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Scientists identify potential new biomarker to better personalize cancer therapy

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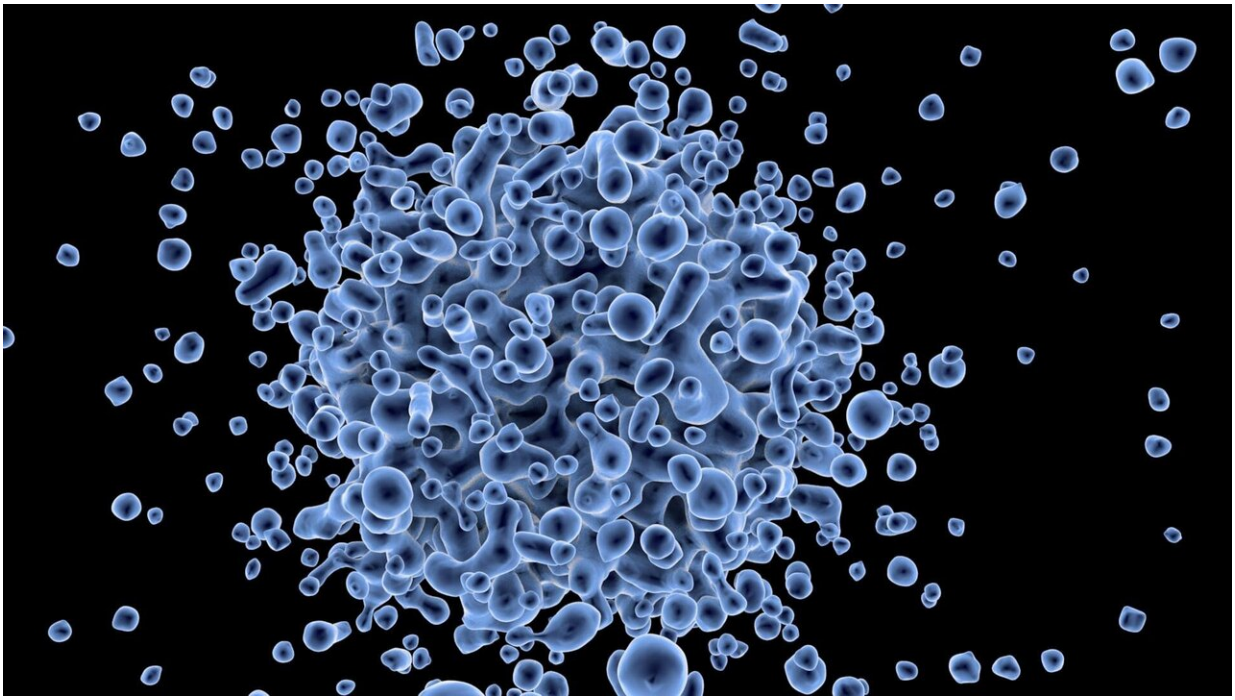

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Researchers from Duke-NUS Medical School, Erasmus University Medical Center, Yale-NUS College and Duke University have found a potential way to predict who will respond to cancer therapies that block Wnt production, such as the novel made-in-Singapore drug ETC-159. This discovery brings the goal of personalized medicine in cancer therapy a step closer to reality.

Wnt proteins are important signaling molecules that help neighboring cells to communicate with each other. However, when the protein is produced in excess, it causes cancers. Wnt has been implicated as a key driver of many common cancers, including colorectal and breast cancers as well as leukemia and pancreatic cancer. Many mutations can trigger an excess activity of Wnt, and finding reliable biomarkers has been challenging.

This findings, published in *Cancer Research*, identify an actionable biomarker—a protein called RNF43—that is altered in a distinct class of Wnt-addicted cancers.

"RNF43 is one instance that can help us predict whether a cancer cell might be dependent on the Wnt pathway," said Assistant Professor Babita Madan, from Duke-NUS' Cancer and Stem Cell Biology (CSCB) Program, the corresponding author of the study. RNF43 is frequently mutated in colorectal, endometrial, mucinous ovarian, pancreatic and gastric cancers.

The drug ETC-159, which was jointly developed by Duke-NUS and Singapore's Agency for Science, Technology and Research, is a novel small molecule drug candidate that targets a range of cancers including colorectal, ovarian and pancreatic cancers. It is currently in Phase 1B human trials and was used in this pre-clinical study to determine whether cancers with RNF43 mutations would respond to Wnt inhibitor therapy.

"It has been shown in the past that RNF43 regulates cell surface Wnt receptors and RNF43 mutations could cause sensitivity to Wnt inhibitor in pancreatic cancers," said Dr. Yu Jia, a research fellow at the CSCB Program and the study's first author.

This study expands the landscape of actionable RNF43 mutations, opening the door for more patients to benefit from these therapies.

Moving forward, the team hopes that their study can help clinicians who are involved in clinical trials for Wnt inhibitors to develop a look-up table based on the team's list of actionable RNF43 mutations.

"This is another major step toward bringing personalized medicine to cancer patients in Singapore and across the globe," said Professor Patrick Casey, Senior Vice-Dean of Research at Duke-NUS. "Being able to tailor treatments to the unique genetic signature of a patient's cancer will allow healthcare providers to better customize treatment plans and greatly increase the chance of real impact on the disease."

More information: Jia Yu et al. The functional landscape of patient-derived RNF43 mutations predicts sensitivity to Wnt inhibition, *Cancer Research* (2020). DOI: 10.1158/0008-5472.CAN-20-0957

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