INTRATUMORAL ADMINISTRATION OF SARS-COV-2 REDUCES TUMOR PROGRESSION AND ALTERS THE TUMOR IMMUNE MICROENVIRONMENT SIMILAR TO THAT OF THE SEASONAL INFLUENZA VACCINE

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Background A significant challenge in using immunotherapies to treat solid tumors is that these treatments are largely ineffective due to lack of immune cell infiltration or are dominated by suppressive immune cell populations. To overcome this, we previously demonstrated that intratumoral administration of influenza converts an immune barren tumor to a tumor that is loaded with inflammatory factors, thus can be targeted by the immune system. With the onset of the COVID-19 pandemic, and there being several shared characteristics between the influenza and SARS-CoV-2 we sought to determine the cancer immunotherapeutic potential of SARS-CoV-2. Here, we have shown that inactivated SARS-CoV-2 can reduce tumor growth in murine tumor models and can shift composition of the tumor microenvironment paralleling that of treatment using the influenza vaccine.

Methods To determine the anticancer response, 4T1 breast cancer and B16 melanoma tumors were induced in BALB/C and C57BL/6 mice, respectively. Tumors were treated with inactivated SARS-CoV-2, seasonal influenza vaccine, or PBS via intratumoral injection. Tumor growth was evaluated via caliper measurements. Determination of immune cell population changes within the tumor following each treatment was determined via flow cytometry analysis.

Results Intratumoral injection of inactivated SARS-CoV-2 and the influenza vaccine showed significant reduction in tumor growth compared to a PBS control ($p < 0.001$) in both 4T1 and B16 tumor models. Within B16 tumors, both SARS-CoV-2 and influenza vaccine increased CD45+ cell populations ($p < 0.0001$) compared to PBS. Notably, both B16 and 4T1 tumors treated with SARS-CoV-2 and influenza experienced a significant increase in CD8+ T-cell infiltration ($p < 0.05$, $p < 0.01$). Additionally, CD11b+ Ly6G/Gr-1+ myeloid derived suppressor cell populations were decreased in B16 melanoma tumors following inactivated SARS-CoV-2 or influenza vaccine treatment.

Conclusions These findings indicate that introducing inactivated SARS-CoV-2 into the tumor microenvironment reduces tumor progression and is able to shift the immune profile of a tumor from an immune-suppressed to a more inflamed, immunologically targeted status. Further, the changes in immune cell populations within the tumor as well, paralleling those of influenza vaccine treated tumors.