nature portfolio

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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Varioskan™ LUX multimode microplate reader (Thermo Fisher Scientific) was used for measurements of luminescence. The Octet Red96e (ForteBio) was used for measuring binding between PD and RBD. Movie stacks were automatically collected using EPU software. The Cryo-EM data of complex were collected by the Titan Krios microscope at 300 kV with a Gatan K3 detector and GIF Quantum energy filter. Particles for all samples were automatically picked using cryoSPARC.
Data analysis	The 50% inhibitory dilution (ID50) or inhibitory concentration (IC50) was calculated using Graphpad Prism 9.0 software by log (inhibitor) vs. normalized response – Variable slope (four parameters) model. Biolayer interferometry data was analyzed by Octet Data Analysis HT 12.0 software. Cryo-EM data processing software usage: cryoSPARC 3.3.1, ChimeraX 1.6.1, MotionCor 2 1.1.0, Phenix 1.11.1, Coot 0.8.2.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Atomic coordinates and cryo-EM density maps of Omicron BA.2.86 S protein in complex with PD of ACE2 (PDB: 8WYH, whole map: EMD-37928), the interface between BA.2.86 RBD and ACE2 (local map: EMD-37927), BA.2.86 S protein in complex with S309 and SA55 (PDB: 8WYJ, whole map: EMD-37930), the interface between BA.2.86 RBD in complex with S309 and SA55 (local map: EMD-37918), cryo-EM density maps of Omicron JN.1 S protein in complex with PD of ACE2 (whole map: EMD-60028), the interface between JN.1 RBD and ACE2 (PDB: 8ZBQ, local map: EMD-39907), have been deposited to the Protein Data Bank and the Electron Microscopy Data Bank, respectively.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	Sex and gender were not considered in study design.
Reporting on race, ethnicity, or other socially relevant groupings	These information were not considered in study design.
Population characteristics	Twenty wild-type vaccine-incubated individuals were infected with Omicron BA.4 or BA.5 subvariant.
Recruitment	All participants were confirmed as positive in RT-PCR test and admitted to Shenzhen Third People's Hospital. We collected their plasma samples in the early stage of breakthrough infection (Visit 1, 0-5 days post a positive PCR test) and another follow-up (Visit 2, 7-15 days after Visit 1).
Ethics oversight	This study was approved by the Ethics Committee of Shenzhen Third People's Hospital, China (approval number: 2021-030). All participants had provided written informed consent for sample collection and subsequent analysis.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	The plasma samples were obtained from 20 BA.4 or BA.5-infected individuals who had received at least two doses of WT SARS-CoV-2 vaccines. This sample size is sufficient for evaluating the neutralization against SARS-CoV-2 variants.
Data exclusions	No data were excluded.
Replication	Neutralization assay were performed two times independently. All attempts at replication were successful.
Randomization	There is no allocation in this study, so randomization is not applicable.
Blinding	No blinding was conducted since there was no specific grouping.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	The 293T cells were obtained from ATCC. The 293T-hACE2 cells were purchased from YEASEN Biotech. The 293F cells were purchased from Life Technologies.
Authentication	All cell lines were frequently checked for cellular morphologies, growth rates and functions.
Mycoplasma contamination	We confirmed that all cell lines were negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*