Genetic Mechanisms Of Resistance To Anti-Pd-1/L1

Tech ID: 27628 / UC Case 2016-075-0

SUMMARY

UCLA researchers have identified a rare genetic mutation in the interferon receptor signaling pathway that can be used as a diagnostic to predict whether a patient will be or has become resistant to a cancer immunotherapy.

BACKGROUND

Clinical responses to programmed death-1 (PD-1) blockade therapy have revolutionized cancer care with evidence of durable tumor responses in at least 15 different cancers. However, only a minority of patients respond, and some who respond eventually become resistant.

Researchers at UCLA have discovered that rare genetic mutations in the interferon receptor signaling pathway can result in lack of PD-L1 upregulation upon interferon exposure and result in innate resistance to PD-1 blockade. These include loss of function mutations that truncate, inactivate, or alter the proper splicing of JAK1 or JAK2, leading to a lack of downstream signaling from the interferon receptor. Additionally, this would include epigenetic changes that prevent IRF1 protein expression and subsequent PD-L1 induction upon interferon gamma exposure.

INNOVATION

Current methods to predict whether a patient will become or has become resistant to cancer immunotherapy do not exist. Assessment by immunohistochemistry (IHC) is the current approach to determine if patients may respond to anti-PD-1 or anti-PD-L1 antibodies. UCLA researchers have developed a method for determining a patient's risk for cancer progression due to resistance to immunotherapy. These biomarkers may be used as predictors for determining patient risk for cancer progression or regression. By assessing PD-L1 by immunohistochemistry they can determine whether a patient may respond to anti-PD-1 or anti-PD-L1 antibodies. This method can lead to individualized management of patients and optimized treatment which can result in decreased toxicity and a significant reduction in cost of by avoiding use of unnecessary therapy.

APPLICATIONS

- Personalized medicine: determine proper course of treatment for patients undergoing cancer immunotherapy
- Enriching patient population: identify patients likely to respond to treatment

ADVANTAGES

Can be used to predict whether a patient will become or has become resistant to cancer immunotherapy

Individualized management of patients can lead to optimized treatment for each patient:

- Toxicity may be decreased by avoiding unnecessary therapy
- Cost of care may be significantly reduced by avoiding unnecessary therapy
- Efficacy may be optimized by selecting treatments for patients who would experience the maximal benefit

STATE OF DEVELOPMENT

This invention has been shown to be able to detect PD-L1 by immunohistochemistry.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10711312	07/14/2020	2016-075

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OTHER INFORMATION

KEYWORDS

Cancer immunotherapy, immunotherapy resistance, PD-1 blockade-based therapy, cancer therapy diagnostics, immunohistochemistry, anti-PD-1 antibodies, anti-PD-L1 antibodies, pharmacogenetics, personalized medicine, individualized medicine, molecular analysis, molecular profiling, companion diagnostics

CATEGORIZED AS

- **Medical**
  - Diagnostics
  - Disease: Cancer

RELATED CASES

2016-075-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- PAK4 in Cancer Immune Exclusion
- A Codon-Optimized Lentiviral Vector For Stem Cell Reprogramming

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