

Sun damage causes genetic changes that predispose children and adolescents to melanoma

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The St. Jude Children's Research Hospital—Washington University Pediatric Cancer Genome Project found that melanoma in some adolescent and adult patients involves many of the same genetic alterations and would likely respond to the same therapy. The research appears in the March issue of the *Journal of Investigational Dermatology*.

The similarities involved adolescents with conventional melanoma tumors and included the first genetic evidence that sun damage contributes to melanoma in children and adolescents as well as adults. The findings stem from the most comprehensive analysis yet of the genetic alterations responsible for pediatric melanoma, which is the most



common skin cancer in children and adolescents.

"This study shows that unlike many cancers, conventional melanoma is essentially the same disease in children and adults. That means we need to make it easier for adolescents to access promising therapeutic agents being tried in adults," said co-corresponding author Alberto Pappo, M.D., a member of the St. Jude Department of Oncology. "These results also underscore the importance of starting sun protection early and making it a habit for life."

Researchers also identified distinct genetic alterations associated with other pediatric melanoma subtypes, including those associated with large congenital nevi (CNM) and spitzoid tumors. The alterations include a mutation that might help identify spitzoid <u>patients</u> who would benefit from aggressive therapy as well as those who could be cured with less intensive treatment.

"Until now the genetic basis of pediatric melanoma has been a bit of a mystery," said co-corresponding author Armita Bahrami, M.D., an assistant member of the St. Jude Department of Pathology. "With this study, we have established the molecular signatures of the three subtypes of this cancer, signatures that have implications for diagnosis and treatment."

The National Cancer Institute (NCI) estimates that melanoma is diagnosed in 425 U.S. residents age 19 and younger each year. While the cancer remains rare in young people, the incidence has risen about 2 percent annually in recent decades, primarily in those ages 15 to 19. That age group makes up the majority of current pediatric melanoma patients. For the 75 percent of pediatric patients whose disease has not spread, long-term survival rates now exceed 90 percent.

"We were surprised to see that so many of the pediatric melanomas had



genetic changes linked to UV damage," said co-author Richard K. Wilson, Ph.D., director of The Genome Institute at Washington University School of Medicine in St. Louis. "This in-depth look at the genomics of pediatric melanoma is extraordinarily important for diagnosis and for selecting treatments that give young patients the best chances of a cure."

This study included 23 melanoma patients ranging in age from 9 months to 19 years old. Researchers used whole genome sequencing and other techniques to compare the normal and tumor genomes of patients with three different types of melanoma for clues about the genetic alterations that underlie their disease. The genome is the blueprint for life that is encoded in the DNA found in almost every cell.

The group included 15 patients with conventional melanoma. Unlike many pediatric cancers, their tumors included numerous <u>genetic</u> <u>alterations</u>, more than any of the childhood cancers studied so far by the Pediatric Cancer Genome Project. More than 90 percent of the tumors had genetic changes consistent with damage caused by ultraviolet light. More than 60 percent of the tumors had mutations in the BRAF oncogene, the PTEN tumor suppressor gene or the promoter region of a gene called TERT. The same alterations are found in melanoma in adults and promoted the unchecked cell division and other changes that are hallmarks of cancer.

In contrast to conventional melanoma, the three patients with the CNM subtype had mutations in the NRAS oncogene and no defects in PTEN. The patients all died of their disease.

In comparison, cancer caused the death of just one of the five spitzoid melanoma patients studied. That patient was also the only one with widespread disease and the only one whose tumor had a TERT promoter mutation. TERT promoter mutations are common in conventional



<u>melanoma</u>. The finding has led to a larger study to determine if TERT promoter mutations can serve as a marker for spitzoid tumors that are destined to become clinically aggressive. The results are expected soon.

Provided by St. Jude Children's Research Hospital

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