Common Genetic Variants Associated with Development of High-risk Neuroblastoma, Poorer Treatment Outcomes

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- African ancestry linked to increased rates of high-risk disease.
- Variants may be found in patients of any ethnic makeup.

WASHINGTON, D.C. — Patients with a high degree of African ancestry had a greater incidence of high-risk neuroblastoma and poorer outcomes, according to preliminary results presented at the Fourth AACR Conference on The Science of Cancer Health Disparities, held here Sept. 18-21, 2011.

“There are common genetic variants that are associated with the development of high-risk neuroblastoma and a poor outcome,” said Navin R. Pinto, M.D., instructor of pediatrics at the University of Chicago in Chicago, Ill. “These variants are more common in patients of African origin, but have the potential to be present and affect patients of all ethnic backgrounds. Identifying patients with these variants at the time of diagnosis may one day allow us to modify treatment for those who are genetically at risk for treatment failure with standard therapies.”

Neuroblastoma is a childhood cancer with a widely variable clinical outcome, Pinto said. Some children do well with no therapy, while others die despite aggressive chemotherapy, surgery, stem cell transplant and immunotherapy.

In a previous study of 3,539 children with neuroblastoma, Pinto and colleagues found that patients who self-reported as black were much more likely to have high-risk disease and have an increased incidence of late relapses, suggesting that germline genetic differences linked with ethnicity or ancestry may influence disease development.

For this follow-up study of 3,508 racially mixed children with neuroblastoma, the researchers obtained germline genotypes from investigators at the Children’s Hospital of Philadelphia. They then created an ancestral map using the patients’ genotypes and the publicly available genotypes of three ancestral populations: African, Asian and white.

Children with a higher degree of African ancestry had increased rates of high-risk disease and lower survival rates following chemotherapy, according to the study’s preliminary findings.

“This indicates that African ancestors may have passed along common genetic variants that are associated with the development of the aggressive form of

neuroblastoma and perhaps a relative intrinsic chemotherapy resistance that is associated with the observed inferior outcomes," Pinto said.

Armed with these findings, researchers can now focus on the specific genetic variants linked with inferior outcome, Pinto said. These variants may be found in patients of any ethnic makeup, not just African ancestry.

"The remarkable improvements in cure rates for childhood malignancies over the past 50 years have, in large part, come from recognizing clinical or biological features that are associated with a poor outcome and intensifying therapy for patients at high risk of non-response," Pinto said. "Germline genetic variables will likely one day be included in risk stratification algorithms for the treatment of neuroblastoma. I believe we are on the cusp of discovering these variants."

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