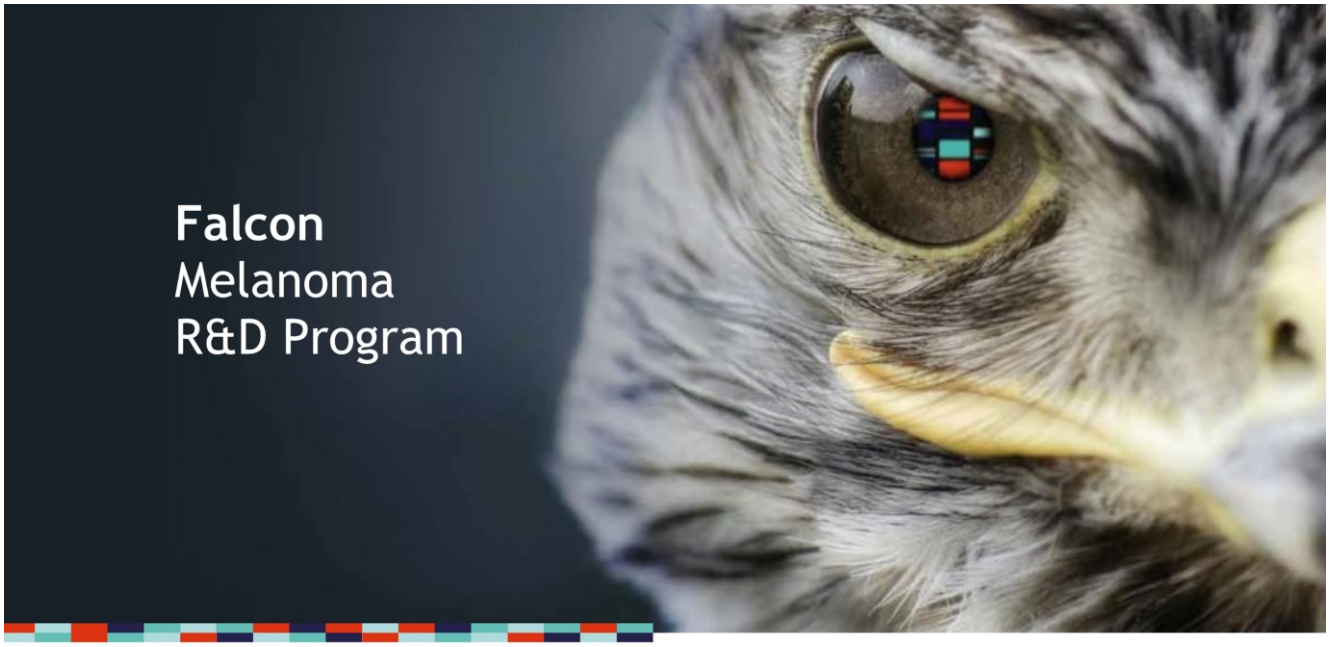

Merlin

A molecular model to identify patients who can safely forgo sentinel lymph node biopsy in primary cutaneous melanoma

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Abstract at CIM 2019

Purpose

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.

Patients and Methods

Genes with functional roles in melanoma metastasis were discovered by analysis of next-generation sequencing data, case-control studies, analysis of publicly available genomic datasets and a review of the cancer literature. Of 192 candidate biomarkers discovered, 108 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 LASSO regularization was applied to clinicopathologic variables and molecular data in a cross-validation training-validation scheme. Three models were built using: only clinicopathologic features (CP); only gene expression profiling (GEP); and both clinicopathologic and gene expression profiling (CP-GEP).

Results

128/754 patients (17%) were SLN positive. Expression of genes with roles in extracellular matrix remodeling (glia-derived nexin, growth differentiation factor 15, integrin ß3, interleukin 8, lysyl oxidase homolog 4, TGFß receptor type 1 and tissue-type plasminogen activator) and melanosome function (antigen recognized by T-cells) were associated with SLN metastasis. The predictive ability of a model that only considered CP or GEP variables was outperformed by a model which included molecular variables in combination with the clinicopathologic predictors Breslow depth and patient age. CP-GEP achieved a SLN biopsy reduction rate of 80% for clinical stage T1b melanoma with an NPV >95% across all T stages.

Conclusion

A combined model including clinicopathologic and gene expression variables improved the identification of melanoma patients who can safely forgo SLN biopsy due to their less than 5% risk of nodal metastasis.