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Duke/Singapore scientists find new way to classify gastric cancers

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An international team of scientists has discovered a new way to classify stomach cancers, and researchers say it may be an important step toward designing more effective treatments and improving long-term survival.

Stomach (gastric) cancer is particularly prevalent in Asia and represents the second leading cause of cancer deaths worldwide.

The research is based upon clinical findings from patients in Singapore, Australia and the United Kingdom and represents the largest genomic analysis of gastric cancers to date. The new system classifies gastric cancers by the signaling pathways the tumors use to grow and spread, as opposed to the more traditional approach that describes them by cell type or structure.

The findings, appearing online in the Public Library of Science journal *PLoS Genetics*, come from a group of scientists at the Duke-National University of Singapore Graduate Medical School in Singapore.

"We identified three oncogenic pathways that were activated in over 70 percent of the gastric tumors we examined," said lead author Chia Huey Ooi, PhD, Research Fellow in the Duke-NUS Graduate Medical School. "We also found that combinations of these pathways are significantly related to patient survival."

Stomach cancer is notoriously resistant to chemotherapy and newer biologic-based therapies have not proven very effective. With current

treatments, less than a quarter of patients live longer than five years after surgery.

Study authors say the new classification system offers physicians the opportunity to stratify patients according to their tumors' pathway profiles and then apply the treatment that is designed to interrupt the signals those pathways use.

"These findings may give us the first way to truly offer our gastric cancer patients personalized medicine," says Patrick Tan, MD, PhD, the senior author of the study and a member of the Duke-NUS Graduate Medical School and the Genome Institute of Singapore.

Investigators obtained 301 gastric tumors from three independent patient groups. They used computational methods to map the activation levels of 11 different cell signaling pathways already known to be active in the development of gastric cancer. They found that three pathways - primary drivers of cell growth and death (NF-kappaB, Wnt/β-catenin and proliferation/stem cell) were deregulated in most of the tumors.

The researchers found that stratifying patients by single pathways did not predict outcomes, but stratifying them by combinations of pathways did.

"We feel that the ability to perform 'high-throughput pathway profiling' opens up a number of interesting possibilities, says Tan, who is also a member of the Institute of Genome Sciences & Policy at Duke University Medical Center. "It suggests that pathway combinations, rather than single pathways alone, may play a more critical role in influencing tumor behavior. We feel our findings that the NF-kappaB pathway may be especially important, because this pathway has been understudied in gastric cancer. Finally, our methods could certainly be used to study pathway profiles in other cancers, which could lead to new insight into tumor behavior and outcomes."

Source: Duke University Medical Center (news : web)