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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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For	r all statistical analyses, confir	m that the following items are present in the figure legend, table legend, main text, or Methods section.
n/a	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	er measurements were taken from distinct samples or whether the same sample was measured repeatedly
	The statistical test(s) us Only common tests should	sed AND whether they are one- or two-sided I be described solely by name; describe more complex techniques in the Methods section.
\boxtimes	A description of all cov	ariates tested
	A description of any ass	sumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	A full description of the AND variation (e.g. star	estatistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient Indard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
	For null hypothesis test	ring, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted us whenever suitable.
\boxtimes	For Bayesian analysis, i	nformation on the choice of priors and Markov chain Monte Carlo settings
\times	For hierarchical and co	mplex designs, identification of the appropriate level for tests and full reporting of outcomes
X	Estimates of effect size	s (e.g. Cohen's d , Pearson's r), indicating how they were calculated
	1	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

UNICORN 7.3 software was used to collect FPLC data. Octet BLI Discovery 12.2.2.20 software was used to collect the bio-layer interferometry data. Gen5 3.08.01 software was used to collect the ELISA data.7500 Fast Software v2.3 was used to collect the Differential scanning fluorimetry data.

Data analysis

- GraphPad Prism 9.3.1.
- Octet Analysis Studio 12.2.2.26 Software.
- XDS Package (version January 10, 2022), Phenix 1.16 and 1.20 (includes Phaser, AutoBuild, and Phenix.refine), Coot 0.9.8.1 and PyMol 2.5.1 curated by SBGrid.
- Protein Thermal Shift software v 1.4

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 data generated or analyzed during this study are included in this published article, source data file and supplementary information files. Atomic coordinates and structure factors have been deposited in the Protein Data Bank with PDB IDs 8GID, 8GIE, and 8GIF. Source data are provided with this paper.

Human research participants

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Reporting on sex and gender	Not applicable
Population characteristics	Not applicable
Recruitment	Not applicable
Ethics oversight	Not applicable

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 belo	w 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 <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>

Life sciences study design

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

Sample size	Sample sizes were chosen based on animal availability and the ability to see trends in the event of one or two outlier animals. The group sizes are sufficient to support the primary conclusion of the manuscript by showing statistically significant improvement in % GIA elicited by SBD1 immunogen compared to AMA1 DI-DII-RON2L complex.
Data exclusions	No data points were excluded from statistical analysis.
Replication	In vitro assays were independently replicated at least twice to ensure reproducibility, and all replication attempts were successful. Animal studies were not repeated to conform with proper animal usage guidelines. All data from the rat immunogenicity study are reported in the manuscript.
Randomization	Animals were randomly assigned to receive the indicated immunizations.
Blinding	All groups were blinded for the growth inhibition assay.

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	Methods
n/a Involved in the study	n/a Involved in the study
Antibodies	ChIP-seq
Eukaryotic cell lines	Flow cytometry
Palaeontology and archaeology	MRI-based neuroimaging
Animals and other organisms	
Clinical data	
Dual use research of concern	
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Antibodies	
from Jackson ImmunoRese 37-2900, Lot: WC318953) p mouse antibody conjugate	conjugated to Horseradish Peroxidase (HRP) (catalog no.: 112-035-071, Polyclonal, Lot: 153607) purchased arch was used as a secondary antibody in ELISA. The mouse 6x-His Tag Monoclonal Antibody (catalog no.: burchased from Thermo Fisher Scientific was used as a primary antibody in western blotting. The goat antidoto HRP (catalog no.: 115-035-164, Polyclonal, Lot: 156577) purchased from Jackson ImmunoResearch atibody in western blotting. The immunoglobulin new antigen receptor (IgNAR) 14I-1 was expressed in ells).
interferometry. The goat ar 153607) purchased from Ja manufacturer. The mouse of Scientific was validated in r conjugated to HRP (catalog	Intigen receptor (IgNAR) 14I-1 was validated in this study by sequencing, ELISA, and Biolayer nti-rat antibody conjugated to Horseradish Peroxidase (HRP) (catalog no.: 112-035-071, Polyclonal, Lot: ckson ImmunoResearch was validated in numerous previous scientific publications and by the Sx-His Tag Monoclonal Antibody (catalog no.: 37-2900, Lot: WC318953) purchased from Thermo Fisher numerous previous scientific publications and by the manufacturer. The goat anti-mouse antibody no.: 115-035-164, Polyclonal, Lot: 156577) purchased from Jackson ImmunoResearch was validated in ic publications and by the manufacturer.
Eukaryotic cell lines	

Policy information about <u>cell lines and Sex and Gender in Research</u>			
Cell line source(s)	Expi293F™ cells were purchased from Thermo Fisher Scientific (cat#A14527).		
Authentication	Expi293F™ cells were authenticated for Viability and Mycoplasma (Mycoplasma qPCR Assay) by Thermo Fisher Scientific. Expi293F™ cells were more than 90 % viable and negative for Mycoplasma.		
Mycoplasma contamination	The cells were not tested for Mycoplasma contamination. No previous case of contamination was ever detected in our laboratory.		
Commonly misidentified lines (See ICLAC register)	No commonly misidentified lines were used.		

Animals and other research organisms

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

Laboratory animals	12-14-week-old CD (Sprague Dawley) IGS female rats, Crl:CD(SD) (Charles River Laboratories) were used for immunogenicity study.
Wild animals	The study did not involve wild animals.
Reporting on sex	Sex was not considered in the study design.
Field-collected samples	The study did not use field-collected samples
Ethics oversight	Rat immunogenicity study were performed in an American Association for Accreditation of Laboratory Animal Care-accredited facility under the guidelines and approval of the Institutional Animal Care and Use Committee at the National Institutes of Health.

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