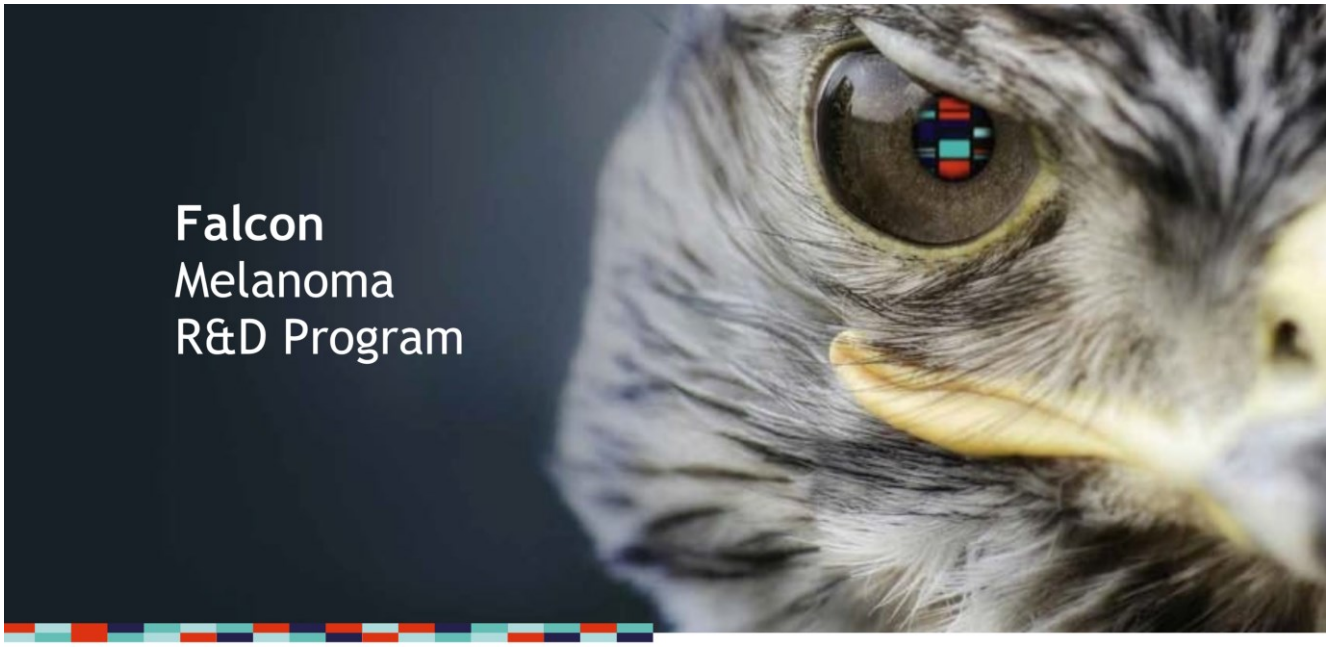


Merlin

# Stromal gene expression predicts sentinel lymph node metastasis of primary cutaneous melanoma

**Sindhuja Sominidi-Damodaran, Suzette Arias-Mejias, Mark R. Pittelkow, Mark A. Cappel, Julia S. Lehman, Tina J. Hieken, Martin H. van Vliet, Jvalini Dwarkasing, Domenico Bellomo, Alexander Meves**

*Abstract at EADO 2019*

**Introduction & Objectives:** Greater than 80% of melanoma patients who undergo sentinel lymph node (SLN) biopsy are SLN negative. Our objective was to use molecular markers crucial in the reciprocal and bidirectional interaction between integrins and the tumor microenvironment to distinguish between high-risk patients and patients who can safely forego SLN biopsy due to their low risk of metastasis.

