# Broad spectrum anti-cancer agents

Tech ID: 32221 / UC Case 2020-132-0

## BACKGROUND

One of the main problems in using immune checkpoint inhibitors (e.g. PD-L1/PD-1/PD-L2/CTLA4) as a cancer treatment is that there is a large percentage of patients (~60-70%) who do not respond to the treatment or become resistant to it. Researchers all over the world are looking for ways to increase response to immunotherapy in this large population of patients, such as identifying new signaling pathways and/or new targets involved in this process as well as identifying synthetic molecules that can modulate the functions of those pathways and targets.

## TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have identified compounds that bind to relevant targets related to the N6-methylation of adenosine (m6A) in RNA which affect immunotherapy response in cancer patients. Different inhibitors identified by the researchers bind to different targets specifically. For example, a first group of compounds binds specifically to certain methyltransferases, which install m6A on RNA (e.g. METTL3/14). A second group binds to specific demethylases which remove methyl groups from m6A. A third group of compounds binds to a demethylase involved in alkylated DNA repair. Then a fourth group binds to a certain family of proteins that promote translation via interaction with translation initiation factors or promote RNA degradation via recruitment of m6A modified mRNA to nuclear processing bodies. Finally, a fifth group of inhibitors bind to a phosphatase in tumor cells and increase the efficacy of immunotherapy by enhancing IFN-g mediated effects on antigen presentation and tumor growth suppression. The inventors have predicted the compounds will have a good pharmacokinetics profile based on in vitro parameters of selected compounds.

## APPLICATIONS

The identified inhibitors will be useful to treat patients with glioblastoma, colon, lung, pancreatic, gastric, resistant breast cancer, and esophageal cancers by sensitizing those tumors to immune checkpoint inhibitors.

## ADVANTAGES

The use of these inhibitors will increase the response rate to existing cancer immunotherapies.

## STATE OF DEVELOPMENT

Experimental stage with in vitro and in vivo data in relevant animal disease models.

## INTELLECTUAL PROPERTY INFO

The invention is patent-pending and is available for licensing.

## RELATED MATERIALS

▶ L. Wang, H. Hui, K. Agrawal, Y. Kang, N. Li, R. Tang, J. Yuan and T. Rana. m6A RNA methyltransferases METTL3/14 regulate immune responses to anti-PD-1 therapy. EMBO J (2020) 39:e104514.

▶ N. Li et al., ALKBH5 regulates anti-PD-1 therapy response by modulating lactate and suppressive immune cell accumulation in tumor microenvironment. Proc Natl Acad Sci U S A, (2020).

## PATENT STATUS

Patent Pending

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**OTHER INFORMATION**

**CATEGORIZED AS**

▶ **Medical**

▶ Disease: Cancer

**RELATED CASES**

2020-132-0