SKIN

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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]

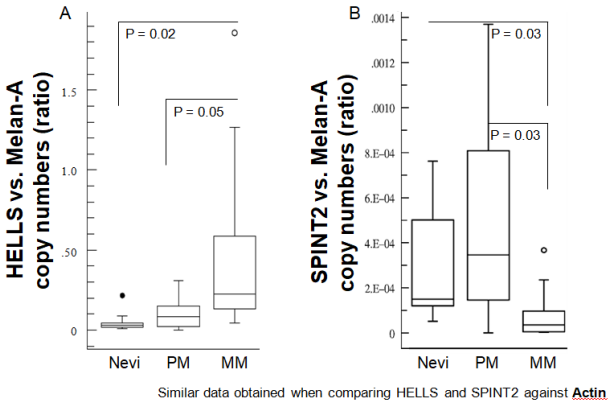
In this study, we sought to evaluate the potential utility of melanoma progression-associated genes as biomarkers for disease burden in human skin tissue samples. Based on previous microarray studies, primary genes of interest were *HELLS*, *NCAPH*, and *SPINT2*.[4] *HELLS* and *NCAPH* have been shown to be cell cycle activators upregulated in aggressive metastatic tumor cell lines in comparison to less-aggressive primary tumor cell lines. *SPINT2* has been implicated as a tumor suppressor gene in multiple cancers; its expression induces cell apoptosis and tumor suppression in vivo.

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).



Similar data obtained when comparing HELLS and SPINT2 against **Actin**

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