FINAL REPORT

Patient: John Doe
Sex: Male
DOB: 12/16/1935
Client: Sample Site
Provider: Dr. Castle

Tumor Site: R Medial Upper Back
Specimen ID: AD21-123123 (FFPE)
Collected: 02/18/2022
Received: 02/21/2022
Reported: 02/24/2022

Final Test Result

Gene expression profile suggestive of benign neoplasm	**-2.6**

RESULT DESCRIPTION

myPath Melanoma utilizes a molecular signature measured by qRT-PCR that classifies a sample as malignant, benign, or indeterminate. The number shown above is this patient's score relative to the myPath Melanoma scores according to the range of benign and malignant lesions in the independent validation cohort with a threshold of zero.

A score range of -16.7 to +11.1 was established in a validation study and scores within this range will be reported. For scores from -16.7 to -2.1 the resulting classification is benign; for scores from -2.0 to -0.1, classification is intermediate*; for scores from 0 to +11.1, the classification is malignant. Scores outside the validated range require follow-up with the ordering health care professional.

*For purposes of reporting herein, the terms intermediate and indeterminate are equivalent.

TEST VALIDATION AND PERFORMANCE METRICS

Based on an analysis of 437 melanocytic lesions in the validation study, a score threshold of zero was established to classify a sample as malignant, benign, or indeterminate. In the validation cohort, the gene expression signature had a sensitivity of 94% and a specificity of 90%[1].

BACKGROUND AND INTENDED USE

Background: Current methods used for definitive diagnosis of melanoma are sufficient for most lesions. However, histopathologic assessment can be challenging, even for experienced dermatopathologists. High rates of diagnostic discordance have been reported[2-6]. myPath Melanoma refines the diagnosis of nevi and melanoma by providing an objective tool to aid in classification of pigmented lesions.

Intended Use: The **myPath-Melanoma** gene expression test is intended for the in vitro analysis of primary cutaneous melanocytic lesions for which malignant potential is uncertain. This ancillary test aids in characterizing these lesions as benign or malignant and should be interpreted in the context of other clinical, laboratory and histopathologic information. **myPath Melanoma** has not been validated on metastatic melanomas, recurrent tissue specimens, non-melanocytic neoplasms, or biopsies from a patient receiving immunosuppressant therapy or radiation treatment. Analysis of these samples may result in incorrect test interpretation; therefore, these specimens will not be accepted for testing.

Castle Biosciences, Inc. | Sherri Borman, PhD, HCLD, Lab Director

ADDITIONAL INFORMATION ABOUT THE TEST

The 14 discriminating genes are: PRAME, S100A7, S100A8, S100A9, S100A12, PI3, CCL5, CD38, CXCL10, CXCL9, IRF1, LCP2, PTPRC, SELL. Nine control genes consist of CLTC, MRFAPI, PPP2CA, PSMA1, RPL13A, RPL8, RPS29, SLC25A3, and TXNLI.

The melanocytic lesion submitted is identified for microdissection by a board-certified dermatopathologist using H&E analysis. Analysis is then performed on total RNA extracted from FFPE tissue. The expression levels of 14 genes are measured and normalized by 9 housekeeping genes.

The assay performance was determined by comparing the myPath-Melanoma score to the consensus diagnosis (as determined by the pathology report, and one independent, blinded review by a board-certified dermatopathologist with discordant diagnoses adjudicated by a third independent board-certified dermatopathologist)[1].

REFERENCES

1. Clarke L, et al. Clinical validation of a gene expression signature that differentiates benign nevi from malignant melanoma. *J Cutan Pathol* 2015; 42:244-252.
2. Warf MB, et al. Analytical validation of a melanoma diagnostic gene signature using formalin-fixed paraffin-embedded melanocytic lesions. *Biomark Med* 2015; 9(5):407-416.
3. Elmore JG, et al. Pathologists' diagnosis of invasive melanoma and melanocytic proliferations: observer accuracy and reproducibility study. *BMJ* 2017; 357:j2813.
4. Shoo BA, Sagebiel RW & Kashani-Sabet M. Discordance in the histopathologic diagnosis of melanoma at a melanoma referral center. *J Am Acad Dermatol* 2010; 62:751-756.
5. Farmer ER, Gonin R & Hanna MP. Discordance in the histopathologic diagnosis of melanoma and melanocytic nevi between expert pathologists. *Hum Pathol* 1996; 27:528-531.
6. Patrawala S, et al. Discordance of histopathologic parameters in cutaneous melanoma: Clinical implications. *J Am Acad Dermatol* 2016;74:75-80.
7. Warycha MA, et al. Changes in the presentation of nodular and superficial spreading melanomas over 35 years. *Cancer* 2008;113:3341-3348.

For additional details, please visit www.CastleTestInfo.com or scan the QR code.

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