# Genomic Profiling of Lentigo Maligna within an Interim Registry Analysis

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## Abstract

Background:
Pigmented lesion analysis remains a challenging aspect of dermatology. The DermTech Melanoma Test ('the test') is a non-invasive gene-expression test designed to rule-out melanoma. It consists of the pigmented lesion assay, which detects RNA products of Long Intergenic Non-Coding RNA 00518 (LINC00518) and Preferentially Expressed Antigen in Melanoma (PRAME), and an add-on assay for DNA promoter mutations in telomerase reverse transcriptase (TERT). In previous studies, the test was found to have a negative predictive value ≥99%. This registry study examines the genomic patterns of the Lentigo Maligna (LM) subtype of melanoma.

Methods:
Between April 2021 and March 2022, multiple geographically diverse sites throughout the US submitted data to a registry to assess real-world use of the test. Approximately 8,000 clinically atypical lesions were tested. After receiving the test result, providers followed their clinical judgement for biopsy decision. Histopathologic diagnoses for biopsied lesions were correlated with test results and all melanomas were sorted into LM subtype vs non-LM subtype. In addition, lesions that were noted to be on sun exposed skin and/or noted to have solar elastosis and called atypical melanocytic hyperplasia were evaluated.

Results:
At the 1-year mark of the registry, there were roughly 8000 unique entries. Of those, 1003 expressed one or more genomic markers from the DMT and had records available, and 134 (13.2%) were found to be melanoma or melanoma in-situ. More than a third (n=46, 34.3%) of the melanomas were of the Lentigo Maligna sub-type, with 7 of those being Lentigo Maligna Melanoma (LMM). Seven additional lesions were called atypical junctional melanocytic hyperplasia (AJMH) on sun-damaged skin. This group of 53 LM, LMM, and AJMH lesions were all evaluated for correlations to the DMT markers. LINC was the most commonly expressed genomic marker (n=45, 84.9%), with PRAME (n=36, 67.9%) and TERT (n=24, 45.3%) following. Most invasive tumors (LMM) expressed all three markers (n=4) and all 7 expressed LINC.

Conclusions:
While the original validation study included the LM subtype, this interim registry analysis demonstrates real-world use of the DMT in assessing pigmented macules concerning for LM. Over 1/3 of the melanomas reported in the registry were LM subtypes. LINC had a higher correlation with the lentigo maligna subtype of melanoma and was present in all invasive tumors. While AJMH is considered borderline, it may be worthwhile in the clinical context to group AJMH lesions with LM due to similarities in treatment.

## Introduction and Objective

The gene expression test is designed to rule out melanoma by analyzing non-invasively collected skin cells from pigmented lesions for genomic atypia (LINC00518, PRAME, and/or TERT). The results of the test are designed to guide biopsy decisions on clinically suspicious pigmented lesions that violate one or more of the ABCDE criteria. This approach improves pigmented lesion management beyond visual inspection with a negative predictive value of ≥99% and a sensitivity of 91-97%, and by enriching melanoma among biopsied lesions almost 5-fold.[1-3] The real-world performance of the test and its impact on clinical practice has been addressed in a previously completed 2020 patient registry, and summarized in 2 peer reviewed publications.[3,4]

The objective of this study was to examine the genomic makeup of the LM subtype of melanomas, as well as AJMH which are histopathologically borderline but often treated similarly to LM.

## Methods

Between April 2021 and March 2022, approximately 8000 lesions were entered into a nationwide registry from 63 unique sites. Sites were encouraged to enter all results, including corresponding histopathology.

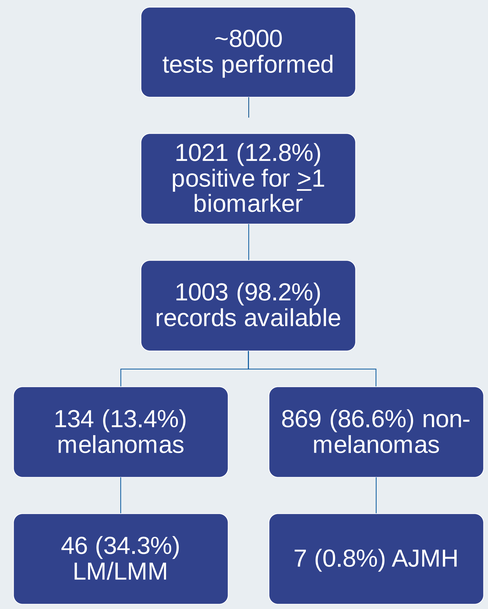
Histopathologic diagnoses were categorized first into melanoma and non-melanoma. Among melanomas, the number of LM subtype was determined, including the number of LMM subtype. Among non-melanomas, the number of SDN/AJMH was determined. All uncertain cases were reviewed by a board-certified dermatopathologist.

Furthermore, correlation between genomic markers present and LM/LMM/AJMH diagnoses was calculated.

## Results

Of the approximately 8000 lesions entered into the registry from April 2021 to March 2022, 1021 (12.8%) were positive for at least one genomic biomarker. Eighteen of these lesions did not have histopathologic diagnoses available. Of the 1003 complete cases, 134 (13.4%) were diagnosed as melanoma; 46 (34.3%) were LM subtype, with 7 of those being LMM. Of the non-melanoma lesions, an additional 7 (0.8%) were classified as AJMH. These results are depicted in the Figure.

Figure 1




LM = Lentigo maligna
LMM = Lentigo maligna melanoma
AJMH = atypical junctional melanocytic hyperplasia

The group of 53 LM/LMM/AJMH were analyzed for genomic marker correlation. LINC was the most commonly expressed genomic marker (n=45, 84.9%), with PRAME (n=36, 67.9%) and TERT (n=24, 45.3%) following. Most invasive tumors (LMM) expressed all three markers (n=4) and all 7 expressed LINC. These data are included in the Table.

Table 1.

**Table: Correlation of Genomic Markers with LM/LMM/AJMH**

| | Total | % | LMM | LM | AJMH |
|---|---|---|---|---|---|
| **LINC/PRAME/TERT** | 17 | 32.1% | 4 | 9 | 4 |
| **LINC/PRAME** | 14 | 26.4% | 1 | 12 | 1 |
| **LINC** | 10 | 18.9% | 2 | 7 | 1 |
| **PRAME** | 5 | 9.4% | 0 | 5 | 0 |
| **LINC/TERT** | 4 | 7.5% | 0 | 4 | 0 |
| **TERT** | 3 | 5.7% | 0 | 2 | 1 |

## Conclusion

This interim registry analysis demonstrates use of the DMT in assessing atypical pigmented macules and patches on chronically sun-exposed areas. While the original validation studies included the LM subtype, this data represents a larger real-world set. Over 1/3 of the melanomas reported were classified as LM subtype. LINC has a higher correlation with LM and was present in all 7 invasive tumors. While AJMH is considered borderline, it may be helpful in the clinical context to group AJMH lesions with LM due to similarities in treatment.

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

## References

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