Merlin

A GENE EXPRESSION-BASED TEST

Some melanoma patients should be referred for sentinel lymph node biopsy.

Far more may forgo the procedure.

Merlin spots who's who.

Merlin

Introducing Merlin

The Merlin Test takes its name from a bird of prey in the Falcon family, with high intelligence and unparalleled detection skills. Like its namesake, the Merlin gene expression profiling test is unique in its ability to detect targets, unveiling insights into the genomic, biologic, and clinical nature of a patient's melanoma.

Merlin addresses important challenges in dermatology practice

Approximately 100,000 Americans[1] are diagnosed annually with melanoma. Each patient requires staging to determine an optimal treatment strategy. It is crucial to assess whether the cancer has spread to the sentinel lymph nodes which might indicate additional risk for patients. While patients with very thick primary tumors should be referred for sentinel lymph node biopsy, NCCN guidelines 2021[2] for lower risk patients do not recommend biopsy.

The challenge for physicians is the group of patients in the middle for whom the effectiveness of a sentinel lymph node biopsy (SLNB) is uncertain. Currently, in 80-85%[3] of cases referred for SLNB, no nodal metastases are found, and there is no patient benefit. Yet these patients incur a >10%[4] risk of complications related to an unneeded, invasive surgical intervention requiring general anesthesia.

The Merlin Test may reduce the uncertainty in SLNB referral by clearly identifying patients who are at low risk of nodal metastasis and may safely forgo the surgery.

Merlin Test at a glance

- Developed in the U.S. by SkylineDx in collaboration with Mayo Clinic
- Validated in multi-center clinical trials in the US and EU
- Enhances clinicopathologic findings with critical tumor biology insights
- Stratifies patients who are at low risk of metastatic melanoma and can avoid SLNB
- Identifies patients at higher risk of metastases who may benefit by SLNB
- Delivers test results in just 5 days

> The Merlin Test seeks to improve risk assessment and individualized care for patients with a primary thin melanoma (pT1-pT3). Merlin can aid patients at risk of surgical complications, such as those with comorbidities or a lower extremity melanoma location. Reducing the need for surgery will facilitate clinical care delivery in lower resource settings, underserved populations, and during times of healthcare crises. The addition of novel diagnostics like the Merlin test aims to positively impact patient care.

Alexander Meves, MD
Mayo Clinic

Merlin is a powerful tool in personalized melanoma care

The clinical utility of individualized gene expression profiling (GEP) in the care of melanoma patients with T1-T3 cutaneous malignant melanoma is well-documented. NCCN guidelines state that GEP may help "differentiate melanomas at low versus high risk for metastases." However, current NCCN guidelines[2] note that GEP alone should not replace pathological staging procedures. Importantly, Merlin incorporates both clinicopathologic variables and GEP to provide valuable insights into a patient's metastatic risk. In this way, the test helps reduce biopsy rates.

Merlin provides clarity with a high Negative Predictive Value (NPV).

