Combination Immunotherapies for Treatment of Liver Cancer

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BACKGROUND

Primary liver cancer, with the majority being hepatocellular carcinoma (HCC), is now the second leading cause of cancer mortality and the fifth most common cancer worldwide, claiming approximately 800,000 life every year. HCC is a chemotherapy resistant tumor with limited treatment options including surgical resection, liver transplantation and local ablation at the early stages. Sorafenib, a multi-kinase inhibitor, remains a first-line systemic drug for advanced HCC even with poor outcomes, and similar low therapeutic benefits were reported for regorafenib, lenvatinib, and cabozantinib. Over 100 clinical trials that tested other compounds or approaches have failed to show therapeutic benefit to HCC patients.

Immunotherapy by blocking inhibitory pathways in T lymphocytes, such as the PD-L1/PD-1 axis, is being widely tested in various solid tumors. Notably, this emerging therapeutic approach is already in clinical trials for advanced HCC in multi-centers around the globe. Two latest reports on open-label, non-randomized, phase 1/2 trials with pembrolizumab or nivolumab indicated manageable safety in advanced HCC patients with or without prior sorafenib treatment, albeit with very limited therapeutic benefits observed so far. The outcome of immunotherapy for liver cancer can be compounded by the unique immunotolerant microenvironment in the liver. A variety of clinical trials are ongoing to evaluate combination of immune checkpoint inhibitors or with other drugs, without clear justification or support by preclinical data.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have developed a combination immunotherapy and found that co-injection of the two reagents effectively suppressed HCC progression in animal models, although neither of them alone showed any therapeutic effect. These preclinical data may be instrumental for design of combination therapy for HCC, using the tested reagents or other similar approaches which boost both innate and adaptive immunity.

More importantly, the new concept or idea developed from this combination immunotherapy in mouse HCC models is that orchestrated activation of both innate and adaptive immune function is a most powerful approach for treatment of primary liver cancer. Based on this concept and rationale, one can systematically search for reagents or specific molecular targets that can lead to maximal activation of innate and adaptive anti-tumor immune activities.

APPLICATIONS

The reagents would be used to treat liver cancer

ADVANTAGES

The combination therapy is more effective than treatment by single reagents.

STATE OF DEVELOPMENT

The current work has been carried out on several animal models as well as in induced liver tumors in mice which demonstrate potent tumor-inhibitory effects and should be beneficial for designing successful clinical trials.

INTELLECTUAL PROPERTY INFO

This technology is patent pending and available for licensing and/or research sponsorship.

PATENT STATUS

Country	Type	Number	Dated	Case
Patent Cooperation Treaty	Published Application	2020/077077 A1	04/16/2020	2019-090

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OTHER INFORMATION

KEYWORDS

HCC, combination therapy, liver cancer, mouse models for liver cancer, anti-tumor therapy

CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Disease: Metabolic/Endocrinology
  - Therapeutics

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