

# Attacking metastatic tumors in the brain

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Rakesh Jain, PhD, Director of the Edwin L. Steele Laboratory for Tumor Biology at the Massachusetts General Hospital and supported by the National Foundation for Cancer Research, has discovered a novel mechanism behind the resistance to HER2- or PI3K-targeted therapies, and a treatment strategy that may overcome treatment resistance. This significant finding was reported in the latest issue of the journal *Science Translational Medicine*.

Rakesh Jain's discovery could be very important for [cancer patients](#) whose cancers have spread to the [brain](#). About 20% to 25% of all breast cancers have an excess of a protein known as Human Epidermal Growth Factor Receptor 2 (HER2). HER2-positive (HER2+) [breast cancer](#) spreads more quickly than other types of breast cancer, and while several targeted therapies are now available to treat HER2+ breast cancer, putting this cancer into remission for years or longer in many patients, up to 50% of patients treated with these targeted therapies eventually develop [brain metastases](#), which are inevitably fatal.

This research project directed by Dr. Jain may have unlocked a key as to why brain metastases are resistant to HER2+ targeted therapies, and have uncovered a potential treatment strategy to overcome this resistance.

Using tumor models and human cancer samples, the researchers found an overexpression of Human Epidermal Growth Factor Receptor 3 (HER3) in breast cancer-associated brain lesions, and that inhibiting HER3 could help overcome [treatment resistance](#). Dr. Jain's team found

that using drugs that target HER3 combined with those that target HER2 significantly slowed brain metastatic tumor growth and improved survival of the tumor models. These results are the collaborative efforts between Rakesh Jain and Jeffrey A. Engelman, MD, PhD, Global Head of Oncology at the Novartis Institutes for BioMedical Research (formerly with the MGH Cancer Center), an expert in targeted therapies and co-senior author of the publication.

Cancer therapies that target specific proteins often fail to reign in tumors that have metastasized to the brain, and Rakesh Jain's collaboration with Jeffrey Engelman could well have revealed the mechanism behind therapeutic resistance of brain metastases in HER-2 positive breast cancer. This breakthrough research "has identified new treatment strategies to overcome this problem which is often lethal to the patients," says Dr. Jain. "We believe our discovery could have a substantial impact on the future development of therapeutic strategies and ultimately, patient survival from this deadly disease."

Dr. Jain hopes that clinical trials and future therapeutic strategies for [metastatic breast cancer](#) will include HER3 targeted therapies in treating brain metastasis in HER2+ (or PIK3CA mutant) [breast](#) cancer. And since HER3 has been associated with treatment resistance in several types of cancer, this discovery could potentially benefit a much broader group of patients.

"The impact of the microenvironment on tumor growth is a major focus of Rakesh Jain's research, and NCFR is proud to have supported his research since 1998," says Franklin C. Salisbury, Jr., Chief Executive Officer of NCFR. Research cures cancer, and "NCFR's support of outstanding scientists like Rakesh Jain is making possible whole new approaches to treating cancer, giving hope and promise to patients with cancer."

Provided by National Foundation for Cancer Research

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