Reliable

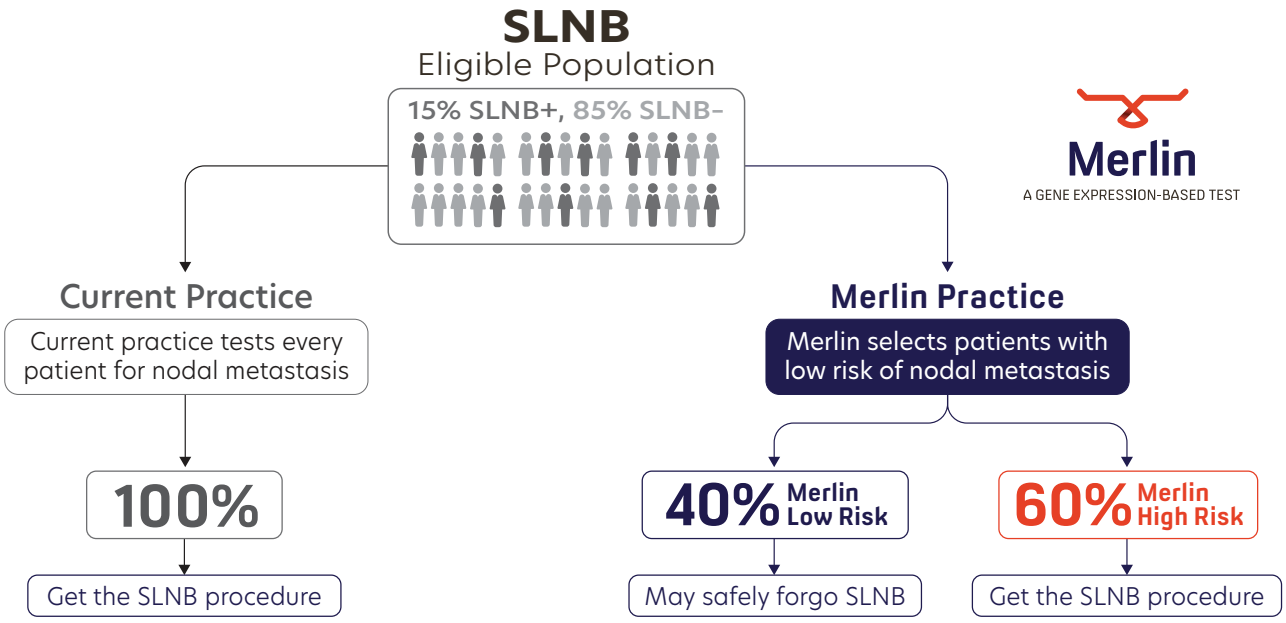
Co-developed by SkylineDx and Mayo Clinic, Merlin is rooted in the Falcon Melanoma R&D program—which develops and validates gene expression-based signatures. The test investigates the genes of interest that directly correlate to metastatic risk, integrating patient age and tumor thickness factors into the analysis.

Validated

Validated in multicenter clinical trials, Merlin has been shown to deliver a high NPV (Negative Predictive Value). The test enables physicians to optimize the clinical management of each patient by making an informed go or no-go decision on SLNB based on the individual disease characteristics.

Clinically relevant and actionable

The Merlin test provides a binary result, helping physicians distinguish low-risk patients, who may safely forgo SLNB, from patients at increased risk who may benefit from the procedure. After timely receipt of a Merlin test result, a physician may choose appropriate therapies sooner.



Current Results
All SLNB patients are exposed to >10% risk of intervention-related complications.

Merlin Results
The number of **unnecessary surgeries** is **reduced by 40%**

The intended use population is newly diagnosed pT1, pT2 and pT3 cutaneous melanoma patients prior to SLNB.

US validation studies confirm Merlin's clinical utility

Numerous studies have reported on Merlin's performance, including the following validation study highlighted below.

Confirming the Potential of CP-GEP to Reduce Unnecessary SLNB Procedures[5]

METHODS

A cohort of 208 US patients (age ≥18 years) with primary cutaneous melanoma from the Mayo Clinic and West Virginia University—subgroup analysis in patients ≥65 years (known to have the highest incidence of melanoma while their sentinel lymph positivity rate remains low). Patients were stratified according to their risk for nodal metastasis: CP-GEP (clinicopathologic-gene expression profiling) High Risk and CP-GEP Low Risk. The main performance measures were SLNB (sentinel lymph node biopsy) RR (reduction rate) and NPV (negative predictive value).

RESULTS

The SLNB positivity for the entire cohort was 21%. Of 153 patients in the T1-T2 patient group, CP-GEP showed an SLNB reduction rate of 41.8% at an NPV of 93.8%. Subgroup analysis of T1-T2 patients ≥65 years (51 patients) showed an SLNB positivity rate of 9.8% and SLNB of 43.1% at an NPV of 95.5%.

CONCLUSION

Confirmed the potential of CP-GEP to reduce unnecessary SLNB procedures in all relevant ages. Findings are especially pertinent in patients ≥65 years, where surgery is more elective. CP-GEP may be used to guide SLNB decisions in clinical practice.

