

Abnormalities in HER2 gene found in wide variety of advanced cancers

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The HER2 growth-factor gene is known to be over-active in breast and gastro-esophageal cancers. But now, irregularities in the genes 's expression—among them mutations, amplifications, substitutions, and translocations—have been found in 14 different advanced solid tumors.

The results of the study of more than 2,000 tumors, being presented at the annual meeting of the [American Society of Clinical Oncology](#) (ASCO), both surprised researchers and provided hope that some of these tumors might benefit from the three anti-HER2 therapies now in clinical use.

"No one ever thought that there would be such a variety of genomic alterations in HER2 in this many [solid tumors](#)," says Massimo Cristofanilli, MD, FACP, Professor of [Medical Oncology](#) and Director of the Jefferson [Breast Center](#) at the Kimmel Cancer Center and Thomas Jefferson University Hospital.

"But this may be good news, both clinically and scientifically," he says. "It tells us that these tumors might benefit from treatment that we already have on hand, and, from a research perspective, it builds on the idea that it is the genomic profile of a tumor that is relevant in providing biological information for planning of personalized treatments—not where the cancer is located or where it develops.'

Dr. Cristofanilli is presenting the results of the study in an oral presentation at the ASCO meeting. He is one of a group of co-authors

from many institutions who donated tumor samples to Foundation Medicine, a [cancer diagnostics](#) company in Cambridge, Massachusetts. Foundation Medicine led and paid for the study.

Dr. Cristofanilli contributed about 50 metastatic [breast tumor](#) samples for the analysis, and found out that one of his patients with advanced triple negative breast cancer had a HER2 mutation. "My patient was treated with Herceptin as well as chemotherapy, and derived [clinical benefit](#)," he says. "No one looks for HER2 mutations in this form of [breast cancer](#). To me, this makes the case for the value of genome-driven therapy."

In the study, Foundation Medicine conducted a genetic screen of more than 182 genes and 14 genetic rearrangements known to be linked to cancer in 2,223 tumor specimens. Twenty different advanced solid cancers were represented.

Researchers found HER2 alterations in 14 types of solid tumors, including 29 percent of esophageal, 20 percent of uterine, 14 percent of breast, 12 percent of stomach carcinomas, and 6 percent of all lung cancer samples.

They also found HER2 irregularities varied widely—4.9 percent of specimens had 116 different HER2 alterations. That included 58 percent with amplifications, 25 percent with substitutions, 14 percent with indels (insertions/deletions of DNA), 2 percent with splice site variants, 2 percent with translocations, 5 percent with multiple alterations, and 2 tumors had both HER2 substitution and amplification.

Anti-HER2 therapies such as [Herceptin](#) can also treat HER2 mutations, and may also help block HER2 that is altered in the ways seen in the study, Dr. Cristofanilli says.

"This study highlights the need to study a broad range of genes at a high level of sensitivity and specificity when searching for novel targets of therapy," he says. "Widespread use of this approach could provide more treatment options and enable more rapid accrual to ongoing and planned trials of agents targeting pathways under study."

Provided by Thomas Jefferson University

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