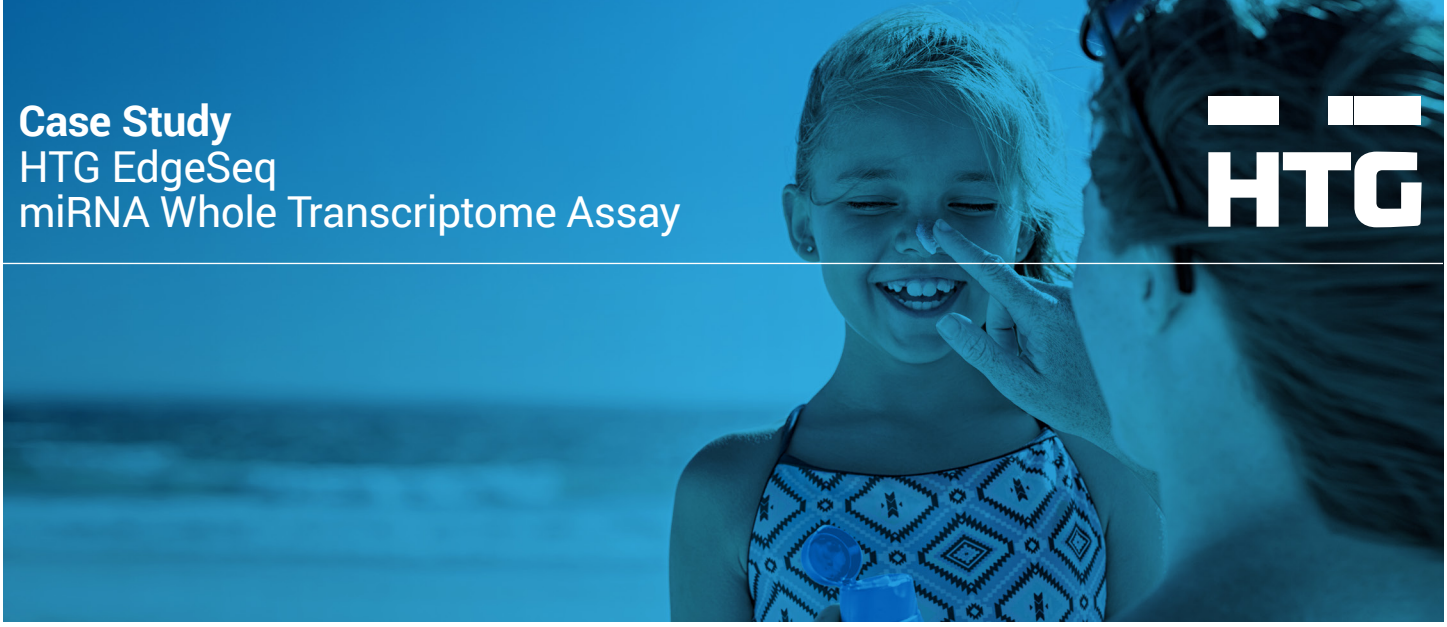
Case Study
HTG EdgeSeq
miRNA Whole Transcriptome Assay



HTG EdgeSeq miRNA Whole Transcriptome Assay identifies miRNA expression signature for differentiating UV-damaged melanocytes

Problem: UV radiation damages skin cells in a variety of ways, and it is difficult to determine which factors directly lead to skin cancer

Ultraviolet (UV) radiation causes damage to DNA within skin cells[1]. Both UV A and UV B can directly induce DNA lesions and indirectly generate reactive oxygen species[2]. In response to UV exposure, cells activate DNA repair pathways and checkpoints that can induce cell cycle arrest until DNA damage has been repaired. Both direct damage and indirect damage may contribute to the transition from melanocytes to melanocytic nevi to clinical melanoma.

Superficial melanocytic nevi are closer to the surface and are therefore more likely to incur direct UV damage. Deep melanocytic nevi are less likely to develop into melanoma due to direct UV damage, but more likely to incur damage from other sources. Therefore, differentiating between the cellular processes of deep and superficial melanocytes could help shed light on what genes are involved in the transition to melanoma as a result of direct UV damage.