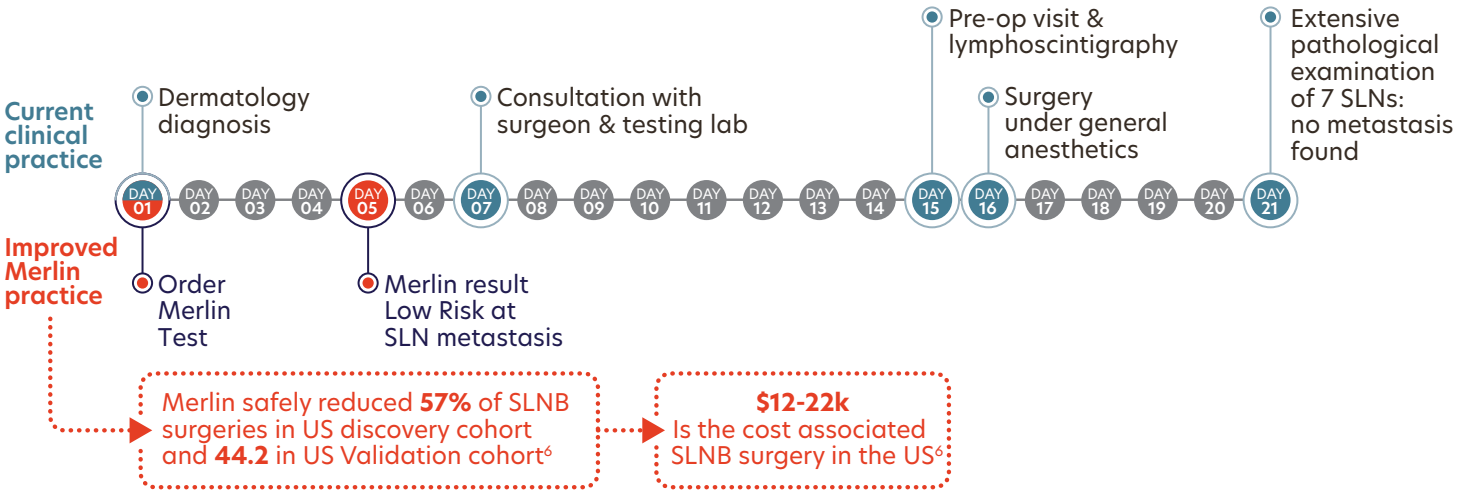
Merlin's Performance on the Subgroup of Patients 65 Years and Older[5]

Performance characterized by calculating sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), sentinel lymph node reduction rate (RR), true positive (TP), true negative (TN), false positive (FP), and false negative (FN).

Patient Subset	n	SLNB positivity rate	NPV	SLNB reduction rate
T1-T2	153	21%	93.8%	41.8%
T1-T2 ≥ 65	51	9.8%	95.5%	43.1%

