Clinical Utility and a Guide for Using Gene Expression Profile Ancillary Diagnostic Testing for Cutaneous Melanocytic Neoplasms

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Background

- Diagnostic discordance in suspicious cutaneous melanocytic lesions is well documented and particularly prevalent among difficult-to-diagnose cases, for which histopathology may be insufficient for a definitive diagnosis.[1-4]
- The **23-gene expression profile (GEP)** and **35-GEP** tests are clinically available objective ancillary diagnostic tools (collectively, dGEP) that facilitate diagnosis of melanocytic lesions with ambiguous histopathology. The tests use proprietary algorithms to produce results of: **suggestive of benign neoplasm**; **intermediate** (**cannot rule out malignancy**); or **suggestive of malignant neoplasm**.[5-7]
- The dGEP tests have demonstrated accuracy metrics of 90.4 – 94.9% sensitivity and 92.5 – 96.2% specificity for 23-GEP, and 94.7 – 99.1% sensitivity and 89.5 – 94.3% specificity for 35-GEP.[5-8]
- Clinical utility has been demonstrated with benign and malignant dGEP test results. For lesions that receive a benign dGEP test result, decreases in treatment intensity have been observed. Specifically, a reduction in the number of excisions performed was noted in two studies (76.7 – 80.5%). A malignant dGEP result prompted 95.2% of dermatologists to increase office visit frequency and a 75% increase in recommendations to excise.[9,10]

Objective

- Provide a framework for use of dGEP testing in clinical practice
- Demonstrate how GEP results can alter patient management plans

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Results

Figure 1. A proposed post-biopsy clinical workflow for the use of dGEP for the treating dermatology clinician and the diagnosing dermatopathologist, including situations of diagnostic and clinical use to achieve personalized management and treatment plans.

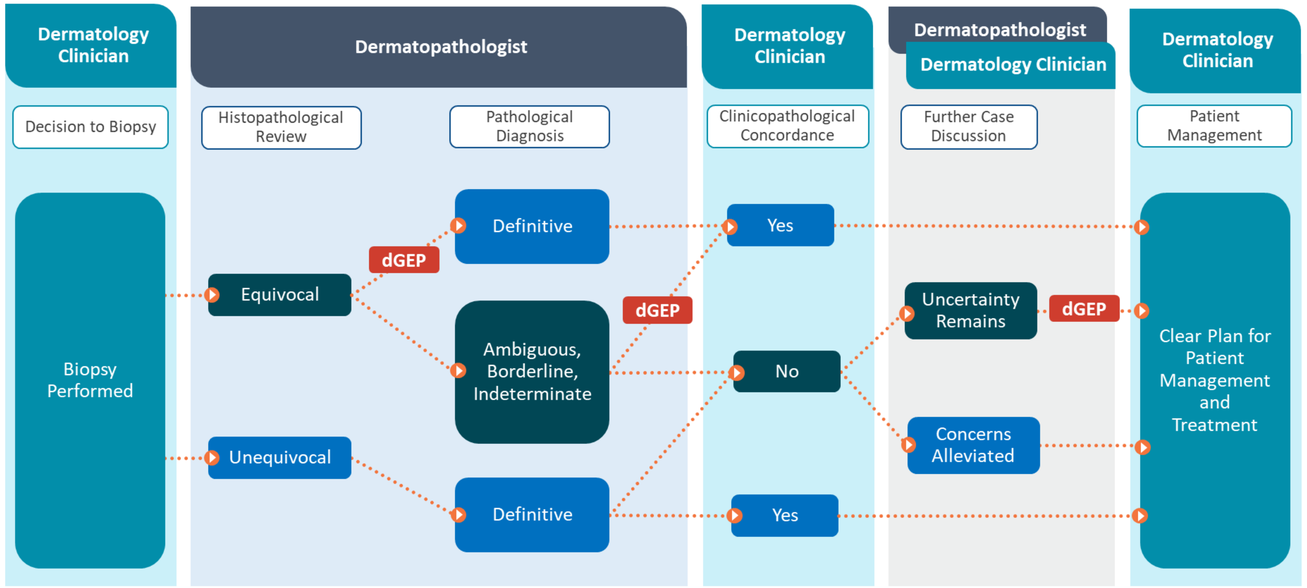

Figure 2. Common provider-based scenarios to consider dGEP testing

Dermatopathologist-driven dGEP requests
1. Atypical melanocytic proliferations
2. Severely dysplastic nevi
3. Atypical blue nevi
4. Clark's or congenital nevi with unusual features
5. Limited tissue availability

Dermatologist-driven dGEP requests
1. Significant clinical concern for melanoma e.g., suspicious dermoscopy, confocal, serial imaging
2. Ambiguous pathology report received
3. Personal history of melanoma
4. Cosmetically sensitive areas

Figure 3. Overall Summary of dGEP Diagnostic and Treatment Utility

Diagnostic Utility Is it melanoma or not?	Treatment Utility Should an excision be performed?
	Benign dGEP Result
› **43% reduction in indeterminate diagnoses**[11]	› 76.7%-80.5% reduction in excisions[9,10] › 74.1% of dermatologists reduce office visits[10] › Demonstrated safe to forego re-excision[12]
	Malignant dGEP Result
› **51% increase in diagnostic confidence**[10]	› 75% increase in excisions[9,10]
› **High accuracy**[5,8]	› 95.2% of dermatologists increase office visits[10]

Conclusions

- GEP testing and results can be incorporated into diagnostic clinical use at various points during the patient journey.
- Optimal dGEP use takes place during the diagnostic process and involves the dermatopathologist to alleviate ambiguous diagnoses.
- Clinical concerns that raise uncertainty may necessitate utilization of dGEP to achieve clinicopathological correlation.
- Treatment decisions have been shown to be dGEP result-dependent and can alter patient management plans such as excision and office visit frequency.

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