

# Letters

## OBSERVATION

### Noninvasive Gene Expression Testing in Amelanotic Melanoma

Not missing melanomas in daily practice keeps dermatologists up at night and is a challenge even for dermatologists who see pigmented lesion cases regularly. Ferris et al<sup>1</sup> describe the utility of a noninvasive gene expression test capable of differentiating primary melanomas from nonmelanoma pigmented skin lesions. However, neither the article by Ferris et al<sup>1</sup> nor the underlying validation study by Gerami et al<sup>2</sup> describe scenarios where the *LINCO0518* and *PRAME* melanoma gene expression test, termed *pigmented lesion assay* by the authors, is used in even more difficult cases to diagnose amelanotic melanomas.

**Report of a Case** | A woman in her 20s with a family history of melanoma presented with a 10 × 11-mm pink papule close to her medial right ankle (Figure). She had no clear recollection of how long the lesion had been present or if it had changed. A suggested surgical biopsy was refused, but the patient agreed to a noninvasive adhesive patch biopsy and gene expression testing.<sup>1,2</sup> This test revealed detectable levels of *LINCO0518* consistent with the gene expression observed in melanoma. The test's second target gene, *PRAME*, was not detected.

After being informed that the detection of 1 or both of these target genes was consistent with melanoma, the patient agreed to undergo a shave biopsy to confirm the diagnosis and provide information on desirable excision margins. Histopathologic analysis established a diagnosis of malignant melanoma with a Breslow thickness of 0.6 mm. The nonulcerated melanoma was found arising over an intradermal nevus and blending with it. Under staining, the tumor was found to be positive for HMB45. To further corroborate these findings, a second gene expression test from tissue block samples was performed, the Myriad myPath Melanoma test,<sup>3</sup> a 23-gene algorithmic gene expression test that includes *PRAME* but not *LINCO0518*. The results of this test indicated a likely benign lesion (myPath Melanoma score, -5.9; range for benign gene signature classifications, -16.7 to -2.1). The amelanotic melanoma lesion was excised with appropriate margins, and follow-up visits were scheduled.

**Discussion** | Offering actionable gene expression testing to patients when appropriate appears helpful. Companies developing such tests should include amelanotic melanoma cases in future studies whenever possible. Further research is needed

Figure. Clinical Appearance of Amelanotic Melanoma



A pink papule is present anterior of the medial ankle.

to determine how well existing tests (including their current off-label use) perform on amelanotic lesions. A positive gene expression result in a case like the present one would be helpful. However, this case emphasizes that a negative melanoma gene expression result on a lesion where differential diagnoses include tumors where gene expression signatures are expected to be different, such as basal cell carcinoma, squamous cell carcinoma, or Merkel cell carcinoma, should not be used as a reason to not biopsy such a lesion. The case highlights the unmet need for additional gene expression signatures for these tumor types.

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