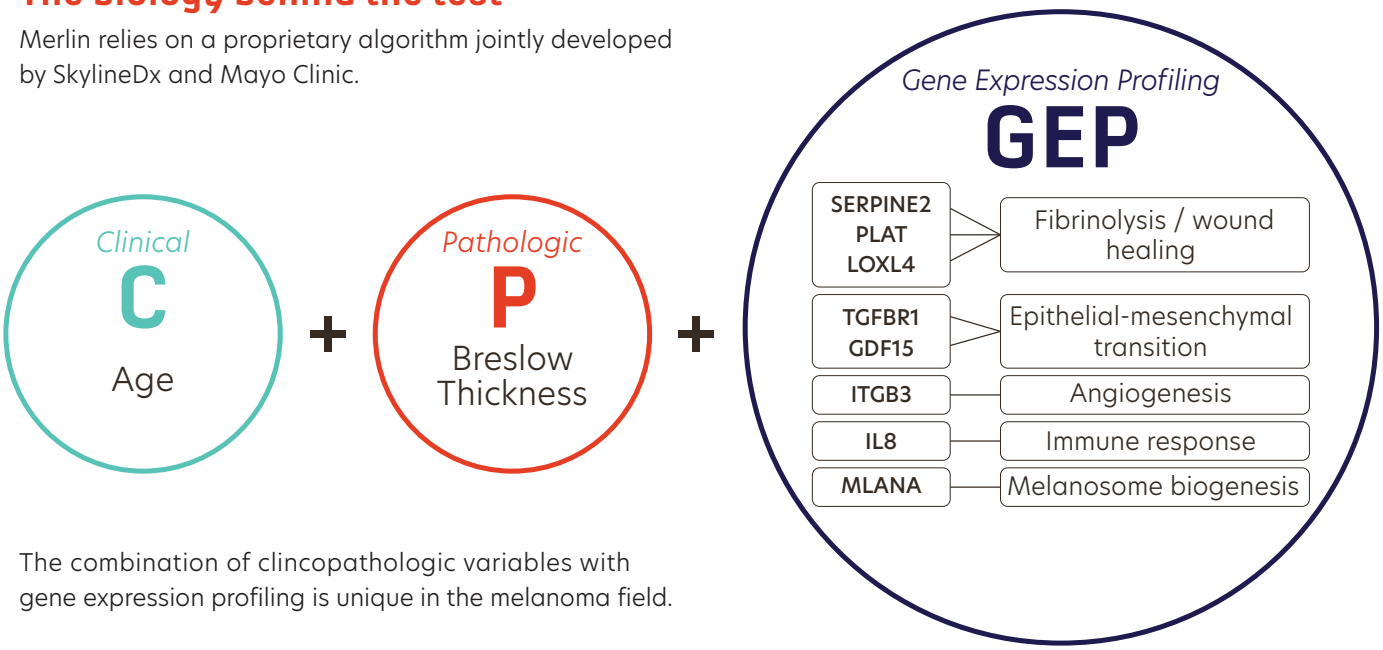
Case study[6]:

Merlin may help treating physicians reduce the number of office visits and associated patient anxiety, while accelerating the initiation of treatment up to 16 days.



The biology behind the test[7]

Merlin relies on a proprietary algorithm jointly developed by SkylineDx and Mayo Clinic.

