VISTA Inhibitor CA170 Synergizes With KRAS Vaccine in Lung Cancer in a Single-Cell RNA Sequencing Analysis

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Immune checkpoint inhibitors (ICIs) have emerged as a promising therapy for late-stage lung cancer. However, the response rate to ICIs remains low. As a result, there is a need to better understand the diversified intervention pathways to optimize antitumor efficacy. Small molecule CA170 targets immune checkpoint V-domain Ig Suppressor of T cell Activation (VISTA), which is highly expressed in the lungs, and overcomes the limitations of existing antibody-based ICIs due to its membrane permeability. I hypothesized that CA170, an antigen-independent small molecule, would work synergistically with Kvax, an antigen-specific vaccine targeting the KRAS mutation in lung cancer, to promote antitumor immune response pathways. I analyzed publicly available single-cell RNA sequencing (scRNA-seq) data of primary mouse lung cancer samples to examine the effects of the treatment on immune cell compartments using the Seurat package in R. I evaluated immune cell response pathways in our receptor-ligand analysis via CellChat. I found that the synergy between CA170 and Kvax promoted plasma and memory B cell proliferation, enhanced helper T cell function, and improved cytotoxic T lymphocyte infiltration. This study suggests that therapies combining antigen-specific vaccines and ICI could enhance the antitumor response in lung cancer. This could pave the way for developing better strategies to extend the efficacy of immunotherapy for lung cancer patients.

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