Recently, a 23-gene signature was developed to produce a diagnostic score capable of differentiating malignant melanoma from benign melanocytic lesions. The objective of the study was to independently assess the performance of this gene signature in clinically relevant lesions.

**Gene Expression Testing**

Melanocytic lesions were submitted for gene expression testing (Myriad Genetic Laboratories, Inc.) as part of normal healthcare operations. The expression of 14 tumor marker genes and 9 housekeeping genes was measured by qRT-PCR to obtain a melanoma diagnostic score (Table 1).

**Study Design**

A set of 1,400 melanocytic lesions was selected from samples prospectively submitted for gene expression testing at a clinical laboratory (Figure 1).

Each sample was subjected to independent histopathologic evaluation by three experienced dermatopathologists, who were blinded to:
- Gene expression testing
- Diagnosis of submitting dermatopathologist
- Diagnoses of other reviewing dermatopathologists
- A primary diagnosis (benign or malignant) was assigned to each sample
- A fourth dermatopathologist reviewed all cases for which there was a triple-concordant diagnosis of melanoma and assigned a subtype
- A threshold for minimum tumor volume was established at 10%

**Validation of the Gene Expression Signature**

The association between the score and the triple-concordant histopathologic diagnosis was assessed by sensitivity and specificity.

Exact 95% confidence intervals were computed for sensitivity (proportion of correctly identified positive/malignant cases) and specificity (proportion of correctly identified negative/benign cases).

The score was used to assess the sensitivity of the gene expression signature within specific melanoma subtypes of lesions with triple-concordant diagnoses of melanoma.

**RESULTS**

A total of 736 cases with triple-concordant histopathologic diagnosis and >10% tumor volume were included in the analysis (Figure 2).

This cohort included all major clinical-histopathologic melanoma and nevus subtypes, as well as many histopathologic variants (Table 2).

Many cases with an indeterminate diagnosis from the submitting dermatopathologist received a definitive score that agreed with the triple concordant diagnosis (Figure 3).

In numerous instances the score was discordant with the submitting dermatopathologist’s favored pre-test diagnosis.

Apparent false positives occurred in several cases in which the triple concordant diagnosis was malignant, in agreement with the score.

Apparent false negative results were most common in lentigo maligna.

**REFERENCES**


**DISCLOSURE**