New studies aim to improve melanoma diagnosis

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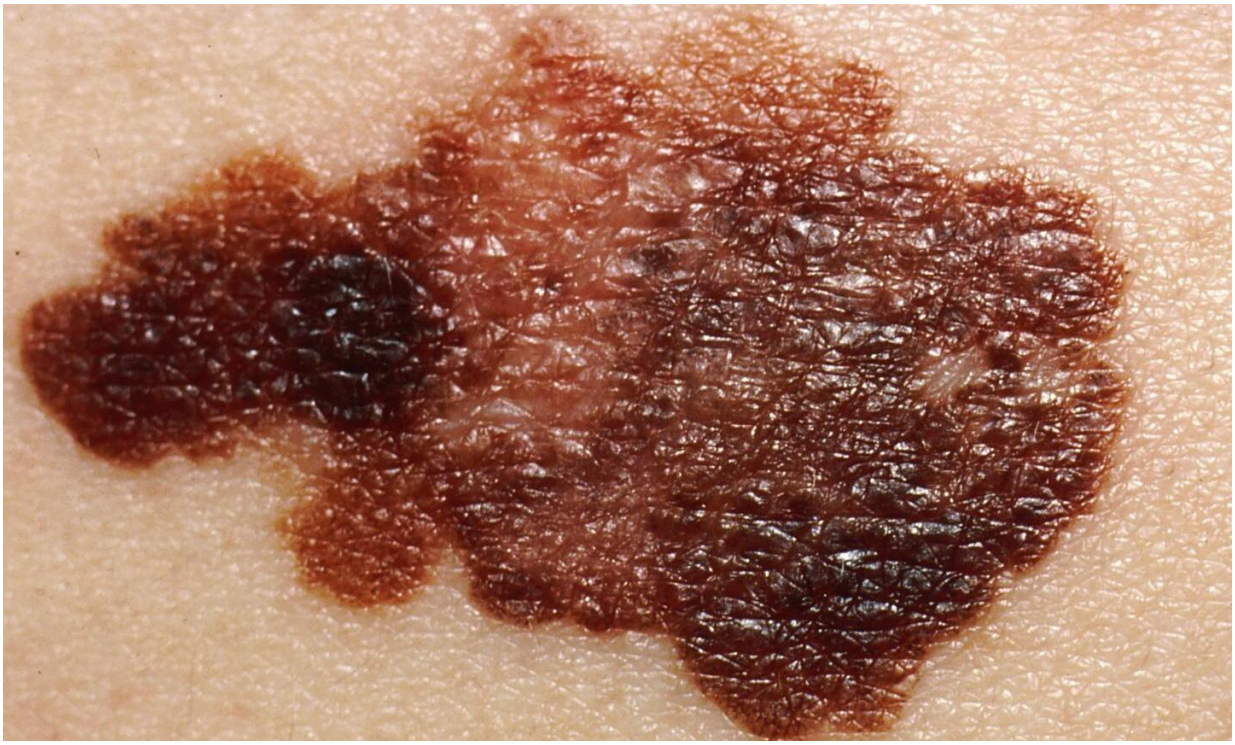

Melanoma. Credit: Wikimedia Commons/National Cancer Institute

A pair of studies led by University of North Carolina Lineberger Comprehensive Cancer Center researchers could aid in improved diagnosis for melanoma, the deadliest form of skin cancer.

The studies, led by UNC Lineberger's Nancy Thomas, MD, Ph.D., Irene

& Robert Alan Briggaman Distinguished Professor and Chair in the UNC School of Medicine Department of Dermatology, and UNC Lineberger's Kathleen Conway Dorsey, Ph.D., associate professor in the UNC Gillings School of Public Health and UNC School of Medicine Department of Dermatology, are needed as early detection of cutaneous melanoma is critical.

"For a certain percentage of melanomas, there is some diagnostic uncertainty," Thomas said. "If we could classify more growths as melanoma or as non-cancerous, this has direct implications for therapy, and could help us prevent under and over diagnosis."

In the first study, published in the *Journal of Investigative Dermatology*, researchers reported on findings into a potential tool that could aid in early diagnosis of melanoma. While new treatment advances have led to promising results for some patients with melanoma, researchers say they are not curative for all.

UNC Lineberger researchers developed a diagnostic test for melanoma based off changes to DNA that researchers have observed in melanoma. These "epigenetic" changes, which are also known as methylation, involve changes that cause DNA to either be tightly coiled or unwound, which determines whether the genetic code is "off" or "on," – meaning it can either be read and translated into proteins, or not.

"Epigenetic changes to the DNA, such as methylation, are among the earliest events that occur as cells become cancerous, so it makes sense that they could be used to diagnose melanoma," Dorsey said.

In their study, researchers trained their test using 60 melanomas and 48 benign molesand then ran it using 29 melanomas and 25 benign moles. They found the test was able to identify 96.6 percent of cases in which a sample was melanoma, and it accurately identified 100 percent of cases

that were not.

"If we converted it to a clinical test, it might be the most accurate ancillary lab test to aid in melanoma diagnosis out there," Thomas said.

Next steps include additional validation of their results, and efforts to convert the test into a version that could be used in a clinical laboratory.

The study's findings build on previous work, published in the American Journal of Dermatopathology, to study a common mutation in melanoma tissues that might be used to aid in diagnosis. Thomas, Dorsey and their collaborators found that while mutations in the genetic sequence for the promoter of the TERT gene, which stands for telomerase reverse transcriptase, were common in cancerous melanoma, these mutations were rarely found in benign moles.

They investigated whether they could use this mutation to better distinguish melanoma from benign moles. The test was able to identify 78 percent of cases of melanoma and exclude 99 percent of benign moles.

"Based on the high specificity of the test for melanoma, if you have this mutation, it's very likely to be melanoma," Thomas said.

Researchers are evaluating if the TERT test can improve melanoma diagnosis at UNC's Clinical Molecular Genetics Laboratory.

"The TERT promoter mutation test offered in the Clinical Molecular Genetics Laboratory can potentially be used to aid in diagnosis of melanoma," said Margaret Gulley, MD, professor in the UNC School of Medicine Department of Pathology and Laboratory Medicine.

More information: Kathleen Conway et al. Identification of a Robust

Methylation Classifier for Cutaneous Melanoma Diagnosis, *Journal of Investigative Dermatology* (2018). DOI: 10.1016/j.jid.2018.11.024