Barkataki S, Joglekar-Javandekar M, Brandfield P, Murphy T, Dickson-Witmer D, van Golen KL. Inflammatory Breast Cancer: a Panoramic View. *Journal of Rare Diseases and Treatment*. 2018;3(2):37-43.
- Hester RH, Hortobagyi GN, Lim B. Inflammatory Breast Cancer: Early Recognition and Diagnosis is Critical. *American Journal of Obstetrics and Gynecology*. October 2021:392-396.
- KFF. Women's Health Policy. Accessed June 16, 2025. <https://www.kff.org/womens-health-policy/fact-sheet/coverage-of-breast-cancer-screening-and-prevention-services/>
- Takahashi Y, Sridhar, N., Iwase, T. et al. Inflammatory breast cancer, best practice in the community setting. *npj Breast Cancer*. 2025;11(52)
- Woodward WA. Deescalation Perils in Inflammatory Breast Cancer. Invited Commentary. *JAMA Network Open*. Feb 26 2025;8(2)
- Chippa V, Barazi H. *Inflammatory Breast Cancer*. StatPearls [Internet]; updated 2023 April 16. Accessed 2025. <https://www.ncbi.nlm.nih.gov/books/NBK564324/>
- Advocates in Research Working Group: Recommendations (2011).
- Porter L, Goodman K, Mailman J, Garrett W. Patient Advocates and Researchers as Partners in Cancer Research: a Winning Combination. *American Society of Clinical Oncology Educational Book*. 2023:1-8.
- Spears PA. Patient Engagement in Cancer Research from the Patient's Perspective. *Future Oncology*. 2021;17(28):3717-3728.
- Donahue J, Earls J, Fraser V, Mason G, Pirowski H, Stephens P. Inflammatory breast cancer (IBC) advocacy - past, present and future! *International Review of Cell and Molecular Biology*. 2023;doi:https://doi.org/10.1016/bs.ircmb.2023.11.001
- Inflammatory Breast Cancer International Consortium. Accessed June 17, 2025. <https://ibcic.org/about-ibc-ic/>
- The IBC Network Foundation. June 17, Accessed June 17, 2025. <https://theibcnetwork.org/>
- Denu RA, Hampton JM, Currey A, Anderson RT, Cress R. Racial and socioeconomic disparities are more pronounced in inflammatory breast cancer than in other breast cancers. *Journal of Cancer Epidemiology*. 2017;2017(1-8)7574946.
- Fighting 4 the Tatas. Accessed January, 2024 <https://fighting4thetatas.org/>

33. Scientific Peer Review of Breast Cancer Research Applications for the Department of Defense. 2012.
34. Avery J, Thomas R, Howell D, Dubouloz Wilner C-J. Empowering Cancer Survivors in Managing Their Own Health: A Paradoxical Dynamic Process of Taking and Letting Go of Control. *Qualitative Health Research*. 2023;33(5):412-425.
35. The Inflammatory Breast Cancer Foundation. Accessed January, 2024. <https://eraseibc.org/about-us>
36. Hoosier Breast Cancer Advocates. Accessed January, 2024. <https://www.hoosierbcadvocates.com/>
37. Catherine Peachey Fund. Accessed January, 2024. <https://www.peacheyfund.com/>
38. Osborne, B.M., *Granulomatous mastitis caused by histoplasma and mimicking inflammatory breast carcinoma*. *Hum Pathol*, 1989. 20(1): p. 47-52.
39. Dahlbeck, S.W., J.F. Donnelly, and R.L. Theriault, *Differentiating inflammatory breast cancer from acute mastitis*. *Am Fam Physician*, 1995. 52(3): p. 929-34.
40. Chambler, A.F., et al., *Inflammatory breast carcinoma*. *Surg Oncol*, 1995. 4(5): p. 245-54.
41. Dvoretzky, P.M., et al., *The pathology of breast cancer in women irradiated for acute postpartum mastitis*. *Cancer*, 1980. 46(10): p. 2257-62.
42. Charpin, C., et al., *Inflammatory breast carcinoma: an immunohistochemical study using monoclonal anti-pHER-2/neu, pS2, cathepsin, ER and PR*. *Anticancer Res*, 1992. 12(3): p. 591-7.
43. Moll, U.M., G. Riou, and A.J. Levine, *Two distinct mechanisms alter p53 in breast cancer: mutation and nuclear exclusion*. *Proc Natl Acad Sci U S A*, 1992. 89(15): p. 7262-6.
44. Zhang, D., LaFortune, T.A., Krishnamurthy, D., Esteve, F.J., Critofanilli, M., Liu, P., Lucci, A., Singh, B., Hung, M-C., Hortobagyi, G.N., and Ueno, N.T. *Epidermal growth factor receptor tyrosine kinase inhibitor reverses mesenchymal to epithelial phenotype and inhibits metastasis of inflammatory breast cancer*. *Clin. Cancer Res.*, 2009. 15(21): 6639-6648.
