

## Triple Negative Breast Cancer

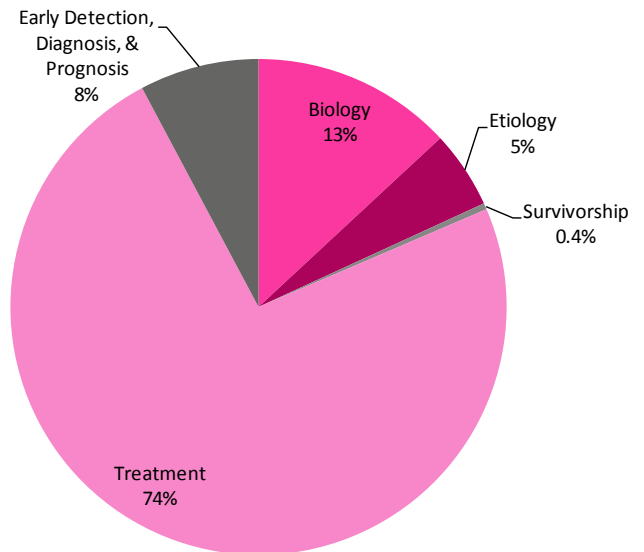
Approximately 15% of all breast cancers are what is commonly called triple negative breast cancer (TNBC). The name refers to three important “receptors” that influence the growth of breast cancer cells: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). Triple negative breast cancers lack all three receptors, which is troublesome because these receptors are critical targets for cancer therapy. As a result, TNBC, which is often very aggressive, does not respond to therapies that target the three receptors.

Though TNBC is not a new type of breast cancer, it was identified only a few years ago as a distinctive type. Research shows that TNBC disproportionately affects certain populations of women; it is more common in African Americans, younger women, and women who carry a BRCA1 gene mutation. One large study showed that African American women are twice as likely to be diagnosed with TNBC as white women (20.8% vs. 10.4%). In another study, 44.5% of the patients with TNBC were under 50 whereas women under 50 represented only 26.7% of patients with other types of breast cancer.

## TNBC and Basal-like Breast Cancer

The presence or absence of receptors is a common way of classifying breast cancers. Recent advances in science and technology, however, have led to new ways of classifying breast cancer based on a tumor’s unique genetic profile. Using this approach, scientists have identified an aggressive type of breast cancer called basal (or basal-like) breast cancer. There is a great deal of overlap between triple negative and basal-like breast cancers but they are not synonymous. About 85% of basal breast cancers are triple negative while the remainder has one or more receptors (ER, PR, or HER2). Similarly, not all TNBCs are basal-like; recent studies have estimated that approximately 71% of TNBCs have at least one basal-like characteristic. As previously mentioned, TNBC is more common among BRCA1 mutation carriers who develop breast cancer, and 75% of these patients’ cancers are basal-like.

**Komen Funded Triple Negative Breast Cancer Awards (2006–2010)**



## Identifying and Treating TNBC

The current approach to treating TNBC typically involves surgery, chemotherapy (oftentimes prior to surgery), and radiation therapy. Chemotherapy is very effective on some TNBC tumors, while others respond initially but quickly begin to re-grow. Women whose tumors respond completely to chemotherapy (called pathologic complete response or “pCR”) have a very good prognosis, similar to women whose tumors are not triple negative. But women whose cancers don’t respond well have lower survival compared to women with other types of breast cancer. More research is needed to understand why responses differ dramatically and to develop more effective treatments and prognostic indicators. Also needed are studies to better understand the risk factors for TNBC and tools to detect it earlier.

## Komen’s Investment in TNBC Research

Komen for the Cure has invested more than \$24 million to TNBC research since it was first identified as a distinct type of breast cancer. Starting in 2006, Komen has awarded 34 grants to researchers looking into the causes of and treatments for TNBC.

