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BRIEF COMMUNICATION

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Genomic Atypia of Lesions Clinically Suspicious for Melanoma Is Confined to Lesional Tissue Within Narrow Margins

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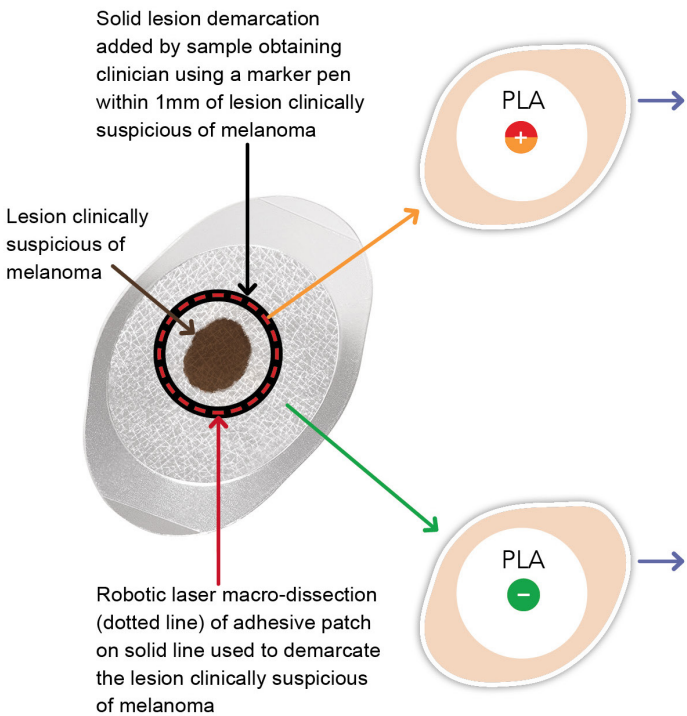
INTRODUCTION

Skin cancer is the most common cancer in the United States. Approximately 200,000 people are diagnosed with in situ and invasive melanoma, the most aggressive sub-set, each year accounting for approximately 7,000 deaths. Distinguishing early-stage melanoma from atypical nevi remains a challenge for many dermatologists; however, technological advances have increased the probability of successful diagnosis and opportunity for early intervention.[1]

The Pigmented Lesion Assay (PLA) is a non-invasive genomic test for the earliest melanoma detection that uses adhesive patches to collect skin samples from lesions clinically suspicious for melanoma. Post sample collection, demarcated adhesive patches are macro-dissected robotically utilizing a CO_2 laser to separate portions of the patches that sampled lesional tissue from non-lesional tissue with an approximate 1mm margin (Figure 1). Total RNA is isolated from the lesional tissue and

FIGURE 1. Genomic atypia and pigmented lesion margins. Samples of randomly selected 15 PLA-positive and 5 PLA-negative skin lesions clinically suspicious for cutaneous melanoma from a real-world use cohort (pathology therefore not available) were obtained via adhesive patches. Patches with epidermal skin tissue were macro-dissected using a robotic CO_2 laser system to separate lesional from non-lesional skin tissue as outlined above and analyzed for the detection of the melanoma markers LINC and PRAME using the PLA. In 12/15 (80%) of PLA-positive cases was genomic atypia (based on LINC and/or PRAME detection) confined to the lesion and narrow narrow margins of approximately 1mm. *Target gene expression detected outside the macro-dissected margin.



Clinical PLA Samples	Lesion Length (mm)	Lesion Width (mm)	Lesional Tissue (LINC/PRAME)	Non-Lesional Tissue (LINC/PRAME)
1 PLA+	9	8	(+/-)	(-/-)
2 PLA+	5	5	(+/-)	(-/-)
3 PLA+	11	12	(-/+)	(-/+)*
4 PLA+	12	8	(+/+)	(-/+)*
5 PLA+	10	7	(+/-)	(-/-)
6 PLA+	9	8	(+/-)	(-/-)
7 PLA+	8	7	(+/+)	(-/-)
8 PLA+	9	8	(+/+)	(-/-)
9 PLA+	5	8	(+/+)	(+/+)*
10 PLA+	6	5	(-/+)	(-/-)
11 PLA+	5	5	(+/-)	(-/-)
12 PLA+	13	10	(+/+)	(-/-)
13 PLA+	13	9	(-/+)	(-/-)
14 PLA+	8	9	(-/+)	(-/-)
15 PLA+	8	8	(+/-)	(-/-)

Clinical PLA Samples	Lesion Length (mm)	Lesion Width (mm)	Lesional Tissue (LINC/PRAME)	Non-Lesional Tissue (LINC/PRAME)
1 PLA-	8	7	(-/-)	(-/-)
2 PLA-	7	6	(-/-)	(-/-)
3 PLA-	7	6	(-/-)	(-/-)
4 PLA-	8	7	(-/-)	(-/-)
5 PLA-	8	8	(-/-)	(-/-)

then analyzed for the expression of LINC (LINC00518, Long Intergenic Non-Coding RNA 518) and PRAME (Preferentially Expressed Antigen in Melanoma), two genes preferentially expressed in melanoma.[2] These genomic markers are used to guide biopsy decisions on pigmented skin lesions clinically suspicious of melanoma.[3] Previous clinical studies have demonstrated that the PLA reduces avoidable biopsies by over 90% while missing fewer melanomas due to its high negative predictive value (NPV) of >99%.[4,5] In most cases, the remaining "donut shaped" patches with non-lesional material are discarded; however, in this study we investigated whether LINC and PRAME were additionally expressed in the non-lesional skin samples (eg, normally appearing skin about 1mm outside the lesion of interest). Upon histopathologic diagnosis of cutaneous melanoma, current clinical practice guidelines recommend surgical excision of the diagnosed lesion with margins of at least 0.5 cm for melanoma in situ and least 1 cm for invasive primary melanoma.[6] One to three millimeters are generally considered appropriate for melanocytic lesions of concern that do not carry morphologic features of melanoma.[6]

For this investigation, 20 non-invasively obtained PLA samples were selected from a real-world use cohort and processed to separate lesional from non-lesional tissue using laser macro-dissection. The lesional and non-lesional tissue samples were then both analyzed for the detection of LINC and/or PRAME to determine whether genomic atypia based on the expression of these melanoma markers extends into non-lesional tissue surrounding the lesion of interest. Figure 1 summarizes the results of this study. Findings demonstrate that detection of the 2 PLA melanoma target genes is generally confined to lesional material within an approximately 1mm margin in 80% (12/15) of PLA positive cases.

CONCLUSIONS

This study demonstrates that genomic atypia assessed by the expression of the 2 melanoma-associated target genes LINC and PRAME is largely confined to concerning lesions without extending into the surrounding area beyond narrow margins. Additionally, this analysis suggests that surgical excision of lesions within established margins will remove cutaneous melanoma and lesions with morphological atypia without residual genomic atypia.

DISCLOSURES

RM and DMS are members of DermTech's Scientific Advisory Board. ZY, MDH, and BJ are employees of DermTech.

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