DermTech

CAP ACCREDITED

PLA Pigmented Lesion Assay

MOLECULAR PATHOLOGY TEST REPORT

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PATIENT INFORMATION

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

TEST RESULTS

GENE EXPRESSION STATUS: POSITIVE

RISK STATUS: HIGH (RED)

***LINC00518*: DETECTED**

***PRAME*: 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:

Risk Status Interpretation:

LOW (GREEN): Melanoma associated gene expression negative. Consider surveillance per standard of care.

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 (LINC only or PRAME only) than in double gene positive samples.

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 (both LINC00518 positive and PRAME positive) than in single gene positive samples.

Joseph Voland, MD FCAP

Laboratory Director: Joseph Voland, MD. FCAP

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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 or lentigo maligna, and the median thickness of invasive melanomas was 0.45 mm. Eighty -one % of nevi were read as atypical nevi. In this study, 91% of melanomas demonstrated detectable levels of LINC00518 and/or PRAME 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 in single gene positive samples (LINC only or PRAME only detected) (92% vs. 12%). These proportions are similar to the ones found in Gerami et al. (*Journal of the American Academy of Dermatology*, 2017). In an additional PLA validation study evaluating hot spot mutations in BRAF, NRAS, and the TERT promoter region in 103 histopathologically confirmed samples relative to PLA results, statistically significant differences were observed between PLA positive and histopathology positive (melanoma) lesions compared to PLA negative histopathology negative (non-melanoma) lesions (75% vs. 15%, $p<<0.0001$) (Data on File, DermTech). There were no statistical differences in mutation frequency between the validation cohort and a 523 real-world test result cohort. 89% 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 calculated 7% melanoma prevalence, the PLA negative predictive value is greater than 99% indicating that, a patient with a negative test has a 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 Ferris et al. (JAMA Dermatology, 2017), pigmented lesion experts biopsy about half as often and miss fewer melanomas when adding the pigmented 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 biopsy ratio declines from >7.5 with visual assessment, to less than 1.9 with the 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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