45. van Golen KL, Davies S, Wu ZF, Wang Y, Bucana CD, Root H, Chandrasekharappa S, Strawderman M, Ethier SP, Merajver SD. A novel putative low-affinity insulin-like growth factor-binding protein, LIBC (lost in inflammatory breast cancer), and RhoC GTPase correlate with the inflammatory breast cancer phenotype. *Clinical cancer research : an official journal of the American Association for Cancer Research*. 1999;5(9):2511-9. Epub 1999/09/28. PubMed PMID: 10499627.
46. van Golen KL, Wu ZF, Qiao XT, Bao LW, Merajver SD. RhoC GTPase, a novel transforming oncogene for human mammary epithelial cells that partially recapitulates the inflammatory breast cancer phenotype. *Cancer research*. 2000;60(20):5832-8. Epub 2000/11/04. PubMed PMID: 11059780.
47. Van Laere, S., Van der Auwera, I., Van den Eynden, G.G., Fox, S.B., Bianchi, F., Harris, A.L., van Dam, P., Van Marck, E.A., Vermeulen, P.B., and Dirix, L.Y. *Distinct molecular signature of inflammatory breast cancer by cDNA microarray analysis*. *Breast Cancer Res Treat* 2005; 93(3): 237-46.
48. Lehman, H.L., et al., *Modeling and characterization of inflammatory breast cancer emboli grown in vitro*. *Int J Cancer*, 2012.
49. Xiao, Y., Ye, Y., Yearsley, K., Jones, S. and Barsky, S.H. *The lymphovascular embolus of inflammatory breast cancer expresses a stem cell-like phenotype*. *Am J Pathol* 173(2): 561-74. 2008
50. Yousefina, S. Forootan, S.F., Forootan, S.S., Esfahani, M.H.N., Gure, A.O. and Ghaedi, K. *Mechanistic pathways of malignancy in breast cancer stem cells*. *Front. Oncol*. 10. 2020 <https://doi.org/10.3389/fonc.2020.00452>
51. Van Laere, S.J., Van der Auwera, I., Van den Eynden, G.G., van Dam, P., Van Marck, E.A., Vermeulen, P.B. and Dirix, L.Y. *NF-kappaB activation in inflammatory breast cancer is associated with oestrogen receptor downregulation, secondary to EGFR and/or ERBB2 overexpression and MAPK hyperactivation*. *Br J Cancer* 97(5): 659-69. 2007.
52. Lehman, H.L., Van Laere, S.J., van Golen, C.M., Vermeulen, P.B., Dirix, L.Y. and van Golen, K.L. *Regulation of inflammatory breast cancer cell invasion through Akt1/PKB phosphorylation of RhoC GTPase*. *Mol Cancer Res* 10(10): 1306-18. 2012.
53. Joglekar, M., Elbazanti, W.O., Wietzman, M.D., Lehman, H.L. and van Golen, K.L. *Caveolin-1 mediates inflammatory breast cancer cell invasion via the Akt1 pathway and RhoC GTPase*. *J Cell Biochem* 116(6): 923-33. 2015.
54. Zhang, H., Bajraszewski, N., Wu, E., Wang, H., Moseman, A.P., Dabora, S.L., Griffin, J.D. and Kwiatkowski, D.J. *PDGFRs are critical for PI3K/Akt activation and negatively regulated by mTOR*. *J Clin Invest*. 117(8): 730-38. 2007.
55. Huang, M., Duhadaway, J.B., Prendergast, G.C. and Laury-Kleintop, L. *RhoB regulates PDGFR-beta trafficking and signaling in vascular smooth muscle cells*. *Arterioscler Thromb Vasc Biol* 27(12): 2597-605. 2007.
56. van Golen, K.L., Bao, L., DiVito, M.M., Wu, Z., Prendergast, G.C. and Merajver, S.D. *Reversion of RhoC GTPase-induced inflammatory breast cancer phenotype by treatment with farnesyl transferase inhibitor*. *Mol Cancer Ther* 1(8): 575-83. 2002.
57. Chatterjee, M. and van Golen, K.L. *Farnesyl transferase inhibitor treatment of breast cancer cells leads to altered RhoA and RhoC GTPase activity and induces a dormant phenotype*. *Int J Cancer* 129(1): 61-9. 2011
58. Joglekar-Javadekar, M., Van Laere, S., Bourne, M., Moalwi, M., Finetti, P., Vermeulen, P.B., Birnbaum, D., Dirix, L.Y., Ueno, N., Carter, M., Rains, J., Ramachandran, A., Bertucci, F. and van Golen, K.L. *Characterization and targeting of Platelet-Derived Growth Factor alpha (PDGFRA) in inflammatory breast cancer (IBC)*. *Neoplasia* 19(7): 564-73. 2017.
