

Differences in subtypes of gastric cancer may determine prognosis and response to treatment

July 26 2017

Molecular classification of the four distinct subtypes of gastric cancer could potentially shape tailored treatment options by helping to predict survival outcomes and patients' response to chemotherapy.

The study was published in *Clinical Cancer Research*, a journal of the American Association for Cancer Research, by Ju-Seog Lee, PhD, an associate professor in the Department of Systems Biology, Division of Cancer Medicine, at The University of Texas MD Anderson Cancer Center in Houston.

In 2014, The Cancer Genome Atlas (TCGA) project discovered that there are four molecular subtypes of gastric <u>cancer</u>: Epstein-Barr virus subtype (EBV); microsatellite instability subtype (MSI); genomically stable subtype (GS); and chromosomal instability subtype (CIN).

Lee said most patients with early-stage gastric cancer are treated with a surgical resection, followed by <u>chemotherapy</u>. "However, outcomes vary significantly, and that difference in clinical outcomes is likely due to biological and molecular differences in tumors. These differences have not been fully understood."

In order to identify the clinical significance of the four subtypes, Lee and colleagues re-analyzed gene expression data for these subtypes using data from the gastric cancer cohort of the TCGA project. They used that



data to develop prediction models and tested the models in two independent cohorts of 267 and 432 gastric cancer patients, respectively, in South Korea and at MD Anderson.

Overall, they found that the EBV subtype was associated with the best prognosis for both recurrence-free survival (RFS) and overall survival, and the GS subtype was associated with the worst prognosis.

The MSI subtype was associated with a moderate prognosis. The CIN subtype was also associated with moderate prognosis, but poorer in the South Korean cohort than in the MD Anderson cohort. Lee said this suggests that the CIN subtype may be less homogeneous and therefore harder to characterize.

The study also sought to examine whether specific subtypes of gastric cancer were associated with a clinical benefit from adjuvant chemotherapy. The researchers based this part of the study solely on the MD Anderson cohort, because more than half of them had received adjuvant chemotherapy, compared with a smaller segment of the South Korean population.

This portion of the study indicated that patients with the CIN subtype received the greatest benefit from chemotherapy; the three-year RFS rate was 58.7 percent for those who had received chemotherapy, compared with 33.5 percent for those who had not. Patients with the GS subtype showed no benefit, while those with the MSI subtype showed a moderate benefit. The effects of chemotherapy on patients with the EBV subtype could not be assessed, because all the patients had received it, leaving no basis for comparison.

Lee said the failure of the GS subtype to respond to chemotherapy was one of the study's most intriguing findings.



"This means that we need to find novel targets and drugs for this subtype," Lee said, adding that patients with the GS subtype could now potentially be spared the damaging side effects of chemotherapy that will most likely not work.

Lee said the study's results indicate that classifying <u>gastric cancer</u> cases according to subtype could provide guidance to physicians as they try to determine the best treatment option for a particular patient.

"These findings, if confirmed, could provide some information for personalized medicine," Lee said. "As we learn more about the biological characteristics associated with each subtype, it will help determine which <u>patients</u> will benefit from immunotherapy, chemotherapy, or other treatment options."

Lee said the primary limitation of the study is that data were collected retrospectively. Further research would be necessary to confirm the findings in a prospective study setting.

More information: *Clinical Cancer Research* (2017). <u>DOI:</u> <u>10.1158/1078-0432.CCR-16-2211</u>

Provided by American Association for Cancer Research

Citation: Differences in subtypes of gastric cancer may determine prognosis and response to treatment (2017, July 26) retrieved 27 April 2024 from <u>https://medicalxpress.com/news/2017-07-differences-subtypes-gastric-cancer-prognosis.html</u>

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