Methods For Predicting Response Patterns To Anti-PD-1 (aPD-1) Therapy In Metastatic Melanoma

Tech ID: 27472 / UC Case 2016-582-0

SUMMARY

Dr. Roger Lo and colleagues in the Department of Medicine at UCLA have identified a method to predict a melanoma patient's resistance to pembrolizumab and other immune checkpoint inhibitors.

BACKGROUND

Immune checkpoint inhibitors are the most recent stars in cancer therapeutics: the first 4+ drugs in the category have received breakthrough designation from the FDA and are showing impressive results in a variety of cancers. However, there are still many patients who do not respond to immune checkpoint inhibitors, reaching 60-70% in the two anti-PD-1 antibodies approved by the FDA.

Finding a predictor of resistance would allow personalization of the patient's drug regimen and prevent unnecessary side effects. Several factors have been shown to correlate with response to immune checkpoint inhibitors, including reduced T cell infiltration into the tumor, pre-therapy PD-L1 expression, and increased overall mutational load in the tumor. But none of these criteria have been successful individually, as they cannot effectively synthesize the multi-factorial influences leading to patient resistance.

INNOVATION

Several factors have been proposed previously as predictors of resistance to immune checkpoint inhibitors: lack of tumor-infiltrating T cells, pre-therapy PD-L1 expression, and increased tumor mutational load. However, no single metric can take into account the multitude of influences that determine patient response. UCLA scientists have established a more effective approach to predicting PD-1 therapeutic resistance in metastatic melanoma by identifying a transcriptional signature called IPRES (innate anti-PD-1 resistance).

Through analysis of melanoma patient RNA-seq data, researchers identified multiple categories of genes that, when observed in total, show distinct differences between resistant and sensitive tumors. By testing the "transcriptome" of a patient's tumor against the known IPRES signature, UCLA scientists can now determine if a melanoma patient will respond to therapy.

The proposed technology could be commercialized as a billable service for hospitals or as analysis software for providers or labs to use directly.

APPLICATIONS

PD-1 and/or PD-L1 therapeutics have been used in clinical trials for many and varied cancers, including the ones listed below. This technology is intended to identify patients who are likely resistant to aPD-1 therapy before they undergo treatment. Because the PD-1/PD-L1 pathway is not specific to one cancer, the proposed method may be applicable to some or all of the other cancers.

- Melanoma
- NSCLC (non-small cell lung cancer)
- SCLC (small cell lung cancer)
- Non-Hodgkin lymphoma
- Hodgkin lymphoma
- AML
- Follicular lymphoma

INVENTORS

▶ Lo, Roger S.

OTHER INFORMATION

KEYWORDS

Cancer immunotherapy; antibody therapy; drug resistance; programmed cell death-1 (PD-1); programmed death ligand 1 (PD-L1); pembrolizumab; nivolumab; RNA-seq; mutatome; transcriptome; proteome; metastatic melanoma; immune checkpoint inhibitor

CATEGORIZED AS

▶ **Medical**
  ▶ Diagnostics
  ▶ Disease: Cancer
▶ **Research Tools**
  ▶ Antibodies
  ▶ Screening Assays

RELATED CASES

2016-582-0

- ▸ Breast cancer
- ▸ Ovarian cancer
- ▸ Cervical cancer
- ▸ Vaginal cancer
- ▸ Vulvar cancer
- ▸ Pancreatic cancer
- ▸ Renal cell carcinoma
- ▸ Bladder cancer
- ▸ Gastric cancer
- ▸ Colon cancer
- ▸ Esophageal cancer
- ▸ Nasopharyngeal cancer
- ▸ HNSCC
- ▸ Glioblastoma
- ▸ Osteosarcoma
- ▸ Rhabdomyosarcoma
- ▸ Ewing sarcoma

ADVANTAGES

UCLA scientists have identified a superior metric for predicting resistance in melanoma patients, verified against patient specimens. By identifying patients who are resistant to aPD-1 therapy before they undergo treatment, patients can avoid unnecessary side effects and toxicities. Providers can also prescribe or suggest more effective treatment modalities.

STATE OF DEVELOPMENT

The IPRES transcription signature has been validated in four cohorts (384 total tumors) of metastatic melanoma RNA-seq: in-house dataset; Hugo et al., 2015; Van Allen et al., 2015; TCGA 2015.

PATENT STATUS

Country	Type	Number	Dated	Case
Germany	Issued Patent	3430171	02/03/2022	2016-582
European Patent Office	Issued Patent	3430171	02/03/2022	2016-582
France	Issued Patent	3430171	02/03/2022	2016-582
United Kingdom	Issued Patent	3430171	02/03/2022	2016-582
United States Of America	Issued Patent	10744116	08/01/2020	2016-582

RELATED MATERIALS

- ▸ Genomic and transcriptomic features of response to anti-PD-1 therapy in metastatic melanoma, Cell 2016.

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