Inherited Genomic Signature Testing for Improved Immune-Checkpoint Inhibition Cancer Therapies

A robust, non-invasive predictive biomarker for personalized selection of cancer treatment options involving immune-checkpoint inhibition (ICI) therapies.

Technology ID
KIR03-03

Category
Life Sciences/Diagnostics

Jane Liew

Authors
Tomas Kirchhoff, PhD

Learn more

Technology

The Kirchhoff Laboratory has developed and validated the use of an inherited genomic signature (HG-sig) as a novel biomarker predictive of ICI response. This biomarker was identified in a first-of-its-kind comprehensive omics analysis of peripheral ICI predictors in metastatic melanoma (MM) as part of a large clinical trial. The team identified differences in genetic signatures associated with distinct baseline peripheral CD8+ T cell phenotypes that may be related to differences in ROS tolerance. Most notably, the team identified that HG-sig, as a novel genomic marker, accurately predicts resistance to nivolumab-based singular or combination anti-PD1 therapies. The team also found the same HG-sig patients respond significantly better to an alternate first-line anti-PD1 therapy. These findings have been validated in a large international consortium of more than 1200 MM patient samples, representing both a clinical trial and the standard-of-care setting, across 3 independent patient populations. This HG-sig represents a novel predictive biomarker for ICI efficacy and resistance which can be determined non-invasively and irrespective of disease stage for a wide range of metastatic cancers.

Background

ICIs have substantially improved metastatic cancer survival, but in MM for example less than 50% of patients respond to the treatments, and only 20-40% shows >5-year overall survival benefit. The current ICI Ipilimumab which targets the B7/CTLA-4 axis only has a 20% response rate, while Nivolumab or Pembrolizumab, which target the PD-L1/PD-1 axis, only have a 40% response rate. Current predictive biomarkers, primarily derived from the tumor and tumor microenvironment, do not sufficiently explain the heterogeneity of outcomes observed in ICI-treated patients. The growing number of ICI combinations and a heterogeneity of the observed clinical efficacies implore the critical clinical need for biomarkers with the capacity to identify the most beneficial treatment options. Current ICI predictors, benefiting < 40% of ICI-treated patients, are not sufficient for this purpose. Also, these tumor-based biomarkers require costly and laborious assessment. The Kirchhoff laboratory's approach which relies on the detection of inherited signatures, overcomes these challenges by offering a non-invasive and disease stage agnostic determination of ICI efficacy.

Applications

- Personalized treatment selection for cancer patients undergoing ICI therapies.
- Routine screening for best ICI combinations in cancer patients.

Advantages

- **Personalized approach:** Predicts ICI efficacy to single-line anti-PD1 and combination therapy (anti-CTLA4/anti-PD1)
- **Novel biomarkers:** Identifies previously undervalued markers of ICI resistance.
- **Improved treatment plans/treatment stratification:** Enables tailored treatment strategies for cancer patients, potentially improving outcomes.
- **Non-invasive:** Inherited genomic signature testing can be performed on non-invasive samples such as saliva and blood, avoiding the need for invasive tumor biopsies.
- **Disease state agnostic:** HG-sig represents a patient's underlying germline genetics and is not contingent on disease state and can accurately be performed at any time

Development Stage

Development of a prototype of a feasible screening method that would be scalable, robust, and applicable for use in the standard clinical labs.

Intellectual Property

NYU has filed a PCT patent application covering the method of determining ICI resistance based on HG-sig.

References

1. Chat V, Ferguson R, Simpson D, et al. , https://pubmed.ncbi.nlm.nih.gov/30863922/