

PATIENT INFORMATION




Patient Name:		Kit ID / Accn ID:	
Reference #:		Body Site:	
MRN #:		Date Collected:	
DOB (Age):		Date Received:	
Sex:		Date Reported:	
Referring Physician:		Fax Number:	
Address:		City/State/Zip:	

TEST RESULTS
Gene Expression Status: Positive
Risk Status: Moderate (Orange)
LINC00518: Detected
PRAME: Not Detected

Expression of LINC00518 and/or PRAME is found in lesions with a histopathologic diagnosis of melanoma. If one or both of the genes are detected, the test is positive.

Macro-dissection Report/Comments: The pre-specimen consists of adhesive patches containing four tissue samples. Except as noted, each patch contained tissue material which was free of obvious contamination with blood, exudate, hair or other contaminants. Each patch had a central circle delineating the margin around the tissue material. Examination of each of the macrodissected specimen revealed that the lesional tissue material was excised at the margin. Each sample was submitted for qPCR analysis. Images of all 4 of the macrodissections are kept on file and are available for review.

Interpretation:

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LOW (GREEN): Melanoma associated gene expression negative. Consider surveillance per standard of care.
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MODERATE (ORANGE): Positive for a single gene (LINC only or PRAME only). Recommend biopsy and histopathologic assessment. The proportion of pigmented lesions that are histopathologically diagnosed as melanoma is lower in single gene positive samples (50% for PRAME only positives and 7% for LINC only positives) than in double gene positive samples.
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HIGH (RED): Positive for both LINC and PRAME genes. Recommend biopsy and histopathologic assessment. The proportion of pigmented lesions that are histopathologically diagnosed as melanoma is higher in two gene positive samples (93% for both LINC and PRAME positives) than in single gene positive samples.



Joseph Voland, MD, FCAP

Laboratory Director: Joseph Voland, MD, FCAP

CAP # 9043605

CLN03ENV1

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ASSAY DESCRIPTION AND INTENDED USE

The DermTech pigmented lesion assay is intended for use under the direction of a physician to provide information on gene expression risk factors for melanoma in pigmented skin lesions. The assay detects gene expression for LINC00518 (Long Intergenic Non-protein Coding RNA518), and/or PRAME (Preferentially expressed Antigen in Melanoma). The test is intended for use on pigmented skin lesions suspicious for melanoma, including those that meet one or more ABCDE criteria, and for which a clinician would like additional information prior to surgical biopsy. If the pigmented lesion assay is positive for gene expression, a surgical biopsy for histologic assessment should follow. The assay is not intended for use on non-melanocytic lesions. The test has been validated in samples collected using the Adhesive Skin Sample Collection Kit and used according to the Instructions For Use (IFU). Lesions should be at least 5mm in diameter. For lesions larger than 16mm, multiple kits should be used. For valid lesion assessment, a careful demarcation of the desired tissue to be analyzed should be provided on the sample collection adhesive patches. The test has not been validated for samples collected from mucosal surfaces, the palms of hands, the soles of feet, sites that have been previously biopsied, areas where hair cannot sufficiently be trimmed, bleeding or ulcerated lesions, pediatric patients, and patients with Fitzpatrick skin type IV or higher. Samples with blood or excessive amounts of non-vellus hair (hair other than 'peach fuzz') on the adhesive patches will not be processed. Clinically obvious or frank melanoma should be surgically biopsied, per standard guidelines. Non-melanoma skin cancers may be negative based on LINC00518 and/or PRAME gene expression. As with all tests, results should be interpreted by the physician in conjunction with clinical findings, histopathologic findings as available, and patient risk assessment.

REFERENCE MATERIAL AND ASSAY PERFORMANCE

Expression of LINC00518 and/or PRAME genes has been studied in a validation set of 398 samples. Of the studied melanomas, 39% were read histopathologically as melanoma in situ of lentigo maligna, and the median thickness of invasive melanomas was 0.45mm. Eighty-one percent (81%) of nevi were read as atypical nevi. In this study, 91% of melanomas demonstrated detectable levels of LINC00518 and/or PRAME gene expression versus only 31% of non-melanoma samples, giving a sensitivity of 91% and a specificity of 69%. In a recent review of adult PLA positive results, the frequency of histopathologically confirmed melanomas in double positive samples, in which both LINC and PRAME are detected, was higher than in single gene positive samples (PRAME only or LINC only detected) (93% vs. 50% vs. 7%). These proportions are similar to the ones found in Gerami et al. (*Journal of the American Academy of Dermatology*, 2017). In a supplemental validation study evaluating hot spot mutations in BRAF, NRAS, and the TERT promoter region in 103 histopathologically confirmed samples, statistically significant differences were observed between histopathology positive (melanoma) lesions compared to histopathology negative (non-melanoma) lesions (77% vs. 14%, $p < 0.0001$) (Data on File, DermTech). In a real-world test cohort of 519 samples, there were no statistical differences in mutation frequency with the validation cohort and a 519 real-world test cohort. Eighty-eight percent (88%) of PLA negative results in the real-world test cohort were mutation negative. Acquired mutations in these genes are well characterized during early stage and metastatic melanoma (*Shain et al., The New England Journal of Medicine*, 2015).

At a melanoma prevalence of 5%, the PLA negative predictive value is greater than 99% indicating that, a patient with a negative test has a less than 1% probability of being positive for melanoma (*Gerami et al., Journal of the American Academy of Dermatology*, 2017). In a review of 280 PLA-negative test results, less than 2% were surgically biopsied at 3-6 months of clinical follow up and none of the biopsied lesions were found to be melanomas consistent with the high negative predictive value and low false negative rate. In a utility study by Ferriset al. (*JAMA Dermatology*, 2017), pigmented lesion experts biopsy about half as often and miss fewer melanomas when adding the pigment lesion assay to their decision process, allowing more melanomas to be found with fewer surgical procedures. Additional studies using the PLA in clinical settings demonstrate that the PLA identifies early stage melanoma (melanoma in situ, Stage 1) and that the number needed to biopsy declines from ~20 with visual assessment, to 2.7 with PLA (Data on file, DermTech).

This test was developed, and its performance characteristics determined by DermTech. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. The DermTech CLIA laboratory is also accredited by the College of American Pathologists (CAP). This test has not been cleared or approved by the US Food and Drug Administration; FDA does not require this test to go through premarket FDA review. This test is used for clinical purposes and is not considered investigational or for research.



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