Non-Invasive Genomic Profiling in Pediatric Patients

Presented at the
Winter Clinical Dermatology Conference
January 13-18, 2023

Allyson G. Perry, PhD[1], Danielle Ruppenthal, PA-C[1], Kellie Hill, CLS (ASCP)[1]

1. DermTech, 11099 North Torrey Pines Road, Suite 150 La Jolla, CA 92037, USA

DermTech

Abstract

Background:
Pigmented lesions with clinical features suspicious for melanoma are not uncommon in pediatric patients. Evaluation of these lesions is complicated by the low prevalence of pediatric melanoma and challenges associated with performing biopsies in children. The DermTech Melanoma Test ('the test') is a non-invasive genomic test designed to rule out melanoma. It consists of the Pigmented Lesion Assay (PLA), which detects RNA gene expression of long intergenic non-coding RNA 00518 (LINC00518, or LINC) and preferentially expressed antigen in melanoma (PRAME), and an add-on assay for DNA promoter mutations in telomerase reverse transcriptase (TERT), which is performed if ordered and if sufficient genomic material is available. Patients younger than 18 years were not included in initial validation studies. In this analysis, we sought to compare genomic biomarker results between uncertain pigmented lesions from adult and pediatric patients.

Methods:
De-identified samples submitted to the clinical lab for the test from May through October 2022 were used for this analysis. Genomic results were available for 36,377 samples. The anatomic locations of the lesions were categorized as head/neck, trunk, or extremities and compared between adult and pediatric patients. Positivity rates for the PLA (and each individual marker) and the TERT add-on assay were calculated for adults and patients younger than 18 years of age.

Results:
The PLA was performed on 34,050 skin samples from adults and 2,327 samples from pediatric patients. There were no differences between adults and pediatric patients in anatomic location of the lesions tested. The proportion of PLA-positive samples was similar between adult (7.0%, n=2,393) and pediatric (8.0%, n=187) patients. Rates of biomarkers detected among PLA-positive adult and pediatric patient samples, respectively, were as follows: LINC only (31.4% vs 69.5%), PRAME only (45.5% vs 14.4%), LINC and PRAME (23.0% vs 16.0%). The TERT add-on assay was performed in 11,084 samples from adults and 613 samples from pediatric patients. Of these, TERT was positive in 830 (7.5%) adult and 3 (0.5%) pediatric patient samples.

Conclusions:
This analysis provides new information about genomic profiling of uncertain pigmented lesions from pediatric patients. While overall PLA positivity rates were similar across adult and pediatric samples, the proportion positive only for LINC was more than two times higher in pediatric samples. Additionally, TERT promoter mutations were rarely detected in pediatric samples. Further investigation of the significance of LINC, PRAME, and TERT abnormalities in lesions from pediatric patients is ongoing.

Introduction and Objective

Pre-biopsy genomic testing is used by providers to non-invasively rule out melanoma in uncertain pigmented lesions.[1,2] Since melanoma is rare in children, validation studies for the test excluded pediatric patients.[1-3] However, pigmented lesions with concerning clinical features are not uncommon in children, in which biopsies can be particularly challenging to perform.[3] The noninvasive nature of genomic testing is attractive for facilitating selection of the subset of pediatric lesions that are appropriate for biopsy.

The test consists of the Pigmented Lesion Assay (PLA), which detects RNA gene expression of LINC00518 (LINC) and PRAME, and an add-on assay for DNA promoter mutations in TERT, which is performed if ordered and if sufficient genomic material is available. The test is positive if one or more genomic markers are detected.[1,2] The objective of this analysis was to compare genomic biomarker results between uncertain pigmented lesions from adult and pediatric patients.

Methods

Between May and October 2022, skin samples were collected using adhesive patches and submitted, along with patient age and anatomic location of the lesion, to the clinical lab for genomic profiling. Samples were assessed for LINC00518 and PRAME RNA (qPCR), and in cases with sufficient material, DNA mutations in the TERT promoter region (Sanger sequencing).

Deidentified samples were categorized by anatomic location (head/neck, trunk, or extremities) and age (pediatric: <18 years, adult: ≥18 years). Positivity rates for the PLA (and each individual marker) and the TERT add-on assay were calculated and compared between adult and pediatric samples.

Results

In total, 34,050 adult and 2,327 pediatric samples underwent PLA analysis. Anatomic locations of the lesions tested were similar between age groups, with the lesions on the trunk accounting for just over 50% of lesions tested (Table 1).

Table 1.

	Adult (≥18 years) N=34,046		Pediatric (<18 years) N=2,326	
Anatomic Location	n	%	n	%
Trunk	17,921	52.6%	1,265	54.4%
Extremities	8,432	24.8%	554	23.8%
Head and Neck	7,693	22.6%	507	21.8%

The anatomic locations of 5 samples (4 adult, 1 pediatric) were not specific enough to be assigned to a category.

Overall positivity rates for the PLA were similar between adult (7.0%, n=2,393) and pediatric (8.0%, n=187) samples. Of PLA-positive samples, the proportion positive for LINC alone was higher in pediatric samples (69.5%) compared to adult samples (31.4%) (Table 2).

Table 2.

	Adult (≥18 years) N=34,050		Pediatric (<18 years) N=2,327	
PLA Results	n	%	n	%
Negative	31,657	93.0%	2,140	92.0%
Positive	2,393	7.0%	187	8.0%
LINC Only	752	31.4%	130	69.5%
PRAME Only	1,090	45.5%	27	14.4%
LINC and PRAME	551	23.0%	30	16.0%

The TERT add-on assay was performed on 11,084 adult and 613 pediatric samples. TERT mutations were detected in 7.5% of adult and 0.5% of pediatric samples (Table 3).

Table 3.

	Adult (≥18 years) N=11,084		Pediatric (<18 years) N=613	
TERT Results	n	%	n	%
Negative	10,254	92.5%	610	99.5%
Positive	830	7.5%	3	0.5%
TERT Only	616	74.2%	1	33.3%
LINC, PRAME, TERT	120	14.5%	1	33.3%
PRAME, TERT	66	8.0%	0	0.0%
LINC, TERT	28	3.4%	1	33.3%

Conclusion

While overall PLA positivity rates were similar across adult and pediatric samples, the proportion positive only for LINC was more than two times higher in pediatric samples than the adult samples. TERT promoter mutations are rare in lesions from pediatric patients. Further investigation of the significance of LINC, PRAME, and TERT abnormalities in lesions from pediatric patients is ongoing.

Scan QR code for additional peer-reviewed publications regarding this genomic test

References

1. Gerami P, Yao Z, Polsky D, et al. Development and validation of a noninvasive 2-gene molecular assay for cutaneous melanoma. *J Am Acad Dermatol*. 2017;76(1):114-120.e2.
2. Jackson SR, Jansen B, Yao Z, Ferris LK. Risk stratification of severely dysplastic nevi by non-invasively obtained gene expression and mutation analyses. *SKIN The Journal of Cutaneous Medicine*. 2020;4(2):105-110.
3. Tracy ET, Aldrink JH. Pediatric melanoma. *Semin Pediatr Surg*. Oct 2016;25(5):290-298.

Funding/disclaimer: the authors are employed by DermTech.