Performance of the 23-gene expression profile (23-GEP) test by histopathological evaluation in an independent, multi-center performance cohort of cutaneous melanocytic neoplasms

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Background

- Histopathologic evaluation can effectively diagnose most melanocytic neoplasms; however, lesions considered to be difficult-to-diagnose pose challenges for accurate classification of malignant potential, which can lead to over- or under-treatment.[1-4] Ancillary tests such as immunohistochemistry, **gene expression profiling (GEP)**, FISH, and aCGH aid in the classification of ambiguous lesions.
- The **23-GEP** test is a clinically available, objective ancillary tool that facilitates diagnosis of melanocytic lesions with ambiguous histopathology. The test uses a proprietary algorithm to produce results of: **suggestive of benign neoplasm**; **suggestive of malignant neoplasm, or intermediate** (**cannot rule out malignancy**).[5-9]
- The 23-GEP test has demonstrated accuracy metrics of 90.0 – 91.5% sensitivity and 91.0 – 92.5% specificity in lesions classified by histopathological majority review[5,6], 93.8 – 96.8% sensitivity and 87.3 – 96.2% specificity in lesions with known outcomes[7,8], and 90.4% sensitivity and 95.5% specificity in equivocal lesions with known outcomes.[9]

Here, we present 23-GEP accuracy from its **current laboratory** in an independent cohort using expert dermatopathology review as the accuracy reference standard.

Methods

- Melanocytic lesions and associated de-identified clinical data from patients were included in this IRB-approved study. Samples were acquired from eight centers, including those previously submitted for clinical testing for the 31-GEP melanoma prognostic test. Lesions were independently reviewed by 3–5 dermatopathologists with designations of benign, malignant, or uncertain malignant potential (UMP) and included in the study if they were fully concordant or non-concordant without opposing diagnoses. Unknown malignant potential lesions (UMPs), opposing and nondefinitive lesions were excluded (**Figure 1**), resulting in a cohort (n=2512) of benign nevi (n=1140) and malignant melanomas (n=1372).
- Accuracy metrics and two-tailed 95% confidence intervals (CIs) were calculated without intermediate results and using resampling x10,000 iterations to establish a balanced number of benign versus malignant samples (**Table 1**).

Results

Table 1. 23-GEP performance accuracy metrics

Performance Cohort, n=2185		
Sensitivity	**91.3%**	95% CI: 89.2% - 93.2%
Specificity	**91.9%**	95% CI: 89.8% – 93.8%
Positive predictive value	**92.2%**	95% CI: 90.3% – 94.0%
Negative predictive value	**91.0%**	95% CI :89.0% – 92.9%
Intermediate result	*7.8%*	

Lesions in which the GEP result did not agree with the dermatopathologists' classification have higher rates of non-concordant diagnoses compared to the full cohort
(27.5% and 12.9%, respectively)

References

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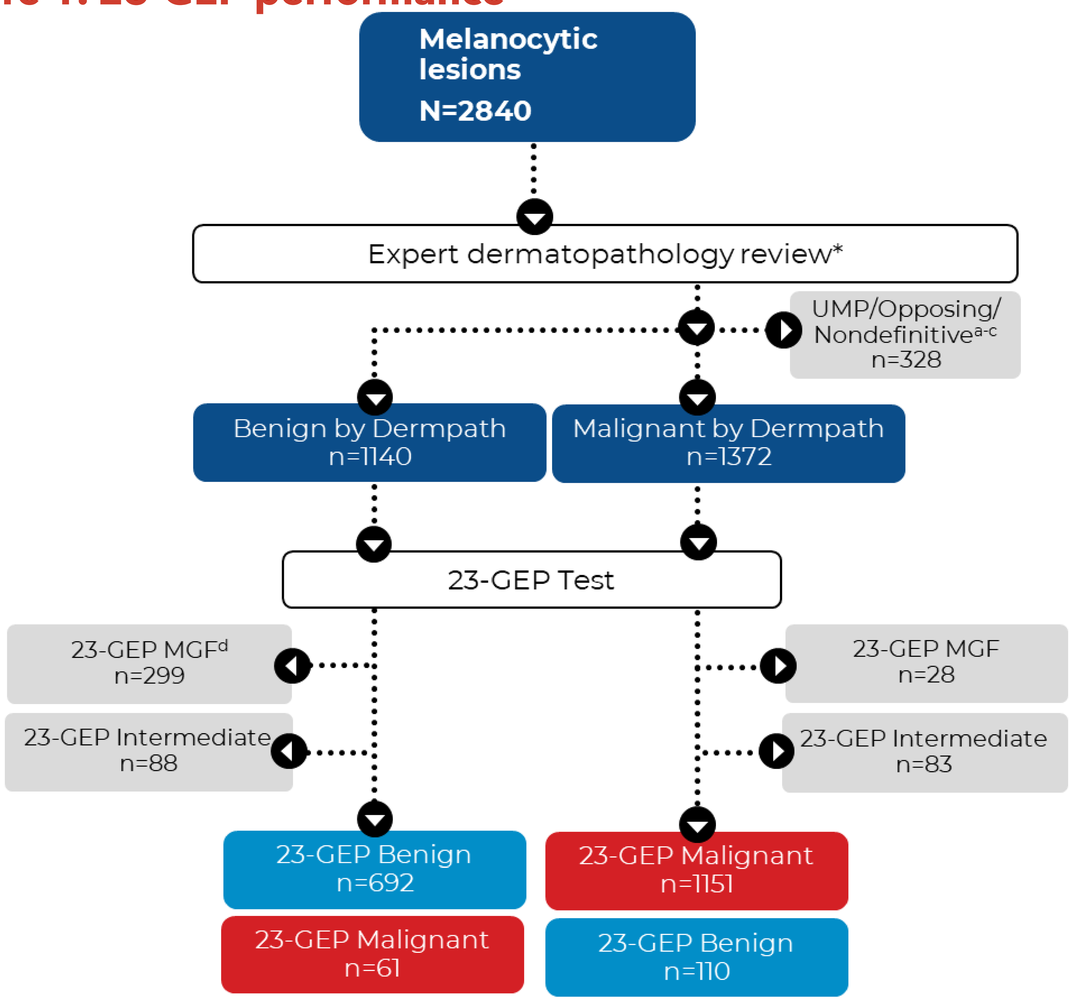
Results

Figure 1. 23-GEP performance



[a]UMP: majority and or ≥2 designations were UMP, [b]Opposing: both benign and malignant designations, [c]Nondefinitive: equal designations of benign or malignant designations, [d]MGF (multiple gene failure)

Conclusions

- These performance metrics do not deviate appreciably from previous studies and demonstrate that the 23-GEP is highly accurate, further supporting its use as an ancillary test which is integrated with clinical, histopathological, and other ancillary test information to guide the final diagnosis.
- Higher rates of non-concordant diagnoses were present in lesions where 23-GEP differed from dermatopathologists' majority assessment, which calls into question the true malignant potential.
- This study relies on subjective histopathologic interpretation without outcomes which allows for larger cohort analyses. Studies utilizing outcomes have confirmed the accuracy of 23-GEP.[7-9]

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