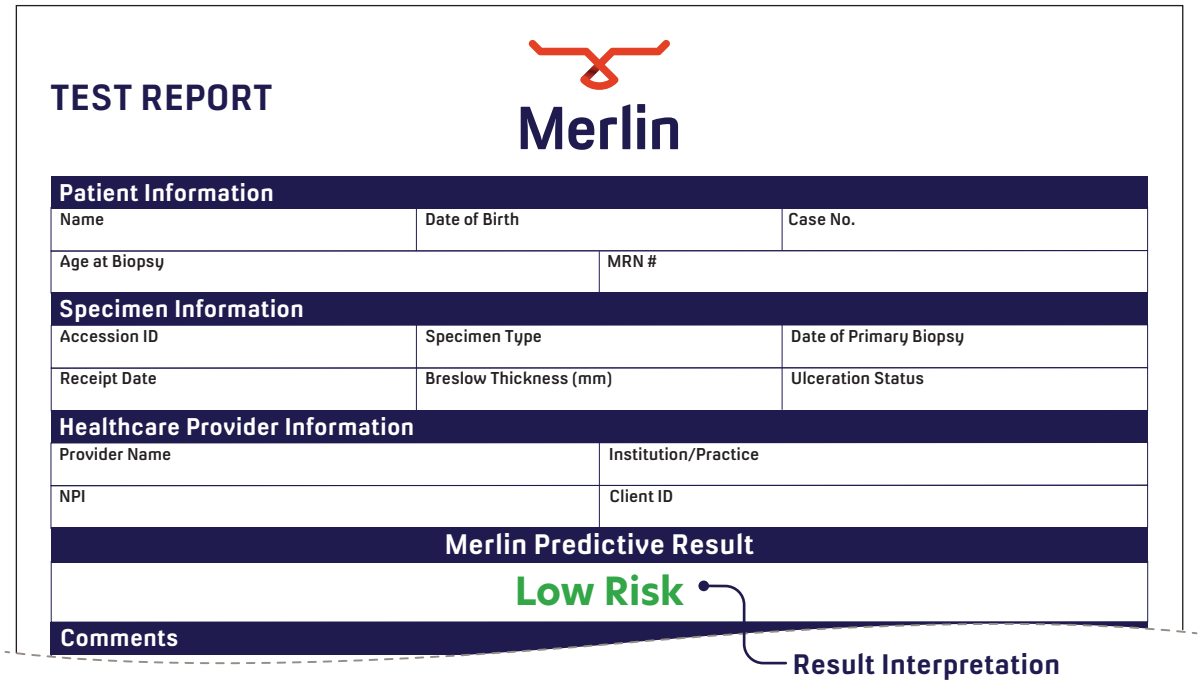


The combination of clincopathologic variables with gene expression profiling is unique in the melanoma field.

Merlin Test Results

Merlin may help treating physicians reduce the number of office visits and associated patient anxiety, while accelerating the initiation of treatment up to 16 days.

Low Risk Report



TEST REPORT

Merlin

Patient Information		
Name	Date of Birth	Case No.
Age at Biopsy	MRN #	
Specimen Information		
Accession ID	Specimen Type	Date of Primary Biopsy
Receipt Date	Breslow Thickness (mm)	Ulceration Status
Healthcare Provider Information		
Provider Name	Institution/Practice	
NPI	Client ID	

Merlin Predictive Result

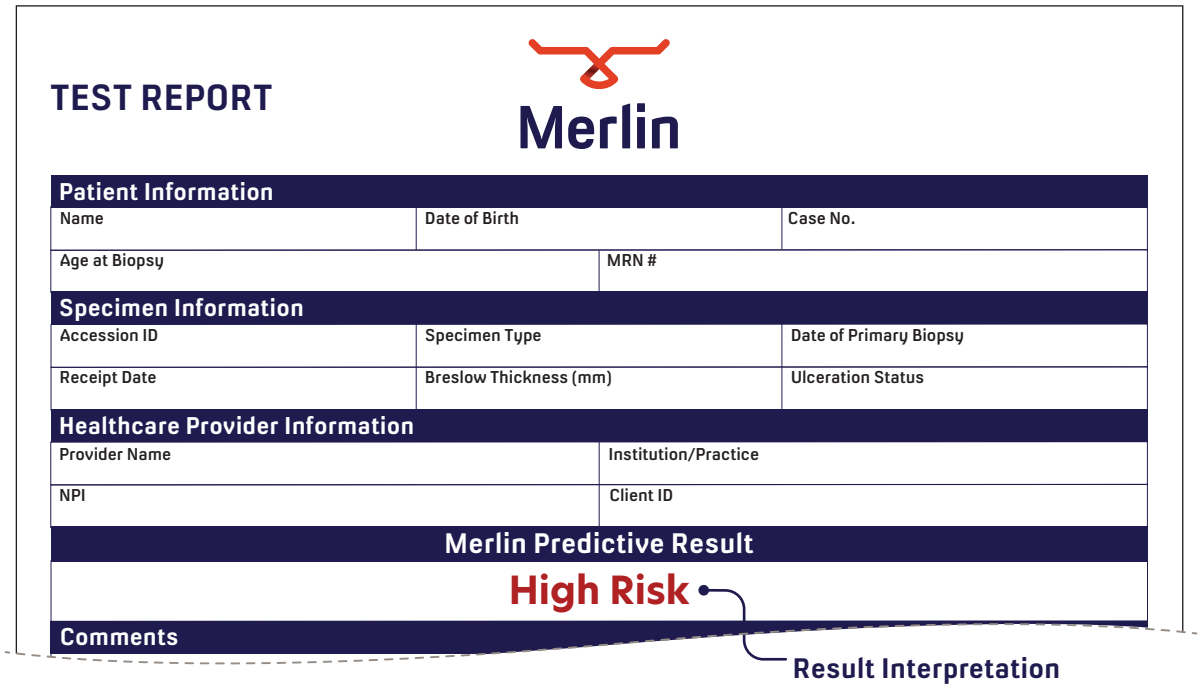
Low Risk

Comments

Result Interpretation

A **Low Risk result** indicates that the patient may have a low probability of metastasis and may not require a surgical procedure of a sentinel lymph node biopsy.