Over

## Specific areas of Komen-funded research include:

- o Study into the underlying biology of TNBC and how it develops
- o Strategies for preventing TNBC, including chemoprevention, mimicking an early pregnancy, and breastfeeding
- o Explaining the connections between BRCA1 gene mutations and triple negative disease
- o Restoring the estrogen receptor so that it can be targeted with ER-specific therapies
- o Enhancing sensitivity of TNBC to chemotherapy
- o Identification of new therapeutic targets (e.g., growth pathways and cellular targets) and developing new therapies for TNBC, including clinical trials
- o New or improved preclinical models of TNBC for testing new therapies and studying the disease
- o Discovery of biomarkers and signatures of risk for TNBC
- o Understanding health disparities related to TNBC, especially the role of African ancestry

## Triple Negative Breast Cancer Research Grants Awarded in 2010

### Investigator Initiated Research

Andrei Goga  
University of California San Francisco  
*Therapy of Receptor Triple-Negative Breast Cancers by Targeting The MYC Oncogene*

Khandan Keyomarsi & Kelly Hunt  
M.D. Anderson Cancer Center, University of Texas  
*CDK2 is a Novel Target for Triple Negative Breast Cancer*

Ann Thor  
University of Colorado Denver  
*Aberrant Glucose Metabolism: Pathogenic Factor and Therapeutic Target in Triple Negative Breast Cancers*

Alexei Kisselev  
Dartmouth College  
*Site-specific Proteasome Inhibitors for the Treatment of Triple-negative Breast Cancers*

### Post Doctoral Fellowship - Basic Research

Jennifer Knight, Fellow  
Morag Park, Mentor  
McGill University  
*Investigation into the Role Of Met, a Receptor Tyrosine Kinase, in the Development of Basal-like Breast Cancer*

Annabell Oh, Fellow  
Douglas Yee, Mentor  
University of Minnesota Twin Cities  
*AIB1 (amplified in breast cancer 1) is a Key Regulator of the IGF Pathway in Triple Negative Breast Cancer*

Vladimir Petrovic, Fellow  
Vincent Cryns, Mentor  
Northwestern University, Feinberg School of Medicine  
*Building a Model of Basal-like Breast Cancer for Discovery of Basal-like Drug Targets*

Fathima Kona, Fellow  
Angelika Burger & Fred Miller, Mentors  
Wayne State University  
*Evaluation of Aldehyde Dehydrogenase Inhibitors for the Prevention and Treatment of Triple Negative Breast Cancer*

Prajjal Singha, Fellow  
Pothana Saikumar & Rajeshwar Tekmal, Mentors  
University of Texas Health Science Center at San Antonio  
*Targeting LC3-SQSTM1/p62 Signaling Axis to Treat Apoptosis-resistant and Metastatic Breast Cancers*

### Postdoctoral Fellowship - Clinical Research

Devika Gajria, Fellow  
Clifford Hudis, Mentor  
Memorial Sloan-Kettering Cancer Center  
*Identifying Oncogenic Targets in Trastuzumab-Refractory HER2-amplified and Triple Negative Breast Cancer: a Phase I/II Trial of EGFR/HER2 and mTOR Inhibition*

### Post Doctoral Fellowship - Translational Research

Antonio F. Santidrian, Fellow  
Brunhilde Felding-Habermann, Mentor  
Scripps Research Institute  
*Role of Mitochondrial Complex I Modulated Tumor Cell NAD<sup>+</sup>/NADH Redox Balance in Breast Cancer Progression*

Jocelyn Reader, Fellow  
Amy Fulton, Mentor  
University of Maryland at Baltimore  
*Prostaglandin E EP1 Receptor in Breast Cancer Metastasis and Disparities*

Roisin Connolly, Fellow  
Vered Stearns, Mentor  
Johns Hopkins University, School of Medicine  
*Phase II Study of 5-Azacytidine and Entinostat (MS-275) in Patients with Advanced Breast Cancer*