



[Targeted therapy](#) has revolutionized breast cancer therapy – allowing doctors to tailor treatments to individual patients while reducing unwanted side-effects. Targeted therapies work by attacking specific proteins that are needed for the tumor to grow. Unlike traditional chemotherapy, targeted therapies only attack proteins that are unique to the tumor, allowing them to kill tumor cells while doing little harm to normal cells. But for many women, targeted therapies can become ineffective as the tumor learns to how to evade the drug. This phenomenon, called “acquired drug resistance,” is a common problem among targeted therapies and the worst fear of many patients. However, research by Komen-grantee Dr. Sabine Brouxhon has revealed a new target for therapy that may overcome drug resistance.



*Dr. Sabine Brouxhon, Associate Professor of Emergency Medicine at Stony Brook University, NY*

One of the most effective targeted therapies for breast cancer is [trastuzumab](#), also known as Herceptin, a drug that attacks a protein called [HER2](#). About 20-25 percent of breast cancer patients have tumors that make too much HER2. These patients, diagnosed as HER2 positive (HER2+), initially respond very well to trastuzumab. Like many targeted therapies, trastuzumab acts like a roadblock, preventing tumor cells from moving along the growth pathway, and forcing them down the “death” pathway. However, some tumor cells find a “detour” around the trastuzumab roadblock, often by finding and using another protein – a “back-up” – that can do the same job as HER2. These breast cancer cells become resistant to trastuzumab treatment and continue to survive and grow.

*“Susan G. Komen has helped me launch a new line of research...and [find] a completely new target for HER2+ breast cancers that has the potential to transform cancer therapeutics,” says Dr. Brouxhon.*

Finding ways to block these detours and stop resistance is a major focus of Dr. Sabine Brouxhon’s research. With funding from a Komen Career Catalyst Research grant, Dr. Brouxhon has been able to show that resistance can be overcome by targeting the “back-up” proteins that cancer cells use to avoid targeted therapy. Her studies showed that in many women with HER2+ breast cancers, a small piece of a protein called E-cadherin is cut off, resulting in a protein fragment called sEcad. The sEcad fragment helps tumor cells grow by stimulating not only HER2, but also

other “back-up” proteins that help cancer cells evade death by trastuzumab. When Dr. Brouxhon treated resistant breast cancer cells with an antibody against this fragment, she was able to kill the resistant cancer cells and reduce tumor growth in mice, without serious side effects. The most important discovery was this antibody-based therapy not only affected HER2, but many of the back-up proteins as well. This makes sEcad antibodies a potentially more effective therapy than trastuzumab, and an attractive treatment option for patients who no longer respond to trastuzumab.

“Our innovative therapy has the potential to revolutionize cancer care, especially for those patients who become resistant to current HER2 targeted therapies,” says Dr. Brouxhon. For patients who have become resistant to trastuzumab, antibodies against specific regions of sEcad are an encouraging step forward. Dr. Brouxhon is continuing to test the sEcad antibodies and hopes to test them in trastuzumab-resistant breast cancer patients in future Phase I clinical trials.

Dr. Brouxhon’s work was recently published in the scientific journals *Clinical Cancer Research and Molecular Carcinogenesis* in June, 2013.