**Material & Methods:** Differentially expressed genes with functional roles in melanoma metastasis were discovered by next-generation sequencing, analysis of publically available genomic datasets and a review of the cancer literature. Of 192 candidate biomarkers discovered 109 were quantified by quantitative PCR in a cohort of 754 consecutive thin and intermediate-thickness melanomas. Outcome of interest was SLN metastasis within 90 days of melanoma diagnosis. Logistic regression with regularization was applied to clinicopathologic variables and molecular data in a Double-Loop-Cross-Validation (DLCV) training-validation scheme. Three models were built using: 1) only clinicopathologic features (CLPA), 2) only gene expression profile (GEP), 3) both clinicopathologic and gene expression profile (CLPA-GEP).

**Results:** 128/754 patients (17%) were SLN positive. Clinicopathologic features associated with SLN metastasis included younger age, thicker Breslow depth, tumor ulceration and mitotic rate. The SLN biopsy reduction rate (RR) of the predictive model that included stromal gene expression (CLPA-GEP) was significantly greater than a model that only considered either clinicopathologic or gene expression variables (see Figure 1), with a negative predictive rate (NPV) of 97% for the entire cohort. CLPA-GEP achieved a SLN biopsy RR of up to 70% for clinical stage T1b melanoma with an NPV >95% across all T stages (see Table 1). A greater SLN biopsy RR can be achieved with a less stringent NPV.

**Conclusions:** A predictive model including stromal gene expression with clinicopathologic variables can be used to identify melanoma patients who can safely forego SLN biopsy.

**Table 1.** Performance of the CLPA-GEP stratified by T stage (SE, sensitivity; SP, specificity; NPV, negative predictive value; SLNB.RR, SLN biopsy reduction rate; AUC, area under the curve).

| Input | SE | SP | NPV | SLNB.RR |
|---|---|---|---|---|
| T1b | 0.47 | 0.71 | 0.98 | 0.7 |
| T2 | 0.89 | 0.38 | 0.96 | 0.34 |
| T3 | 1 | 0.063 | 0.99 | 0.042 |

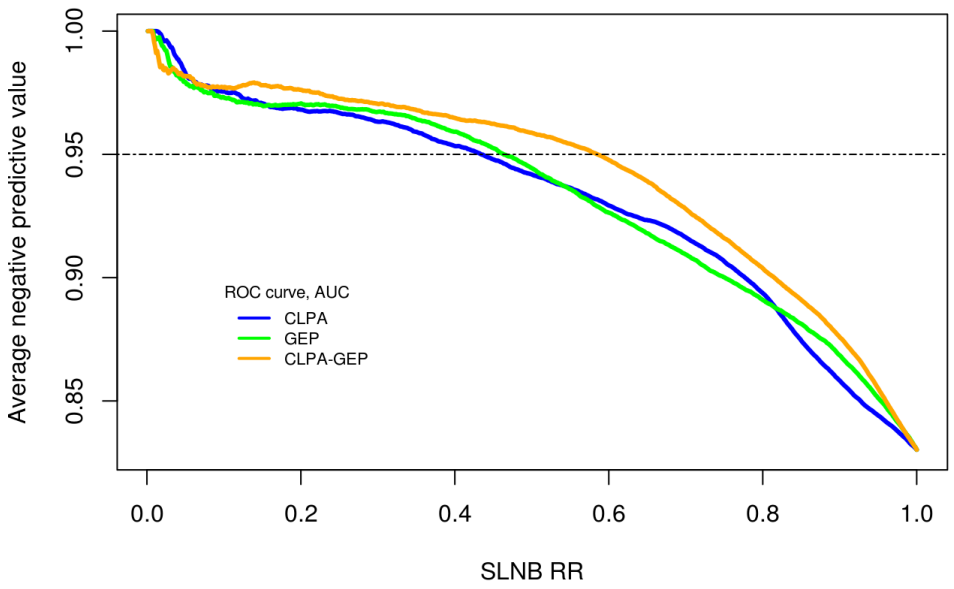


**Figure 1** NPV and SLNB RR curves for CLPA, GEP and CLPA-GEP models

The figure depicts the Negative Predictive Value (NPV) versus the Sentinel Lymph Node Reduction Rate (SLNB RR) for the logistic regression classifiers trained in DLCV on: 1) gene expression, 2) clinicopathological variables, 3) gene expression and clinicopathological variables combined.