Gene Expression Analysis Differentiates Pediatric Melanomas from Spitz Nevi

Burkhard Jansen[1], MD, Doyle Hansen[2], MD, and Zuxu Yao[1], PhD. 1) DermTech Inc, La Jolla, CA, USA; 2) Pacific Pathology, La Jolla, CA, USA.

Introduction

We recently validated a dermatology gene expression platform using adhesive patch biopsies to non-invasively collect skin samples. LINC (Long Intergeneic Non-Coding RNA 518) and/or PRAME (Preferentially Expressed Antigen in Melanoma) gene expression in non-invasively obtained epidermal skin samples from adult patients differentiates primary melanomas from atypical nevi and other pigmented lesions with a Negative Predictive Value of over 99%, a sensitivity of 91% and a specificity of 69% to help clinicians with the management of difficult to assess pigmented lesions. Surgically obtained melanomas (primary lesions and metastases) show the same gene expression pattern in FFPE tissue block samples further corroborating these findings. [1, 2]

Based on feedback from a considerable number of clinicians and dermatopathologists, who asked how pediatric melanomas and pediatric Spitz nevi behaved at a gene expression level, we conducted the study presented here to find answers.

Materials and Methods

In this study, we investigate gene expression patterns of pediatric pigmented lesions from FFPE tissue block samples with a focus on differentiating Spitz nevi from pediatric melanomas. Spitz nevi can pose significant diagnostic challenges to both clinicians and dermatopathologists when the current image-recognition based gold standard is employed. Histopathologically confirmed samples of pediatric melanomas, benign pediatric nevi and pediatric Spitz nevi (n=8-9 per group) were assessed by qRT-PCR for LINC, PRAME and 4 control genes. All analyses were conducted in duplicate.

Results

Figure 1 provides examples of the lesion types investigated. Figure 2 summarizes gene expression data. Consistent with findings in adults, PRAME levels were significantly ($p<0.001$) increased based on normalized Ct cycle counts in pediatric melanomas (mean Ct 33.45 ± 0.61, 95% CI 32.35-34.56) when compared to Spitz nevi (37.45 ± 0.63, 95% CI 36.26-38.65) or common nevi (37.21 ± 0.80, 95% CI 35.73-38.69), respectively. LINC levels were also marginally increased in pediatric melanomas whereas 4 control genes (ACTB, B2M, CMIP and PPIA) showed similar expression levels in all 3 pigmented lesion groups investigated. Clinically and histopathologically, complex pediatric Spitz nevi demonstrated gene expression signatures almost identical to gene expression signatures of common pediatric nevi but clearly different from pediatric melanomas.

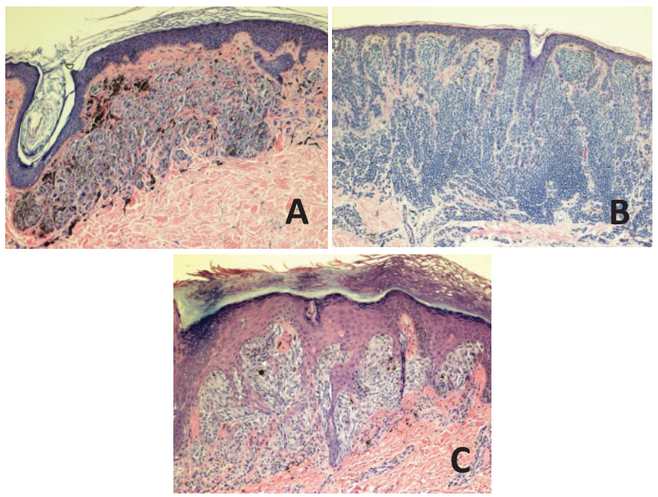

Figure 1. Representative examples of histopathological analyses of pediatric pigmented lesion cases (H&E stained slides from FFP tissue blocks) also assessed for gene expression. A) melanoma, B) common nevus; C) Spitz nevus.

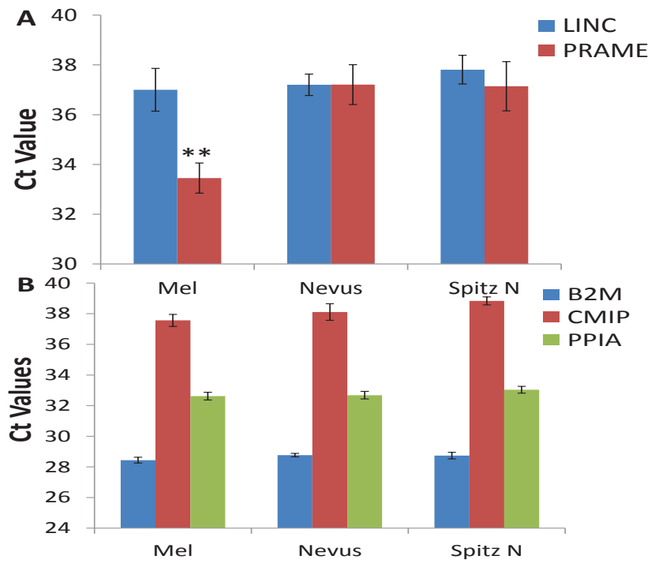

Figure 2. Gene expression analysis of the target genes LINC and PRAME (A) and of control genes (B) in the above described 3 lesion types (FFPE tissue blocks). ** indicates a p-value <0.001 (significant difference with 99% confidence). Low Ct values indicate high gene expression.

Conclusion

PRAME and possibly LINC gene expression can be valuable objective aids to differentiate pediatric melanomas from Spitz nevi, groups of pigmented lesions that can be particularly difficult to assess in children.

References

1. Gerami et al., Development and validation of a non-invasive 2-gene molecular assay for cutaneous melanoma; JAAD-D-16-00647R1, 2016.
2. Yao et al., Analytical Characteristics of a Noninvasive Gene Expression Assay for Pigmented Skin Lesions; ASSAY and Drug Development Technologies, Vol.14 No.6, 2016.
Supported by DermTech, Inc.