

# Personalized medicine: Tumor analysis reveals new opportunities for existing cancer drugs

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Targeted cancer therapies such as trastuzumab (Herceptin), gefitinib (Iressa) and erlotinib (Tarceva) could be used to treat a wider range of cancers than previously thought, according to new research presented today (Wednesday) at the 22nd EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Berlin.

Scientists in the USA have studied 20 [genes](#) that are targeted by existing therapies and found that there are significant changes to these genes in a broad range of patients' tumours, including many for which these drugs are not being used at present. The results suggest that these therapies, which have already been deemed safe and effective by regulatory agencies, may have additional opportunities to benefit [cancer](#) patients.

However, Dr Daniel Rhodes, chief executive officer and co-founder of Scientific Applications at Compendia Bioscience (Ann Arbor, Michigan, USA), told the meeting: "While there may be immediate opportunities to use these new findings to treat patients with few remaining treatment options, broader application of the findings will require large-scale clinical trials to investigate if such personalised medicine could translate into real benefit over existing standard of care."

Genes can play a role in causing cancer in a number of ways, including via mutations that cause them to function incorrectly or via DNA amplifications whereby there are multiple additional copies of a gene.

Normal cells (apart from [germ cells](#)) typically have two copies of each gene, but [cancer cells](#) often create additional copies of specific cancer-causing genes. For the current study, Dr Rhodes and his colleagues were looking for tumours in which there were five or more copies of a particular gene.

Targeted therapies are aimed at blocking the action of the mutated or amplified genes, "but they are often used without detailed knowledge of the [genetic makeup](#) of a patient's tumour," said Dr Rhodes. "The aim of personalised medicine is to understand an individual patient's cancer and select therapies that are most likely to benefit the patient; however, today most patients do not undergo any genetic testing of their tumours. We sought to understand the opportunity to use DNA amplifications, one type of cancer-causing mutation, to select existing targeted therapies that would be most likely to benefit cancer patients.

"We studied 22 genes that are targeted by therapies, either approved or in clinical trials, and found that the targets often show high-level amplifications in small subsets of patients and that particular cancer types show more frequent amplifications, for instance cancers of the brain (21.4% of cases) and breast (23.2% of cases). Our work suggests that some cancer patients should be tested for DNA amplifications and that small subsets of cancer patients harbour specific DNA amplifications that might indicate potential benefit from an existing therapy. We caution that we have not demonstrated that the targeted therapies will benefit all cancer patients with a DNA amplification, but we suspect, given past clinical trials and experimental studies, that some DNA amplifications will be predictive of therapeutic benefit for some patients."

The researchers studied the genes in tumours from 4,086 patients and found 592 significant DNA amplifications in 438 cancer patients, suggesting that 5-10% of cancer patients might be suitable for treatment

with an existing targeted therapy. In addition to brain and breast cancers, they found significant amplifications in cancer of the colon (5.8%), lung (5.8%), ovary (4%) and pancreas (3%). They were rare or non-existent in liver cancer, leukaemia and myeloma. As might be expected, amplifications of the HER2 gene were found in breast cancer (13.7% frequency), at which the drug trastuzumab is targeted, but it was also found in small subsets of colorectal (1.3%) and lung (0.9%) cancer patients. There were examples of other gene amplifications occurring in cancers other than those for which targeted therapies had been tested and approved.

The researchers also checked whether the amplifications were ones that were responsible for driving the growth of the various cancers. "We cannot be sure that in each case the DNA amplifications we studied were 'drivers' of cancer, but we can look for clues that the genes are likely to be the drivers," explained Dr Rhodes. "If the amplifications involved small, focal regions of the genome that included only the target or only a few genes, then it is more likely that the target gene was a 'driver'. Also, if the target gene was more frequently amplified and amplified at higher levels than neighbour genes, then again it is more likely that the target gene is the 'driver'. Thus, we examined the regions of amplification around the target genes and the most commonly amplified genes in the region and in almost all cases, our target gene under study was the most commonly and most highly amplified gene in the region."

Dr Rhodes concluded: "We envision our work motivating a DNA amplification-guided clinical trial that would test advanced cancer patients for DNA amplification of all relevant targets and then partition patients into treatment arms based on their particular amplification. Such an effort would be costly and could require hundreds of patients; however, our study provides the basis and the frequencies of amplifications that could be expected. We hope that this work will motivate clinicians to consider such an approach."

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