

ALTERATION OF T CELL RESPONSES AGAINST SARS-COV-2 OMICRON VARIANT AFTER VACCINATION WITH MRNA BOOSTER IN LUNG CANCER PATIENTS

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Background The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant has demonstrated high transmissibility and possesses several spike protein mutations that allow for evasion of previously established immunity.¹ mRNA vaccines against the spike protein of the ancestral strain of the virus have been reported to induce robust T cell immunity against the omicron variant when examined in healthy individuals.² However, the effectiveness of the booster vaccine doses in late-stage lung cancer patients undergoing active anti-PD-1/PD-L1 agent immunotherapy has yet to be investigated.³

Methods To address this question, we assessed both CD8+ and CD4+ T cell responses using a modified activation-induced marker (AIM) assay that was performed on peripheral blood mononuclear cells (PBMCs), which was coupled with high dimension spectral flow cytometry analyses. The PBMCs were obtained using cryopreserved blood samples collected from The COVID-19 Vaccine Study of Infections and Immune REspoNse (SIIREN) trial, and a total of 51 patient samples (20 non-cancer patients and 31 lung cancer patients) were assessed.

Results Our observations included that booster vaccines induced CD8+ T cell response in both non-cancer subjects and lung cancer patients against ancestral strain and omicron variant, while only marginal induction or trend was detected for CD4+ T cells in normal subjects. Pertinent results also consisted of identification of distinct subpopulation dynamics involving varying degrees of differentiation of antigen-specific CD8+ and CD4+ T cells in lung cancer patients compared to non-cancer subjects, thus demonstrating evidence of dysfunction. Another noteworthy finding included the observation of sex biased T cell responses with female lung cancer patients demonstrating more efficient antigen-specific T cell responses compared to males.

Conclusions We conclude that lung cancer patients in our study cohort have substantial qualitative deviation in their T cell response to mRNA vaccine from the normal individuals. This altered response may be a consequence of altered T cell differentiation states, resulting in the high degree of heterogeneity of AIM+ T cells identified in booster vaccinated individuals. Moreover, the dampened T cell response to omicron in cancer patients could implicate that less protection was established by vaccination for lung cancer patients, especially given that humoral response is also reduced in cancer patients.⁴ This further highlights the need for heightened protective measures for cancer patients to minimize the risk of breakthrough infection with the omicron and other future variants of SARS-CoV-2.⁵

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REFERENCES

1. Hu J. Increased immune escape of the new SARS-CoV-2 variant of concern Omicron. *Cell Mol Immunol.* 2022;**19**:293–295.
2. Liu Y. Robust induction of B cell and T cell responses by a third dose of inactivated SARS-CoV-2 vaccine. *Cell Discov.* 2022;**8**:10.
3. Naranbhai V. T cell reactivity to the SARS-CoV-2 Omicron variant is preserved in most but not all individuals. *Cell.* 2022;**185**:1041–1051.
4. Fendler A. COVID-19 vaccines in patients with cancer: immunogenicity, efficacy and safety. *Nat Rev Clin Oncol.* 2022.
5. Mair MJ. Enhanced SARS-CoV-2 breakthrough infections in patients with hematologic and solid cancers due to Omicron. *Cancer Cell.* 2022.

Ethics Approval All samples and clinical data were collected from patients who consented to the research study and were enrolled under an approved IRB protocol (2021C0041). An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

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