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Researchers discover genes affecting cancer drug

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Genomic research could help doctors better target a drug widely used to treat colorectal cancer patients, according to a study by Genomic Health Inc. and the Translational Genomics Research Institute (TGen).

The drug, oxaliplatin, is widely used in colon cancer. It is used in early disease, following surgery in those cancers that are likely to recur. It is also used in advanced disease to slow progression of the cancer where it has spread to other parts of the body.

However, a significant number of patients experience serious side effects, including prolonged damage to the nervous system, "creating an urgent need to identify genes that are responsible for drug sensitivity or resistance, which results in directing therapy to those most likely to benefit," according to the study published in *Molecular Cancer Research*.

Colorectal cancer is the third most common type of cancer in the U.S., annually diagnosed in more than 146,000 Americans. It also is the third highest cause of cancer death in the U.S., annually killing nearly 50,000 people, more than who die each year on the nation's roadways. This cancer affects men and women in nearly equal numbers.

Nerve damage, or neurotoxicity, associated with oxaliplatin is most commonly manifest as pain or a loss of sensation in the hands and feet and can severely affect a patient's quality of life and ability to work. These symptoms are experienced in some form by the majority of patients receiving this drug and, for some patients, can be permanent.

The TGen/Genomic Health researchers examined the role of individual cancer genes to influence the sensitivity or resistance of colon cancer cells grown in laboratory culture. An interfering RNA screen of 500 genes — with 2,000 unique siRNA sequences —identified 27 genes that, when silenced, altered the sensitivity of colon tumor cells to oxaliplatin, causing damage to the cancer cells' DNA and inhibiting the cancer cells' ability to reproduce and survive, the study said. This study has also showed that diverse gene networks also play a role in the ability of the drug to impact colon tumors.

"These 27 genes, whose loss of function significantly affect the effectiveness of oxaliplatin, may be promising therapeutic biomarkers for oxaliplatin," said Dr. Holly Yin, head of TGen's Cellular Genomics Collaborative Center in Scottsdale, and a co-author of the study.

Dr. Robert J. Pelham, a research scientist at Redwood City, Calif.-based Genomic Health and the study's senior author, said the findings indicate a need for additional clinical studies on tumor specimens in patients treated with oxaliplatin. "Such future clinical studies could eventually lead to potential clinical applications, where patients could benefit," Dr. Pelham said.

Provided by The Translational Genomics Research Institute