High Risk Report



TEST REPORT

Merlin

Patient Information		
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Healthcare Provider Information		
Provider Name	Institution/Practice	
NPI	Client ID	

Merlin Predictive Result

High Risk

Comments

Result Interpretation

A **High Risk result** indicates that the patient may have a high probability for sentinel node metastasis and therefore should be considered for a biopsy.

We promise to provide personalized service

Outstanding customer service

With its U.S. headquarters in San Diego, California, SkylineDx is a highly efficient laboratory with a big heart. We believe it is our job to make a difference by improving the quality of patients' lives. As we continue to innovate and serve your patients, we promise to provide the personalized service—expert, compassionate, and timely—that you and your patients deserve.

Ordering

To order Merlin testing or to set up an account, please email **customerserviceUSA@skylinedx.com** or visit our website at **MerlinMelanomaTest.com**

Tissue Requirements

- **Specimen:** Formalin-Fixed and Paraffin Embedded (FFPE) primary cutaneous melanoma biopsy tissue (skin biopsy required), either as freshly cut curls in a tube provided in kit or mounted on glass slides (unstained, unbaked) and placed in slide box mailer included in kit.
- **Specimen volume:** 5 x 10 microns FFPE tissue as freshly cut curls in tube provided in kit or mounted on glass slides (charged, unstained, unbaked).

Billing

SkylineDx will bill your patient's insurance company or Medicare for the Merlin test. SkylineDx recognizes that a diagnosis of cancer can cause a financial burden so we directly contract with insurance providers to obtain the best coverage possible. Depending on your patient's insurance provider; a copayment, coinsurance, and/or deductible may be indicated. Patients may qualify for the SkylineDx Patient Assistance Program. Please contact your SkylineDx representative, or customer service at (888) 770-9076 with any questions or to inquire about payment options.

The Merlin gene expression profile provides actionable information to complement clinical management decisions and help you improve patient care.

Merlin Test Indication

Utility
Identify patients that may safely forgo SLNB

Intended use population
SLNB eligible patients

Which means
- Intended for patients with newly diagnosed invasive malignant melanoma of the skin (AJCC 8th edition staging guidelines)
- pT1b-pT3 (Breslow thickness ≥0.8 mm to 4.0 mm)
- pT1a (Breslow thickness <0.8 mm) AND one or more of the following:
  - Mitotic rate ≥2/mm^2
  - Patient age at time of primary melanoma biopsy <40 years old
  - Presence of lymphovascular invasion
- Without clinical evidence of nodal involvement or distant metastases (cN0M0)
- Without documented history of another (prior or concurrent) primary invasive melanoma of pT1 or greater at any site within the last five years

References:

1. https://seer.cancer.gov/statfacts/html/melan.html
2. NCCN guidelines 2021
3. Morton DL, Thompson JF, Cochran AJ, et al: Final trial report of sentinel-node biopsy versus nodal observation in melanoma. N Engl J Med 370:599-609, 2014
4. Moody JA, Ali RF, Carbone AC, et al: Complications of sentinel lymph node biopsy for melanoma - A systematic review of the literature. Eur J Surg Oncol 43:270-277, 2017
5. Yousaf & Tjien-Fooh et al., Validation of CP-GEP (Merlin Assay) for predicting sentinel lymph node metastasis in primary cutaneous melanoma patients: A U.S. cohort study. 2021 Int J Dermatol
6. Meves & Eggermont, Deselecting Melanoma Patients for Sentinel Lymph Node Biopsy During COVID-19: Clinical Utility of Tumor Molecular Profiling. 2020 Mayo Clinic Proceedings IQC
7. Bellomo et al. A Model Combining Tumor Molecular and Clinicopathologic Risk Factors Predicts Sentinel Lymph Node Metastasis in Primary Cutaneous Melanoma. 2021, JCO PO

We welcome your inquiries.
To order Merlin or for additional information,
please contact us at:

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MerlinMelanomaTest.com

SkylineDx

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