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Genetic variant may identify pediatric osteosarcoma patients at risk for metastasis

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A genomewide association study (GWAS) has revealed two specific variations in the NFIB gene that may identify which children and adolescents with osteosarcoma have metastatic disease or are at high risk for metastasis, according to results presented here at the American Association for Cancer Research (AACR) special conference on "Pediatric Cancer at the Crossroads: Translating Discovery Into Improved Outcomes," held Nov. 3-6.

Osteosarcoma is the most common malignant bone tumor in children and adolescents, with about 800 new cases in the United States each year. Osteosarcoma has a high rate of metastasis, and the vast majority of patient deaths occur as a result of metastasis.
"We wanted to determine if germline genomewide genetic variation was associated with clinical outcomes such as susceptibility to metastasis, survival, and response to chemotherapy for osteosarcoma," said Lisa Mirabello, Ph.D., investigator in the Division of Cancer Epidemiology and Genetics at the National Cancer Institute (NCI) in Bethesda, Md. "Our results indicate that osteosarcoma patients with specific variants of the NFIB gene are 2.5 times more likely to have metastases at diagnosis. If validated in other populations, these genetic markers may one day serve as a tool to help clinicians identify patients with metastasis or possibly those at risk of metastasis.

"The identification of a genetic prognostic marker could potentially improve patient management," Mirabello said. "In addition, a clearer understanding of the mechanism through which NFIB confers risk of

metastasis could lead to the development of specific treatment strategies for these patients."

Mirabello and colleagues recently completed a GWAS of people of European ancestry and were able to identify two genetic variants associated with osteosarcoma. In the current study, the researchers looked more closely at the data to determine if any inherited genetic variations were associated with clinical outcomes for osteosarcoma.

In the original study, blood or buccal cell genomic DNA was obtained from 1,128 patients with osteosarcoma, and genotyped. For this study, clinical-outcome GWAS analysis was conducted for 550 of the patients of European ancestry for whom complete clinical outcome data were available. Twenty-three percent of these patients had metastatic disease at the time of diagnosis.

The researchers identified two linked genetic variations in the NFIB gene that were significantly associated with a more than twofold increased risk of metastasis.

Mirabello is currently evaluating the association between inherited genetic variants and other clinical endpoints of osteosarcoma, such as survival, response to chemotherapy, tumor location, and subtype. In addition, she is working to replicate the findings of the current study in other osteosarcoma populations.

This study was funded by the intramural research program of the NCI. Mirabello has declared no conflicts of interest.

More information: www.aacr.org/page34138.aspx