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Researchers discover new approach to improve personalized cancer treatments

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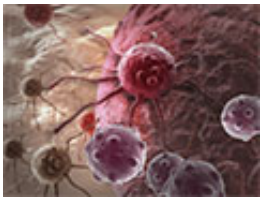

Researchers from the University of Minnesota, Mayo Clinic, and University of Toronto have successfully shown that a new method for targeting mutated cells could create a major breakthrough in a personalized medicine approach to treat cancer.

The team's findings are published in the Oct. 15 issue of *Cancer Research*, a journal of the American Association of Cancer Research.

The new research discovers susceptible genes in the cancer cells using synthetic lethal interactions—pairs of genes in which mutation in either gene alone causes no damage to the cell, but where mutations in both cause the death of the cell.

"When we discover these interactions in human cells, it can hold the key to effective, targeted cancer treatments," said Professor Chad Myers, the lead researcher and computer science and engineering associate

professor in the University of Minnesota's College of Science and Engineering. "Specifically, drugs could be used to target the synthetic lethal interaction partners of cancer-associated genetic mutations. These drugs would then effectively kill cancer cells but spare otherwise identical cells lacking the cancer-related genetic alteration."

Myers and his collaborators used research on yeast genes to find synthetic lethality, and then found genes in humans that were similar in structure and evolutionary origin to the yeast cells. Myers worked with Dr. Dennis Wigle, a practicing thoracic surgical oncologist at Mayo Clinic to test those interactions in human cells.

They found two striking cases where synthetic lethal interactions were similar between yeast and human cells. These interactions involve genes that are frequently mutated in specific types of cancer and provide potential new drug targets for these tumors.

"About 40 percent of yeast genes have homologs in humans, we thought that inferring interactions across species may provide a quick way of getting at these interactions," Myers said. "Given our expertise with the yeast interactions, we developed a strategy for narrowing down the large list of interactions to test, based on sequence similarity between the genes and public databases of genes commonly mutated in cancer as well as other features."

Decades of drug discovery research have produced a limited number of targeted therapies for treating cancer. The most commonly used therapies involve delivering high doses of radiation or toxic chemicals to the patient, which can help to suppress tumor growth but also cause substantial damage to normal tissue.

"The strategy of using synthetic lethal interactions to identify drug targets, particularly for 'undruggable' cancer genes is an attractive

alternative method for drug target discovery," said Wigle. "This technology is an important means to fully leverage information from sequencing projects for clinical application."

More information: "A Comparative Genomic Approach for Identifying Synthetic Lethal Interactions in Human Cancer," cancerres.aacrjournals.org/con … CAN-12-3956.abstract

Provided by University of Minnesota