New genomics tool could help predict tumor aggressiveness, treatment outcomes

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This is James Rocco, M.D., Ph.D. Credit: photo credit to The OSUCCC - James

A new method for measuring genetic variability within a tumor might one day help doctors identify patients with aggressive cancers that are more likely to resist therapy, according to a study led by researchers now at The Ohio State University Comprehensive Cancer Center - Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James).

Researchers used a new scoring method they developed called MATH (mutant-allele tumor heterogeneity) to measure the genetic variability among cancer cells within tumors from 305 patients with head and neck cancer. High MATH scores corresponded to tumors with many differences among the gene mutations present in different cancer cells.

Cancers that showed high genetic variability - called "intra-tumor heterogeneity" - correlated with lower patient survival. If prospective studies verify the findings, MATH scores could help identify the most effective treatment for patients and predict a patient's prognosis.

Researchers have long hypothesized that multiple sub-populations of mutated cells within a single cancer lead to worse clinical outcomes; however, oncologists do not use tumor heterogeneity to guide clinical care decisions or assess disease prognosis because there is no single, easy-to-implement method of doing so in clinical practice.

To address this need, James Rocco, MD, PhD, and his colleagues developed MATH to make it easier for doctors to measure genetic variability in patients' tumors and to help guide treatment decisions.

The new findings, reported in *PLOS Medicine*, confirm that high genetic variability with a patient's tumor is related to increased mortality in head and neck squamous cell carcinoma.

"Genetic variability within tumors is likely why people fail treatment,"

says Rocco, Professor and John and Mary Alford Chair of Head and Neck Surgery and Director of the OSUCCC - James Division of Head and Neck Oncologic Surgery. "In patients who have high heterogeneity tumors it is likely that there are several clusters of underlying mutations - in the same tumor - driving the cancer. So their tumors are likely to have some cells that are already resistant to any particular therapy."

Study Design and Findings

For the current study, Rocco and his team used the MATH tool to analyze retrospective data from 305 head and neck squamous cell carcinoma patients from The Cancer Genome Atlas (TCGA). This National Institutes of Health repository of publicly available data was launched in 2006 as a pilot project and now includes samples from more than 11,000 patients across 33 tumor types. The MATH score was calculated from data obtained by TCGA with a genome sequencing technique called whole-exome sequencing.

Researchers confirmed that high intra-tumor heterogeneity was related to increased mortality in this sub segment of patients. Each 10 percent increase in MATH score corresponded to an 8.8 percent increased likelihood of death.

The relationship between MATH score and mortality was not dependent on HPV (human papilloma virus) status or other molecular characteristics of the tumor.

"Our retrospective analysis showed that patients with high heterogeneity tumors were more than twice as likely to die compared to patients with low heterogeneity tumors," says Rocco. "This type of information could refine the dialogue about how we tackle cancer by helping us predict a patient's treatment success and justify clinical decisions based on the unique makeup of a patient's tumor."

Researchers believe this is the first study to combine data from hundreds of patients treated at multiple institutions in an effort to document intra-tumor heterogeneity and overall survival in any type of cancer.

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