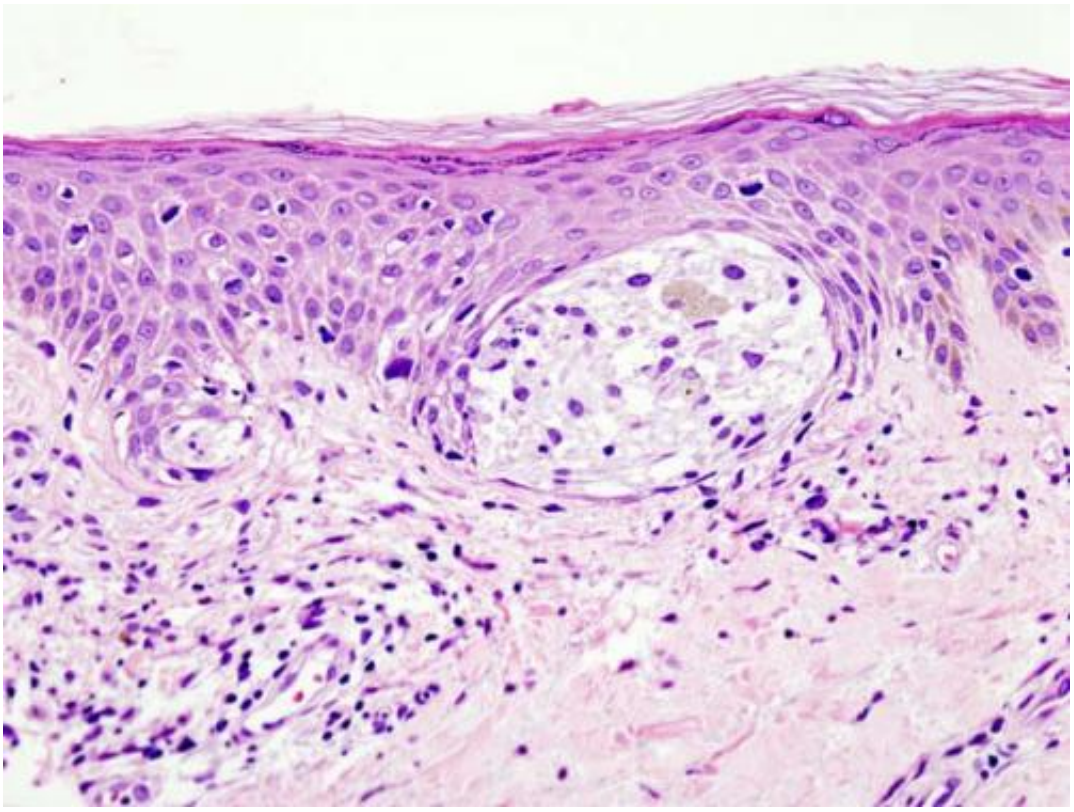
MedicalXpress

Lower survival rates connected with high-risk melanoma with mutations, study finds

April 13 2015



Melanoma in skin biopsy with H&E stain—this case may represent superficial spreading melanoma. Credit: Wikipedia/CC BY-SA 3.0

Researchers from the UNC Lineberger Comprehensive Cancer Center analyzed hundreds of melanoma samples to find out if two genetic mutations more commonly found in melanoma tumors were associated with lower survival rates in patients.

In findings published in the journal *JAMA Oncology* on Thursday, the researchers reported that people with tumors containing either BRAF or NRAS gene mutations whose cancer was at a higher risk of spreading had lower survival rates. That was compared to when people with high-risk tumors lacking either mutation. The study was led by UNC Lineberger researchers, and involved scientists from around the world through the international, population-based Genes, Environment and Melanoma (GEM) Study.

"When you get to higher-risk, primary tumors, it looks like mutational status is associated with lower survival," said Nancy E. Thomas, MD, PhD, a UNC Lineberger member, the Irene and Robert Alan Briggaman Distinguished Professor in the UNC School of Medicine Department of Dermatology and the study's principal investigator. "These findings could help inform treatment decisions for patients, and highlights an area worth further study."

Thomas said the researchers set out to do the study to find out if the BRAF and NRAS mutations could be used as indicators of patients' prognosis. It was done at a critical period before new treatments were approved for melanoma – including before the first BRAF inhibitor was approved in 2011. So she said that means that the researchers were able look at outcomes connected with the mutations without the influence of those treatments.

"With these new medicines coming on board that have been shown to be relatively safe, I'm sure there's going to be pressure to use the drugs earlier as adjuvant treatments," Thomas said. "Our study tells us that certain patients might be at higher risk, and might be better candidates for treatment."

For the study, the researchers followed 912 melanoma patients for seven years. The patients were all diagnosed in 2000, and were enrolled

through the GEM study. Thirteen percent had tumors with NRAS mutations, 30 percent had BRAF mutations, and 57 percent had neither.

Overall, they found there was no statistically significant difference in the five-year survival rates for people with NRAS or BRAF-mutated melanoma tumors compared with survival in people with tumors lacking mutations. However, the researchers did find lower five-year survival rates in people with higher-risk tumors with mutations.

Specifically, they found that 73 percent of people with high-risk, NRAS-mutated tumors survived five years and 71 percent of people with high-risk tumors with BRAF mutations survived five years. That was compared with a five-year survival rate of 82 percent for people with high-risk cancer and lacking either mutation.

Kathleen Dorsey, a UNC Lineberger member, an assistant professor of cancer epidemiology in the UNC School of Medicine and a study co-author, said the findings may have clinical implications for people with the mutations and higher-risk cancer.

"We found an approximately three-fold increased risk of death from NRAS+ and BRAF+ mutations that was limited to higher-stage tumors," she said. "This finding could be useful in identifying patients at high risk of death from melanoma based on their mutational status and primary melanoma tumor characteristics. Mutational status could also be important for determining eligibility for adjuvant trials."

In addition to tracking survival, the researchers also examined characteristics of the tumors. They looked for indicators of tumor growth and at markers of the immune system's response to the cancer.

In tumors with mutations in the NRAS gene, they found a lower number of lymphocytes in and around the cancer cells. Lymphocytes are a type

of white blood cell that can help fight cancer and other diseases.

"One of the major findings of this study is that melanomas with a mutation in the NRAS gene have fewer tumor-infiltrating lymphocytes," Thomas said. "That's important because of the new immunotherapies that require infiltrating lymphocytes to be present in order for the treatments to work."

Provided by University of North Carolina at Chapel Hill School of Medicine