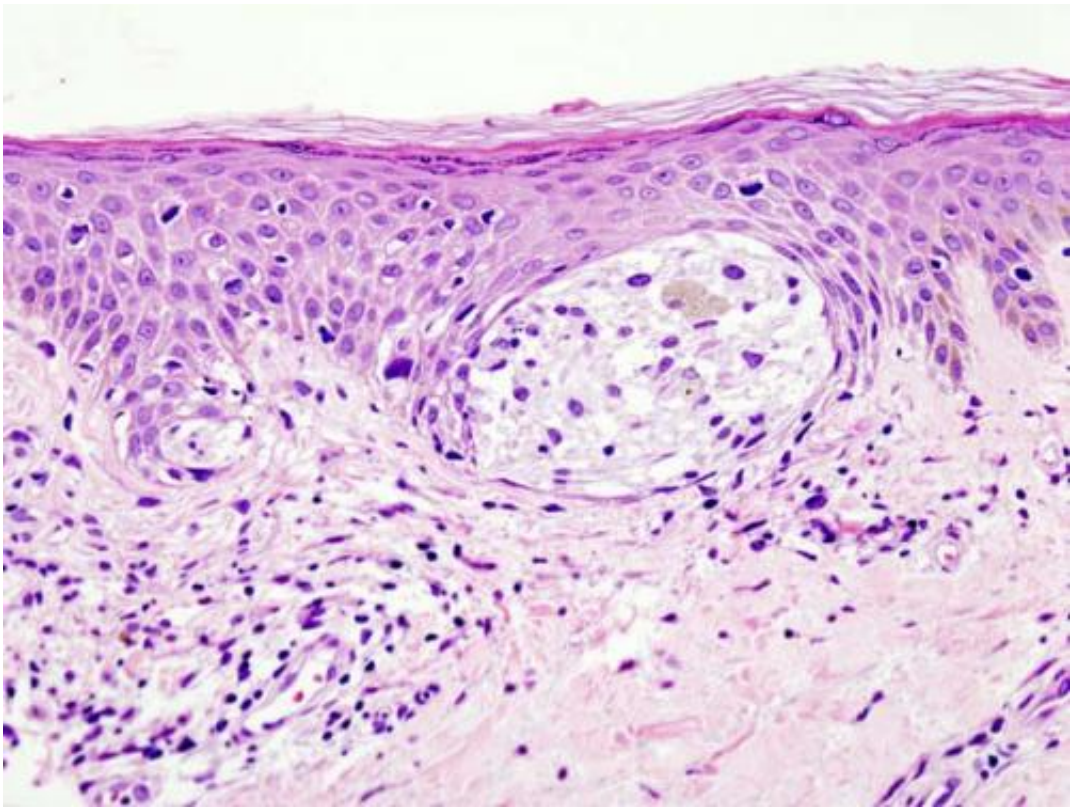
Predicting mutated gene associated with melanoma

April 12 2021, by Rae Lynn Mitchell



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

Although risk for melanoma, the most serious type of skin cancer, is often associated with ultraviolet light exposure, genetic factors are also at play, with some families being more prone to the disease than others.

Moreover, mutations in the gene CDKN2A are also associated with increased risks for other cancers such as pancreatic cancer, making it especially important to identify carriers among melanoma patients. With population-based melanoma incidence rates varying according to geography, clinicians could benefit from a universal, cost-effective tool for assessing mutational status among melanoma patients from the same family. Such a tool could aid in directing patients toward risk counseling and away from expensive and inappropriate genetic testing.

In a study published in the *Journal of the American Academy of Dermatology*, a research team led by Nicholas Taylor, assistant professor in the Epidemiology and Biostatistics Department at the Texas A&M University School of Public Health, used data collected by the international GenoMEL Consortium of melanoma researchers to develop a statistical model for the prediction of germline CDKN2A mutations in a global population of familial melanoma cases. This algorithm (GenoMELPREDICT) gives clinicians a helpful tool for determining the appropriateness of genetic testing and likelihood of the presence of deleterious CDKN2A mutations. It has recently received international recognition and endorsement from the Australian government. The GenoMELPREDICT algorithm has been deployed on the GenoMEL Consortium website in an easy-to-use point-and-click interface.

In this study, Taylor and colleagues began by first testing a well-established prediction model known as MELPREDICT, which has shown good performance predicting the gene mutations among affected members of melanoma-prone families of Northern European descent. The original algorithm performed fairly well in predicting mutational status when applied to the GenoMEL population.

The researchers tested changes in model performance after adding personal or family history of pancreatic cancer, tendency to sunburn and tan, facial freckling, skin type and eye color. Significant prediction

improvement was noted with the addition of any history of pancreatic cancer to the model.

Taylor and colleagues found that the GenoMELPREDICT model could be generalized to the more diverse population of melanoma-prone families found in the GenoMEL dataset. They observed that the model performed better with some populations than others, like among patients in Australia. It performed the poorest for those living in southern Europe or South America. The authors state that this may be due to the larger proportion of Australian subjects in the sample and the classification for melanoma-prone families being too strict for populations with lower overall incidences of melanoma, respectively.

The algorithm has similar performance to other statistical instruments used to predict BRCA1 and BRCA2 mutations in breast cancer patients. It may serve as a quick and robust tool, applicable worldwide, for directing patients away from unnecessary genetic testing, especially in the event of a low carrier probability estimate. A user-friendly web-based interface to calculate the probability of carriage of a CDKN2A mutation will soon be available at www.genomel.org.

More information: Nicholas J. Taylor et al. Estimating CDKN2A mutation carrier probability among global familial melanoma cases using GenoMELPREDICT, *Journal of the American Academy of Dermatology* (2019). DOI: 10.1016/j.jaad.2019.01.079

Provided by Texas A&M University