Cell Cycle Activators and Tumor Suppressors that Correlate with Melanoma Progression

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Background/Objectives: Melanoma accounts for the highest numbers of skin-cancer related deaths, and incidence of cutaneous melanoma continues to rise.1 Good prognosis is highly dependent on early detection and appropriate staging.2 In addition to our current clinical and histological prognostic indicators, there may be a role for gene expression biomarkers in complementing our current melanoma staging and tumor burden assessment.3

Methods: After defining the panel of melanoma biomarkers to evaluate, we optimized a multiplex reaction to efficiently quantify RNA for our genes of interest from small quantities of tissue. Quantitative real-time polymerase chain reaction (qRT-PCR) was performed to quantify and compare RNA levels in human skin tissue samples of nevi (n=12), primary melanoma (n=12), and metastatic melanoma (n=12). While NCAPH expression levels were difficult to measure due to minimal expression in human tissue, we were able to successfully quantify HELLs and SPINT2.

Results: HELLs expression levels were remarkably higher in metastatic melanoma compared to benign nevi (p=0.02) and primary melanoma (p=0.05) (Figure 1A). Meanwhile, SPINT2 expression levels were almost nonexistent in metastatic skin samples; this was evident when comparing metastatic melanoma to nevi (p=0.03) and primary melanoma (p=0.03) (Figure 1B). There was no statistical difference between nevi and primary melanoma (p=0.11 for HELLs, p=0.31 for SPINT2).

Conclusion: Our assay system proved sensitive in detecting differences in expression levels of HELLs and SPINT2 in metastatic melanoma compared to benign nevi and primary melanoma. Such novel biomarkers help us further understand the biology of melanoma, with potential clinical implications in prognosis, therapy, and detection of treatment response and tumor recurrence.
Figure 1. Statistical analysis shows HELLS is upregulated (A) while SPINT2 is downregulated (B) in metastastatic melanoma (MM) compared to benign nevi and primary melanoma (PM).

References: