# Clinical Prognostic Models for Stage II Melanoma Using Tumor miRNA Signatures

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## Technology

NYU researchers from the Polsky Lab have characterized micro RNA (miRNA) expression and identified miRNA signatures in primary melanomas (n=175), enhancing the clinicopathological parameters needed to predict death from melanoma within 5-years from initial diagnosis for patients with stage II disease. Combining these miRNA signatures with clinical staging parameters (i.e., Breslow tumor thickness and tumor ulceration) improved the accuracy of prognostic models based on the staging parameters alone. The unique prediction model, which is based on data from patients with and without recurrence of their melanoma, estimates the probability of a patient's recurrence at clinically relevant time points of 24, 36, 48 and 60 months. Impressively, this innovative statistical tool improves the overall prognostic accuracy from 30% for models based only on the clinical staging factors to 62% for the model combining miRNA expression with the clinical staging factors. Using the miRNA-based assay, 94% of patients with a negative result are expected to have been surgically cured and can be categorized as low-risk (negative predictive value), and 40% of patients with a positive result are expected to recur and be categorized as high-risk (positive predictive value). This compares with 75% negative predictive value and 25% positive predictive value for a model based on staging criteria alone. The study is currently the most comprehensive collection of miRNA expression analysis in primary melanomas.

## Background

Melanoma is the sixth most common cancer in the US with about 97,610 newly diagnosed patients in 2023. The global melanoma therapeutics market was valued at $5.5 billion in 2022, and is projected to reach around USD 14.59 billion by 2032, growing with a compound annual growth rate (CAGR) of 10.3%. There are no approved predictive models focused only on stage II melanoma recurrence. Clinical AJCC staging factors to select high-risk patients are unreliable due to inconsistent clinical outcomes, which may indicate underlying biological differences in the tumors or the patients themselves. Adjuvant pembrolizumab (an anti PD-1 immunotherapy) is currently the treatment strategy for stages IIB and IIC melanoma. Given the risks of anti PD-1 immunotherapy-related toxicity risks (16% of patients will discontinue treatment due to severe adverse effects), the high costs of immunotherapy, and the relatively high cure rate from surgery (estimated to be 75% by 5 years after initial excision) it is crucial to accurately identify stage II melanoma patients who may benefit from adjuvant therapy. This will distinguish patients with ‘high-risk of recurrence’ from surgically cured patients, thereby sparring ‘low-risk’ patients from potential toxicity and costs of unnecessary treatment.

## Development Status

Future work will replicate these results in additional patient cohorts, and adapt the technology for use in clinical laboratories. This technology is one of four projects awarded by the National Cancer Institute (NCI) to NYU Langone Health Melanoma SPORE program to develop better

tools to predict which patients with advanced melanoma will benefit from immune checkpoint inhibitors.

### Applications

Assessment of risk or recurrence in stage II melanoma patients.

### Advantages

- **>90% accuracy** in predicting individuals who are at low risk for melanoma recurrence.
- **Less prone to variations in degradation between different samples.** The technology analyzes miRNAs, which are more stable in Formalin-fixed paraffin-embedded (FFPE) tumor material than messenger RNA (mRNA), and therefore less subject to sample-to-sample variations in degradation.
- **Unique in its approach**, as others typically use DNA or GEP (mRNA gene expression profiles) to assess cancer severity and risk of recurrence combing stages I and II; this model was developed using only stage II patients (the intended-use population) because stage I patients have a very high cure rate and are not offered adjuvant therapy.

### Intellectual Property

NYU has filed a U.S. provisional patent.