Method of Treating Lung Cancer in Patients with LKB1 Genetically-Inactivated Tumors

Technology

Dr. Kwok-Kin Wong at NYU Langone Health has identified a pathway that negatively regulates oncogenic CD38 expression and proposes a method of sensitizing patients with lung adenocarcinoma (LUAD) to the anti-CD38 monoclonal antibody, Daratumumab. The researchers have identified the STK11 gene, which encodes the LKB1 protein, to be genetically inactivated in 20% of LUAD patients. The researchers demonstrated that LKB1-depleted cells express higher levels of CD38, making them more sensitive to anti-CD38 antibody treatment. Downstream of LKB1, in the same pathway, are salt-inducible kinases (SIKs). In cells with intact LKB1 activity, treatment with a SIK inhibitor also increased CD38 expression and sensitized cancer cells to treatment with Daratumumab. The Wong Lab proposes both novel therapy options for targeting the aggressive LKB1-inactivated cancer types and a combinatorial therapy for LKB1-wildtype cancers. Background

Background

Lung cancer is the leading cause of cancer-associated deaths worldwide because of resistance to conventional therapies and recurrent disease. In 2020 alone, there were 2.2 million new cases and 1.7 million deaths recorded globally. In 2019, patients paid a collective 1.35 billion in out-of-pocket expenses. Immunotherapy is a common treatment option including immune checkpoint inhibitors and antibodies against programmed cell death 1 (PD-1) or programmed cell death ligand 1 (PD-L1). Immunotherapies often show initially success, while later tumors will evolve resistance. Inactivating mutations in STK11, encoding the kinase LKB1, are found in 20% of Non-Small Cell Lung Cancer (NSCLC) patients, and promote therapy resistance. Finding a way to sensitize tumors to already existing treatment would increase the efficacy of those treatments and result in fewer relapses.

About the PI

Dr. Kwok-Kin Wong is a world-renowned hematologist, oncologist, and researcher specializing in treating lung cancer. He received PhD and MD degrees from Columbia University and trained at Massachusetts General Hospital and Dana Farber Cancer Institute. In 2016, he joined NYU's Perlmutter Cancer Center as Chief of Hematology and Medical Oncology. His research focuses on understanding the molecular mechanisms of lung tumorigenesis and finding new ways of treating these conditions.

Applications

- Targeting CD38 could be an effective therapy for LUAD patients with LKB1 genetically-inactivated tumors.
- Targeting LKB1-wildtype tumors with SIK inhibitors could be an effective combination therapy to sensitize LUAD tumors to anti-CD38 treatment.

Technology ID

WON02-07

Category

Life Sciences/Therapeutics/Oncology

Jane Liew

Authors

Kwok-Kin Wong, MD, PhD

Learn more

Advantages

- This invention can be quickly translated to clinical applications using the FDA-approved antibody CD38, as well as SIK inhibitors, which are currently under clinical development for other applications.
- There is already evidence that up to 20% of LUAD patients have genetic inactivation of LKB1, resulting in a more aggressive cancer. However, this is the first time CD38 treatment has been shown to be effective in treating this cancer type. Intellectual Property A provisional patent application has been filed.