immunoSEQ®

CASE STUDY

ONCOLOGY

Molecular analysis of primary melanoma T cells identifies patients at risk for metastatic recurrence

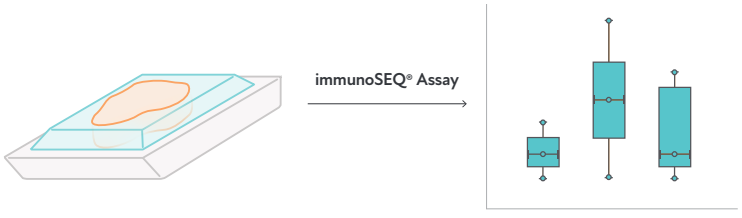
Pruessmann W, et al. (2020) *Nature Cancer* DOI:10.1038/s43018-019-0019-5

Background

Staging of primary melanoma (>1 mm) has not changed in decades. The standard process includes evaluating tumor thickness (Breslow thickness), ulceration, mitotic rate, and regional lymph node disease. Breslow thickness is the main factor currently used to stage primary melanomas. Primary melanomas can be cured by resection but as thickness increases, so does the recurrence rate. With each additional millimeter, the chance of recurrence (developing metastases) increases. In fact, 38.1% of primary melanomas that are >4 mm will recur metastatically within 5 years.[1] The ability to more accurately identify primary melanoma patients at risk for disease progression is an important unmet medical need.

Aims

To investigate if features of the T-cell receptor beta (TCRß) repertoire of tumors correlate with recurrence in primary melanoma patients.



Formalin-fixed paraffin-embedded (FFPE) tumor tissue

Correlate with progression-free survival (PFS) or metastasis

Methods

Using the immunoSEQ® Human TCRB Assay, T-cell fraction (TCFr), which reports the fraction of total nucleated cells that are T cells, was calculated for archived FFPE tumor tissue samples from 199 patients with primary melanoma.

1. FFPE tumor tissue → gDNA → **immunoSEQ hsTCRB Assay**
2. Determine repertoire metrics
3. Investigate correlation to clinical outcomes

WHY IMMUNOSEQ?

- Compatible with archived tissue samples including FFPE
- The quantitative nature enables enumeration of total T cells and nucleated cells, resulting in a robust T-cell fraction metric

1. Elsaesser, O. et al. Prognosis of sentinel node staged patients with primary cutaneous melanoma. PLoS ONE 7, e29791 (2012).

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Results

- TCFr, as measured by the immunoSEQ Assay, could predict PFS and was independent of the standard metrics used to predict melanoma prognosis; further, it improved upon conventional histopathological tumor-infiltrating lymphocytes (TIL) grading for PFS prediction.
- The combination of TCFr and Breslow thickness was better than any other combination in predicting recurrence.
- Most notably, a clinically transferable cut-off of TCFr >20% was determined to be a positive prognostic marker of survival, as melanomas with a low TCFr (<20%) were 2.5 times more likely to recur.

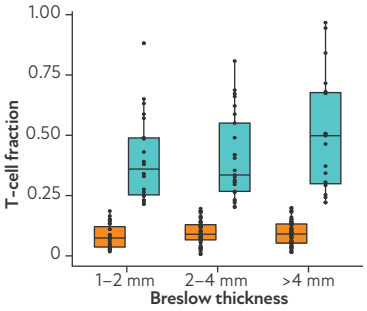

Figure 1. T-cell fraction is an independent predictor from Breslow thickness which is the current standard prognostic factor for melanoma.

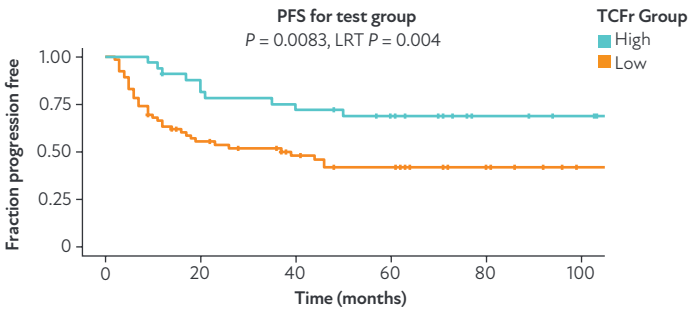

Figure 2. Using the optimized TCFr cut-off of 20% in the held-out test group, patients in the high TCFr group had significantly longer PFS.

Conclusions

Additional prospective studies may elucidate if staging primary melanomas based on the combination of Breslow thickness and TCFr may also be a clinically applicable way to predict patient response to immunotherapies.

Data is available in immuneACCESS at https://doi.org/10.21417/WP2019NC

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