



Combination Immunotherapy

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SUMMARY

UCLA researchers have developed a combination immunotherapy for lung cancer that functions by evoking anti-tumor immune responses in lung cancer patients.

BACKGROUND

Lung cancer is a challenging health problem, claiming more than 1.1 million deaths worldwide annually. Despite incredible medical progress, the long-term survival rate of lung cancer remains low due to the high risk of recurrence. Therefore, immunotherapy which harnesses the immune system to react against tumors can be an attractive approach with potential for long term anti-tumor benefit.

CCL21 (secondary lymphoid chemokine, SLC) is a lymphoid chemokine which, upon binding to the CCR7 gene receptor, functions as a chemo-attractant for mature dendritic, naïve, and memory T cells. PD-L1 (Programmed death receptor-ligand 1) decreases T cell receptor-mediated proliferation and cytokine production by interacting with PD1 (Programmed cell death protein 1). While CCL21 enhances cell-mediated immunity against tumor cells, the PD-L1/PD1 pathway plays a major role in immune evasion of tumor cells.

INNOVATION

Dr. Dubinett’s group has previously developed an immunotherapy which evokes anti-tumor immune responses in lung cancer patients by intratumoral administration of dendritic cells expressing the CCR7 receptor ligand CCL21. Their recent clinical data shows that the efficacy of this immunotherapy is most prominent in patients with low tumor PD-1L expression level. This result indicates that blocking PD-1L/PD1 pathway in combination with the CCL21 therapy can be a very effective treatment for lung cancer.

APPLICATIONS

Immunotherapy for PD-1L-positive lung cancer patients.

ADVANTAGES

- ▶ CCL21 has anti-angiogenic activities in addition to its ability to reduce tumor burden
- ▶ The combination therapy improves the efficacy of the existing cancer immunotherapies
- ▶ The combination therapy may have therapeutic implications for other types of cancers

STATE OF DEVELOPMENT

A phase I clinical trial was carried out using intratumoral injection of CCL21 gene modified autologous dendritic cells in lung cancer. Results from the trial demonstrated that 1) anti-tumor specific immune responses are elicited and correlate with lower PD-L1 expression, and 2) cytotoxic CD8 T cell infiltration into the tumor is induced.

PATENT STATUS

Country	Type	Number	Dated	Case
Japan	Issued Patent	7305300	06/30/2023	2015-348
European Patent Office	Issued Patent	3215182	01/04/2023	2015-348
United Kingdom	Issued Patent	3215182	01/04/2023	2015-348
Germany	Issued Patent	60 2015 082 196.3	12/22/2022	2015-348
France	Issued Patent	3215182	12/22/2022	2015-348

CONTACT

UCLA Technology Development Group
ncd@tdg.ucla.edu
tel: 310.794.0558.



INVENTORS

- ▶ Dubinett, Steven M.
- ▶ Dubinett, Steven M.

OTHER INFORMATION

KEYWORDS

Lung cancer, immunotherapy, therapeutics, immunity

CATEGORIZED AS

- ▶ Medical
 - ▶ Disease: Cancer
 - ▶ Therapeutics

RELATED CASES

2015-348-0

United States Of America	Issued Patent	11,236,139	02/01/2022	2015-348
United States Of America	Published Application	20220162279	05/26/2022	2015-348

RELATED MATERIALS

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UCLA Technology Development Group

10889 Wilshire Blvd., Suite 920, Los Angeles, CA 90095

tdg.ucla.edu

Tel: 310.794.0558 | Fax: 310.794.0638 | ncd@tdg.ucla.edu

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