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Specific gene signature could help predict survival outcomes among children with intermediate-risk RMS

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Among children with intermediate-risk rhabdomyosarcoma (RMS) that is negative for a fusion gene, those who had a high score of a specific gene signature called MG5 had poorer survival outcomes compared with those who had a low score of MG5.

Hingorani explained that RMS is a rare but aggressive malignancy of childhood and is of two types, embryonal and alveolar, based on histology. Most alveolar RMS are positive for PAX-FOXO1 gene fusions, which portends an unfavorable prognosis. For patients with fusion gene-negative RMS, no molecular prognostic factors are currently employed in the clinic to identify those that may have poorer outcomes; hence, all receive similar treatment based on the clinical-pathological features of their tumors.

The study was conducted using archived tumor samples from patients enrolled in the Children's Oncology Group D9803 clinical trial. Hingorani and colleagues used tumor samples obtained from 57 patients enrolled in a study by the Children's Oncology Group. Using a technology called nCounter, the researchers studied a set of five genes (MG5) and compared the expression of these genes and clinical outcomes in these patients.

The researchers were able to stratify the patients into two groups: Those with a low MG5 score had better clinical outcomes and those with a high MG5 score had poorer clinical outcomes.

Patients who had a high MG5 score were seven times more likely to die of the disease and six times more likely to relapse, compared with those who had a low MG5 score.

The MG5 scores did not correlate with any of the clinical-pathological features on which treatment decisions are currently being made for patients with intermediate-risk, fusion gene-negative RMS.

The five genes analyzed in this study are EPHA2, EED, NSMF, CBS, and EPB41L4B.

In an interview, Hingorani said, "We tested whether the expression of a five-gene signature, MG5, in these fusion gene-negative, intermediate-risk patients may be able to divide them into two separate risk groups. MG5 was previously identified and shown in a separate cohort to be associated with outcome. If increased risk of relapse or progression could be identified upfront, treatment might be intensified. Conversely, for patients who are identified as having a decreased risk of relapse or progression, we might be able to decrease their therapy and minimize toxicity."

"We were able to perform this analysis using the nCounter technology on formalin-fixed paraffin-embedded tissues and get equally reliable results as previously obtained on a separate group of patients using frozen tumor samples. This opens up the possibility of large-scale implementation of this test, as paraffin-embedded tissue is much more readily available than frozen tissue," she added.

"While this is a very exciting discovery, caution should be used in implementing it in routine clinical settings. First, it will be important to validate this signature in a larger cohort of patients in which the MG5 score is prospectively determined," Hingorani said. "Second, it is not yet clear whether knowing the MG5 score will allow us to meaningfully improve therapy in either group."

Hingorani identified the retrospective nature of the study and a small sample size as the most important limitations of this study.

Source:
American Association for Cancer Research