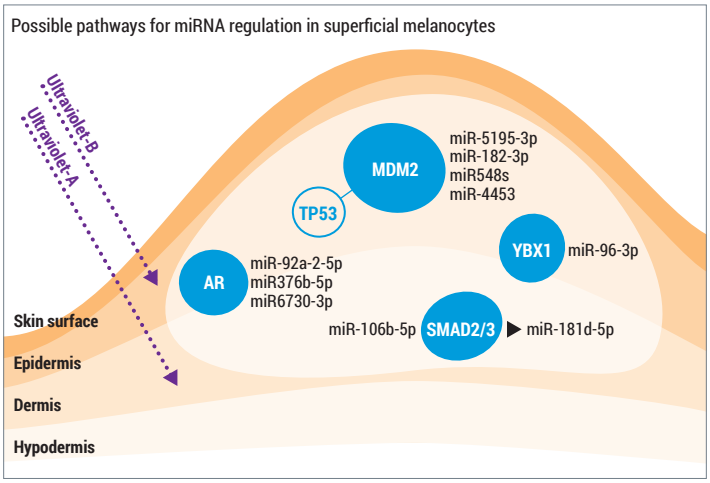
Solution: Differentiating between deep and superficial melanocytic nevi via miRNA profiling

miRNAs are known to be involved in the regulation of a variety of cellular processes and pathways directly related to melanoma development and cancer progression[3]. Therefore, altered miRNA expression profiles could be useful in characterizing cancer development and progression and have the potential to reveal previously uncharacterized regulatory networks[4].

In a recent study, carried out at MD Anderson Cancer Center, Bell *et al*. examined skin melanocytes taken from both superficial and deep tissue biopsy samples of 14 patients to determine differences in miRNA expression profiles downstream of UV exposure[5]. Bell *et al*. used the HTG EdgeSeq miRNA Whole Transcriptome Assay to demonstrate that superficial melanocytic nevi, associated with higher levels of UV exposure, can be differentiated from unexposed deep melanocytes based on the differential expression of 39 miRNAs. Of the 39 differentially expressed miRNAs, 35 were downregulated in the UV-exposed tissue samples, and these particular miRNAs are associated with neoplastic tissue growth and promoting dedifferentiation of cells, thereby promoting epithelial to mesenchymal transition into cancer cells[4,6].

The researchers further examined whether these miRNAs are linked to oncogenes or tumor suppressors. Through Ingenuity Pathway Analysis, the researchers identified AR, MDM2, SMAD2/3, and YBX1 as likely targets of these miRNAs *(Figure 1)*. Follow up experiments using immunohistochemistry confirmed that one of the likely targets, YBX1, is in fact more highly expressed in superficial melanocytes[5].

Figure 1. *Predictions generated by Bell et al. using the program Ingenuity Pathway Analysis[5]*



Significance: miRNA profiling revealed differential expression of miRNA and protein targets associated with cancer in superficial melanocytes

Bell *et al*. used the HTG EdgeSeq miRNA Whole Transcriptome Assay to identify hallmarks of UV damaged melanocytes with increased potential to become malignant melanoma cells. The analysis of human miRNAs revealed 39 miRNAs that were differentially expressed in deep vs superficial melanocyte biopsies, suggesting a miRNA expression profiling signature that can be used to differentiate UV-damaged melanocytes from undamaged tissues.

Therefore, detection of the expression of miRNAs using the HTG EdgeSeq miRNA Whole Transcriptome Assay has the potential to identify biomarkers for malignant transition in UV exposed skin cells. This study demonstrates the utility of using the HTG EdgeSeq miRNA Whole Transcriptome Assay to differentiate cancerous and pre-cancerous cells from closely related cell types based on signatures of miRNA expression that signal differences in pathology; in principle, a similar strategy could be applied to other solid tissue cancers.

References

1: Sun, X., Kim, A., Nakatani, M., Shen, Y. & Liu, L. Distinctive molecular responses to ultraviolet radiation between keratinocytes and melanocytes. *Exp. Dermatol.* 25, 708–713 (2016).

2: Valejo Coelho, M. M., Matos, T. R. & Apetato, M. The dark side of the light: mechanisms of photocarcinogenesis. *Clin. Dermatol.* 34, 563–570 (2016).

3: Holst, L. M. B. *et al*. The microRNA molecular signature of atypic and common acquired melanocytic nevi: differential expression of miR-125b and let-7c. *Exp. Dermatol.* 20, 278–280 (2011).

4: Lu, J. *et al*. MicroRNA expression profiles classify human cancers. *Nature* 435, 834–838 (2005).

5: Bell, A. *et al*. Detection of a MicroRNA molecular signature of ultraviolet radiation in the superficial regions of melanocytic nevi on sun-exposed skin. *Mod. Pathol.* 31, 1744–1755 (2018).

6: Sha, J. *et al*. The Response of microRNAs to Solar UVR in Skin-Resident Melanocytes Differs between Melanoma Patients and Healthy Persons. *PLOS ONE* 11, e0154915 (2016).

HTG Molecular Diagnostics, Inc.
Call 1-877-289-2615
www.htgmolecular.com

Rev 2: 29-APR-2021