MET protein levels show promise as biomarker for aggressive colon cancer

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MET protein levels correlate strongly with epithelial-mesenchymal transition (EMT) phenotype, a treatment-resistant type of colorectal cancer and may be used as a surrogate biomarker, according to new research from The University of Texas MD Anderson Cancer Center.

The study results, which compared MET protein expression with protein/gene expression of EMT markers and evaluated impact on survival, were released today at the annual meeting of the American Society of Clinical Oncology.

"When the epithelial cells that line the colon become cancerous, some of them develop special features to allow migration, causing the cancer to be more aggressive," said Kanwal Pratap Singh Raghav, M.D., fellow in MD Anderson's Division of Cancer Medicine. "Although EMT is a dominant molecular subtype, a biomarker suitable for clinical use has not been found. This research gives us an important step toward learning more about treating this colorectal cancer subtype."

In a bigger picture view, the study provides another piece of the puzzle of personalized cancer diagnosis and treatment.

"While we know there are many of types of colorectal cancer, we're not as advanced as we'd like to be in our understanding of them," said Scott Kopetz, M.D., Ph.D., associate professor in MD Anderson's Department of Gastrointestinal Medical Oncology and senior author of the study. "One of the larger goals of our research is to classify simple biomarkers

that can be used by doctors in the community to identify subtypes. We want to condense sophisticated gene signatures down to single markers and simple tests that can be used to guide therapy."

The data were tested with:

- Mann-Whitney U-test and Spearman rank correlation to determine association between MET protein expression and protein/gene expression of EMT markers and EMT gene signature scores
- Regression tree method and Kaplan-Meier estimates to assess overall survival

Results of the analysis showed higher MET levels were found more often in colon tumors than rectal tumors.

Overexpression of MET was associated with:

- Decreased overall survival
- Higher gene expression of 28 EMT markers
- Higher gene scores derived from three published EMT gene signatures

The researchers also determined that MET protein expression did not correlate with MET gene expression.

Next steps

Going forward, the group plans to apply this approach to other colorectal cancer subtypes, hopefully defining other simple and readily available biomarkers.

"The ultimate success in targeting colorectal cancer requires understanding molecular subsets of the disease," Kopetz said. "If we can identify and group cancers with similar behaviors, we'll be closer to identifying vulnerabilities and optimal therapies for each subset."

Provided by University of Texas M. D. Anderson Cancer Center