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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	No software was used for data collection
Data analysis	Clustering analysis on sequenced IgH and IgL paired sequence was performed using Kymab's proprietary Intellisellect software platform but is not considered central to the paper.

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

All VH/VL paired sequences used to synthesize monoclonal antibodies and using the same unique identifiers in the manuscript are available via the published patent filing WO2023094628A1. A full list of all 951 VH/VL sequences generated in the study is included in the source data file.

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	Details on reporting of sex and gender for clinical studies from which bacteria and associated patient metadata were used in this study are detailed in the following publications. Schultz et al. Repeated local emergence of carbapenem-resistant Acinetobacter baumannii in a single hospital ward. Microb Genom 2, e000050 (2016). Toan, N. D. et al. Clinical and laboratory factors associated with neonatal sepsis mortality at a major Vietnamese children's hospital. Plos Global Public Heal 2, e0000875 (2022). Roberts, L. W. et al. Genomic characterisation of multidrug-resistant Escherichia coli, Klebsiella pneumoniae, and Acinetobacter baumannii in two intensive care units in Hanoi, Viet Nam: a prospective observational cohort study. The Lancet Microbe 3, e857–e866 (2022). Sex and gender based analyses related to strain and patient metadata were not considered for study of monoclonal antibody binding described in the reported research.
Reporting on race, ethnicity, or other socially relevant groupings	Details on reporting of race, ethnicity, or other socially relevant groupings for clinical studies from which bacteria and associated patient metadata were used in this study are detailed in the publications listed above. These analyses were not considered for study of monoclonal antibody binding described in the reported research.
Population characteristics	See above
Recruitment	Participants were recruited as described in the publications listed above.
Ethics oversight	Ethical oversight for clinical protocols for studies from which from which bacteria and associated patient metadata were used in this study are detailed in the publications listed above.

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	For all animal studies, study size was defined in each institutional animal protocol (see online methods section Mouse immunisations and Murine challenge studies) according to power calculations for delivery of a conclusive outcome (n=5). For all in vitro studies a minimum sample size of n=4 was employed in all cases. Sample size was maximised to n=6 whenever possible. These sample sizes were selected to maximise power of the statistical test used for analysis of in vitro data (Mann Whitney for comparison two groups of or Dunnett's one-way ANOVA to compare multiple groups).
Data exclusions	No data was excluded from any of the analyses.
Replication	Individual experiments were repeated three times to assess reproducibility and an individual representative experiment was presented.We confirm that all repetitions of experiments successfully delivered data representative of those presented in the manuscript.
Randomization	Random allocation of samples into experimental groups were not relevant as samples were derived from defined experimental groups for the in vivo and in vitro studies presented.
Blinding	Blinding was not relevant in this study as samples were derived from defined experimental groups for the in vivo and in vitro studies presented.

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

Antibodies

Antibodies used	Information given below is as follows, antibody, application, supplier, Cat#, clone name, Lot#, dilution used. BUV-395-B220, Cell sorting, BD Biosciences, 563793, RA3-6b2, 7177756 1/200 BUV-395-CD19,Cell sorting, BD Horizon, 563557, 1D3, 8206694 1/200 BV451-Anti-Heavy IgG, Cell sorting, BD Horizon, 562581, X40, 9079965 1/40 BV650-Anti-Heavy IgM, Cell sorting, Biolegend, 314526, MHM88, B268198 1/100 BV510-CD8a, Cell sorting, Biolegend, 100752, 53-6.7, B248151 1/500 BV510-CD4, Cell sorting, Biolegend, 100449, GK1.5, B248587 1/500 BV510-Ly6G, Cell sorting, Biolegend, 127633, RB6-8C5, B307304 1/500 BV510-F4/80, Cell sorting, Biolegend, 123135, BM8, B25669 1/500 BV510-CD11c, Cell sorting, BD Biosciences, 562949, HL3, 8011606 1/500 PE-Mouse Lambda, Cell sorting, Southern Biotech, 1175-09L, JC5-1, G1714-VL87C 1/200 FITC-labelled anti-Guinea pig complement C3 C3b depositon MP Biomedicals 855385 PE-conjugated anti-human C3 C3b depositon Cedarlane CL7636PE
Validation	Validation for each use case is supplied in product note supplied by the manufacturer with the following exceptions. Validation for use of FITC-labelled anti-Guinea Pig complement C3 for C3b deposition described in the manuscript is described in Fischinger et al. A high-throughput, bead-based, antigen-specific assay to assess the ability of antibodies to induce complement activation. J Immunol Methods 473, 112630 (2019). BUV-395-B220 https://www.bdbiosciences.com/en-gb/search-results?searchKey=563793# BV510-CD11c https://www.bdbiosciences.com/en-gb/search-results?searchKey=562949 BV451-Anti-Heavy IgG https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv421-mouse-anti-human-igg.562581 BUV-395-CD19 https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv395-rat-anti-mouse-cd19.563557 BV650-Anti-Heavy IgM https://www.biolegend.com/en-us/products/brilliant-violet-650-anti-human-igm-antibody-9650 BV510-CD8a https://www.biolegend.com/en-us/products/brilliant-violet-510-anti-mouse-cd8a-antibody-7992 BV510-CD4 https://www.biolegend.com/en-us/products/brilliant-violet-510-anti-mouse-cd4-antibody-10707 BV510-Ly6G https://www.biolegend.com/en-us/products/brilliant-violet-510-anti-mouse-ly-6g-antibody-9121 BV510-F4/80 https://www.biolegend.com/en-us/products/brilliant-violet-510-anti-mouse-f4-80-antibody-8934

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	HEK293 cells (Expi293™, Gibco, Thermo Fisher Scientific, US, Cat-A14635), CHO-3E7 (National Research Council, Canada NRC file 11992), THP-1 (ATCC TIB-202 ™)
Authentication	All authentication procedures carried out by supplier indicated for HEK293 cells (Expi293™, Gibco, Thermo Fisher Scientific, US, Cat-A14635), CHO-3E7 (National Research Council, Canada NRC file 11992), THP-1 (ATCC TIB-202 ™)
Mycoplasma contamination	All cell lines used tested negatively for mycoplasma
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in this study

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	Kymouse platform mice are true-breeding lines is a randomized mixture of 129S7 and C57BL/6J strains, male and female mice were used in this study. Kymouse platform mice were bred at the Biological Support Unit at the Babraham Research Campus, Cambridge

UK. C57BL6J male and female mice, BALB/c male and female mice were purchased from Charles River Laboratories UK. All mice were housed on a 12-h light/dark cycle at 20-24°C with 55%±10% humidity.

Wild animals | This study did not involve use of wild animals

Reporting on sex | Findings presented in this study do not apply to only one sex. No sex-specific analysis of data were performed.

Field-collected samples | This study did not involve samples collected from the field.

Ethics oversight | For studies used Kymouse platform mice Mice were housed under United Kingdom Home Office License 70/8718 with all procedures carried out receiving approval of the Wellcome Trust Sanger Institute Animal Welfare and Ethical Review Body. Mouse studies carried out at Imperial College were performed under United Kingdom Home Office License PP5168779 and were approved by the Animal Welfare and Ethical Review board at Imperial College London. Mouse studies carried out at the University of Cambridge were performed uUnited Kingdom Home Office License P653704A5 with university approval by a local Animal Welfare and Ethical Review Board (AWERB)

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

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.*