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Bivalent mRNA vaccine-elicited SARS-CoV-2 specific T cells recognise the omicron XBB sublineage

The omicron XBB1.5 sublineage is currently the predominant SARS-CoV-2 variant in circulation. This sublineage differs from XBB by the F486P mutation in spike, which enhances the transmissibility of the virus. While XBB is poorly neutralised by plasma from recipients of the BA.5 bivalent mRNA vaccine,^{1,2} little is known about the susceptibility to vaccine-elicited T cells. Understanding the degree of T-cell cross-recognition is important because T cells from vaccine recipients continue to recognise the omicron BA.1 sublineage even though the virus evades neutralising antibody responses in the same individuals.^{3,4} To determine the degree of T-cell recognition of XBB, we looked at the responses of peripheral blood mononuclear cells (PBMCs) from 21 healthy donors who had received the bivalent booster.

The study was approved by the Johns Hopkins Medicine Institutional Review Boards and informed consent was obtained from all

study participants. Blood was drawn from 21 healthy donors (8 men and 13 women) who had received the bivalent vaccine. Individuals who had tested positive for COVID-19 in the past 3 months were excluded. We performed the interferon gamma (IFN- γ) enzyme-linked immunosorbent spot assay with unfractionated PBMCs as previously described,³ but with a 40-hour incubation period to allow time for antigen processing and presentation. We stimulated PBMCs with recombinant spike from the ancestral virus with D614G, F817P, A892P, A899P, A942P, K986P, and V987P mutations, as well as from XBB. Recombinant extracellular glycoprotein lacritin was used as a control. The three proteins, each with a polyhistidine tag at the C-terminus, were purchased from SinoBiological (Beijing, China) and used at a concentration of 1 μ g/mL. The one-way ANOVA test with multiple comparisons were performed using GraphPad Prism 9.2.0.

T cells from the bivalent vaccine recipients responded vigorously to both spike proteins but not to media alone or extracellular glycoprotein lacritin (appendix; data not shown). There was no statistical difference in the responses and there was a strong correlation between the response to

the two spike proteins (appendix). The single F486P mutation in XBB1.5 is unlikely to affect these responses because T cells target a broad number of epitopes in spike.⁵ Our data suggest that despite extensive evasion of neutralising antibody responses, the XBB sublineage is still susceptible to T cells, which could potentially lead to protection from severe disease.

We declare no competing interests.

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See Online for appendix