

HER2-positive Breast Cancer

Approximately 20% of all breast cancers are what is commonly called HER2-positive (HER2+) breast cancer. The name refers to an important receptor that influences the growth of breast cancer cells: the human epidermal growth factor receptor 2 (HER2). These breast cancers are more aggressive, a characteristic that was first established in the late-1980s, and patients with HER2+ breast cancer tend to have worse outcomes than those with HER2- disease.

The development of trastuzumab (Herceptin®), the first HER2-targeted therapy, dramatically changed the prognosis for many women diagnosed with HER2+ breast cancer. Studies have shown that trastuzumab, which prevents the HER2 receptor from signaling the cancer cells to grow, has reduced recurrences by half and improved survival by up to 41%. Also of great significance was the introduction in 1998 of a test to detect the presence and amount of the HER2 protein, allowing doctors to identify which patients might benefit from trastuzumab and other HER2-targeted therapies developed in more recent years.

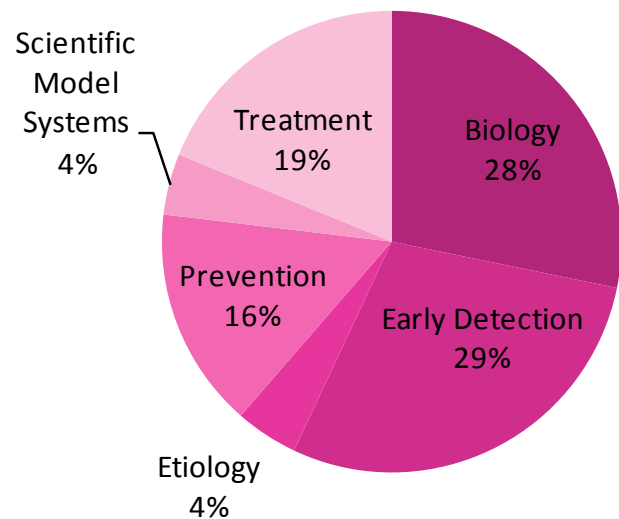
Treating HER2-positive Breast Cancer

In spite of the advances in treating HER2+ disease, challenges remain. Some HER2+ breast cancers do not respond to trastuzumab or develop resistance to the drug. This may be because there are multiple HER proteins and other proteins that interact with HER2, and trastuzumab targets only the HER2 protein. Newer therapies, many still in development, target more than one protein and may prove to be effective therapies for HER2+ disease. Some of these drugs are being tested in combination with trastuzumab to address problems of drug resistance and improve outcomes for patients with HER+ breast cancer.

Komen's Investment in HER2 Research

Komen for the Cure has funded 109 grants totaling \$41,263,715.00 on HER2 research. The first such grant was awarded in 1992 to Dr. Edison Liu to

**Komen Funded HER2-positive
Breast Cancer Awards (1992–2010)**



explore the role of HER2 gene amplification in breast cancer progression. Three Komen Promise Grants are looking at HER2+ disease:

- Researchers at University of Kansas and University of Texas are collaborating on a project to look at the preventive effects of an active compound found in flax seed, and their research is using a laboratory model of ER-negative, HER2+ breast cancer.
- A team of researchers at M.D. Anderson Cancer Center and Duke University are investigating the role of HER2 signaling in the progression from atypia (pre-cancerous cells) to ER- breast cancer. Their goal is to identify and test prevention strategies for HER2+, ER- breast cancer.
- University of California researchers are studying the way HER3, another protein in the HER family, interacts with HER2 and whether this promotes tumor growth. The results of their research could become the foundation for a new drug to block interaction between these HER proteins.

Over

Other topics of research funded by Komen include

- Determining how HER2 overexpression leads to breast cancer progression and metastasis
- Investigating the role of HER2 in breast cancer metastasis to bone
- Developing and testing new drugs that target HER2, including small molecules, gene therapy, and vaccines
- Identifying drugs that improve the response to HER2-directed therapies
- Identifying strategies for overcoming resistance to trastuzumab and other HER2-directed therapies
- Developing and validating biomarkers of response to HER2-directed therapies
- Identifying predictors of cardio-toxicity (which potentially leads to heart damage) resulting from treatment with anthracyclines followed by trastuzumab
- Prevention strategies for HER2+ breast cancer
- Determining whether HER2 is a marker of high-risk for progression in DCIS

HER2-Positive Breast Cancer Research Grants Awarded in 2010

Career Catalyst Research

Bin Wang
Temple University
Targeted Multidrug Delivery System to Overcome Chemoresistance in Breast Cancer

Rebecca Muraoka-Cook
Vanderbilt University Medical Center
Overcoming Resistance to HER2-targeted Therapies Through Inhibition of HER3-induced PI3K Activity

Investigator Initiated Research

Jonathan Serody
University of North Carolina at Chapel Hill
Combined Modality Therapies for the Treatment of Metastatic Breast Cancer

Dmitri Artemov
Johns Hopkins University, School of Medicine
Novel Two-component Delivery System Based on HER-2/neu Receptor Internalization Strategy

Brittney-Shea Herbert
Indiana University, Indianapolis
Targeting Telomerase for the Treatment of Refractory Breast Cancers

Keith Knutson
Mayo Clinic and Foundation, Rochester
The Role of the Immune Response in the Clinical Efficacy of Combination Trastuzumab and Chemotherapy

Post Doctoral Fellowship - Basic Research

Lavakumar Karyampudi, Fellow
Keith Knutson, Mentor
Mayo Clinic and Foundation, Rochester
Combination Therapy for Breast Cancer Using Anti-PD-1 Antibody and "Infrastructure" Vaccine.

Kideok Jin, Fellow
Zaver Bhujwalla, Mentor

Johns Hopkins University, School of Medicine
The Role of HOXB13 in the Development of Tamoxifen Resistance

Kakajan Komurov, Fellow
Pralhad Ram, Mentor
M.D. Anderson Cancer Center, University of Texas
Targeting Acquired Lapatinib-resistance in Breast Cancer

Brian Van Tine, Fellow
Matthew Ellis, Mentor
Washington University in St. Louis, School of Medicine
The Role of Taspase1 in HER2/Neu Driven Tumorigenesis

Post Doctoral Fellowship - Translational Research

Delphine Boulbes, Fellow
Francisco Esteva, Mentor
M.D. Anderson Cancer Center, University of Texas
Mechanisms of Action and Biological Significance of EGFR, HER2 and HER4 Mutations in HER2-Overexpressing Breast Cancer

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

Promise Grants

Carol Fabian
University of Kansas Medical Center
Stephen Hursting
University of Texas at Austin
The Lignan SDG as a Prevention Strategy for Pre-Menopausal Women at High Risk for Development of Breast Cancer