59. Martin B. *Dermatology Secrets*. In: James E, John L, editors. *Dermatology*. New Delhi: Jaypee Brothers; 1997. p. 310-20.
60. Cristofanilli M, Valero V, Buzdar AU, Kau SW, Broglio KR, Gonzalez-Angulo AM, Sneige N, Islam R, Ueno NT, Buchholz TA, Singletary SE, Hortobagyi GN. *Inflammatory breast cancer (IBC) and patterns of recurrence: understanding the biology of a unique disease*. *Cancer*. 2007;110(7):1436-44. Epub 2007/08/19. doi: 10.1002/cncr.22927. PubMed PMID: 17694554.

61. Perrot, C.Y., D. Javelaud, and A. Mauviel, *Insights into the transforming growth factor beta signaling pathway in cutaneous melanoma*. *Ann Dermatol*, 2013. 25(2): p. 135-144.
62. Schmid, P., P. Itin, and T. Ruffli, *In situ analysis of transforming growth factor- β s (TGF- β 1, TGF- β 2, TGF- β 3 and TGF- β 3 type II receptor expression in malignant melanoma*. *Carcinogenesis*, 1995. 16(7): p. 1499-1503.
63. Barcellos-Hoff, M.H., *Radiation-induced Transforming Growth Factor β and Subsequent Extracellular Matrix Reorganization in Murine Mammary Gland*. *Cancer Res*, 1993. 53(17): p. 3880-3886.
64. Cichon, Magdalena A., Evette S. Radisky, and Derek C. Radisky, *Identifying the Stroma as a Critical Player in Radiation-Induced Mammary Tumor Development*. *Cancer Cell*, 2011. 19(5): p. 571-572.
65. Ehrhart, E.J., et al., *Latent transforming growth factor beta1 activation in situ: quantitative and functional evidence after low dose gamma-irradiation*. *FASEB*, 1997. 11: p. 991-1002.
66. Giampieri, S., et al., *Localized and reversible TGFbeta signalling switches breast cancer cells from cohesive to single cell motility*. *Nat Cell Biol*, 2009. 11(11): p. 1287-96.
67. Gotzmann, J., et al., *Molecular aspects of epithelial cell plasticity: implications for local tumor invasion and metastasis*. *Mutat.Res.*, 2004. 566(1): p. 9-20.
68. Mukai, M., et al., *RhoC is essential for TGF-beta1-induced invasive capacity of rat ascites hepatoma cells*. *Biochem Biophys Res Commun*, 2006. 346(1): p. 74-82.
69. Lehman, H.L., et al., *Modeling and characterization of inflammatory breast cancer emboli grown in vitro*. *Int J Cancer*, 2012.
70. Yang, H., Zhou, J., Mi, J., Ma, K., Fan, F., Ning, J., Wang, C., Wei, X., Zhao, H. and Li, E. *HOXD10 acts as a tumor-suppressive factor via inhibition of the RhoC/Akt/MAPK pathway in human cholangiocellular carcinoma*. *Oncol Rep* 34(4): 1681-91. 2015.
71. Ma, L., Teruya-Feldstein, J. & Weinberg, R. *Tumour invasion and metastasis initiated by microRNA-10b in breast cancer*. *Nature* 449, 682–688 (2007). <https://doi.org/10.1038/nature06174>
72. Wang, J., Yan, Y., Zhang, Z., & Li, Y. (2019). Role of miR-10b-5p in the prognosis of breast cancer. *PeerJ*, 7.
73. Al-Qadi, N., Halim, A.S., Mackie, H., Sempere, L.F., & Moore, A. (2023). Exploring the effects of inhibiting miR-10b on breast cancer stemness and metastasis. *Journal of Clinical Oncology*.
74. Guo, D., Guo, J., Li, X., & Guan, F. (2018). Enhanced motility and proliferation by miR-10b/FUT8/p-AKT axis in breast cancer cells. *Oncology Letters*, 16, 2097 – 2104
75. Wang, X., Gu, J., Miyoshi, E., Honke, K. and Taniguchi, N. *Phenotype changes of Fut8 knockout mouse: Core fucosylation is crucial for the function of Growth Receptor(s)*. *Methods Enzymology* 417: 11-12. 2006.
76. Halim, A., Al-Qadi, N., Kenyon, E., Conner, K.N., Mondal, S.K., Medarova, Z. and Moore, A. *Inhibition of miR-10b treats metastatic breast cancer by targeting stem cell-like properties*. *Oncotarget* 15: 591-606. 2024