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>.

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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted Give <i>P</i> 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 <u>statistics for biologists</u> contains articles on many of the points above.
Software and code

Policy information about <u>availability of computer code</u>

Data collection

no software used

Data analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows (Version 24.0. Armonk, NY: IBM Corp) and GraphPad Prism version 7.00 for Windows (GraphPad Software, USA, www.graphpad.com)

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 <u>availability of data</u>

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

Data available on request from the authors

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	Sex was recorded according to the biological sex stated in the medical record. Proportion of male/female participants is recorded only.
Population characteristics	Children aged 5 to 16 years with a recorded diagnosis of asthma on the practice register and prescribed regular inhaled corticosteroids were eligible for inclusion in the study. Eligible patients were invited for their routine annual asthma review by telephone call or letter. The project was conducted as a quality improvement project in primary care.
Recruitment	Eligible participants were identified in the Primary Care database and invited for review via telephone call or letter. Attenders may be a self-selected population and may be more proactive with their disease management. The cohort attending for review had higher adherence compared to those who didn't. Additionally, the patient population may be a very heterogenous group e.g., quartile 1 might include dormant asthma, those misdiagnosed, as well as patients who are extremely non-adherent.
Ethics oversight	None required

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guidelines.

Blinding

Please select the o	ne below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.			
X 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 scier	nces study design			
All studies must dis	sclose on these points even when the disclosure is negative.			
Sample size	No sample size calculation performed. This is an observational cross-sectional study that reports on findings over the time period the project was undertaken.			
Data exclusions	Data was excluded if patients were not able to complete lung function testing according to the criteria described.			
Replication	Findings not replicated as this was an observational study, but the findings are in keeping with previous studies referenced.			
Randomization	No randomisation required as this was not an experimental study. This was an observational study according to current established practice guidelines.			

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.

No blinding required as this was not an experimental study. This was an observational study according to current established practice

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			

Antibodies

Antibodies used

Authentication

Describe all antibodies used in the study; as applicable, provide supplier name, catalog number, clone name, and lot number.

Validation

Describe the validation of each primary antibody for the species and application, noting any validation statements on the manufacturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

State the source of each cell line used and the sex of all primary cell lines and cells derived from human participants or

Vertebrate mode

Describe the authentication procedures for each cell line used OR declare that none of the cell lines used were authenticated.

Mycoplasma contamination

Confirm that all cell lines tested negative for mycoplasma contamination OR describe the results of the testing for mycoplasma contamination OR declare that the cell lines were not tested for mycoplasma contamination.

Commonly misidentified lines (See ICLAC register)

Name any commonly misidentified cell lines used in the study and provide a rationale for their use.

Palaeontology and Archaeology

Specimen provenance

Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information). Permits should encompass collection and, where applicable, export.

Specimen deposition

Indicate where the specimens have been deposited to permit free access by other researchers.

Dating methods

If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.

Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight

Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

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

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 Research</u>

Laboratory animals

For laboratory animals, report species, strain and age OR state that the study did not involve laboratory animals.

Wild animals

Provide details on animals observed in or captured in the field; report species and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.

Reporting on sex

Indicate if findings apply to only one sex; describe whether sex was considered in study design, methods used for assigning sex. Provide data disaggregated for sex where this information has been collected in the source data as appropriate; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex-based analyses where performed, justify reasons for lack of sex-based analysis.

Field-collected samples

For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.

Ethics oversight

Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

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

Clinical data	
Policy information about clin	
	ith the ICMJE guidelines for publication of clinical research and a completed <u>CONSORT checklist</u> must be included with all submissions. Provide the trial registration number from ClinicalTrials.qov or an equivalent agency.
	Note where the full trial protocol can be accessed OR if not available, explain why.
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	Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.
Outcomes	Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.
Dual use research	of concern
Policy information about <u>dua</u>	luse research of concern
Hazards	
Could the accidental, deliberable in the manuscript, pose a t	erate or reckless misuse of agents or technologies generated in the work, or the application of information presented hreat to:
No Yes Public health National security Crops and/or livestod Ecosystems Any other significant	
Experiments of concern	
Does the work involve any	of these experiments of concern:
No Yes	
	render a vaccine ineffective therapeutically useful antibiotics or antiviral agents
	therapeutically disertifiantiblotics of antiviral agents the of a pathogen or render a nonpathogen virulent
Increase transmissib	
Alter the host range	of a pathogen
	agnostic/detection modalities
	ation of a biological agent or toxin
Any other potentially	harmful combination of experiments and agents
ChIP-seq	
Data deposition	
Confirm that both raw a	and final processed data have been deposited in a public database such as GEO.
Confirm that you have o	deposited or provided access to graph files (e.g. BED files) for the called peaks.
Data access links May remain private before publica	For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.
Files in database submissio	n Provide a list of all files available in the database submission.

Methodology

(e.g. <u>UCSC</u>)

Genome browser session

Replicates

Describe the experimental replicates, specifying number, type and replicate agreement.

Sequencing depth

Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and

enable peer review. Write "no longer applicable" for "Final submission" documents.

Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to

Sequencing depth	(whether they were paired- or single-end.		
Antibodies	Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.		
Peak calling parameters	Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index file used.		
Data quality	Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.		
Software	Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.		
Flow Cytometry			
Plots			
Confirm that:			
The axis labels state the	he marker and fluorochrome used (e.g. CD4-FITC).		
The axis scales are cle	arly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).		
All plots are contour p	plots with outliers or pseudocolor plots.		
A numerical value for	number of cells or percentage (with statistics) is provided.		
Methodology			
Sample preparation	Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used.		
Instrument	Identify the instrument used for data collection, specifying make and model number.		
Software	Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details.		
Cell population abundance	Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.		
Gating strategy	Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined.		
Tick this box to confirm	m that a figure exemplifying the gating strategy is provided in the Supplementary Information.		
Magnetic resonar	nce imaging		
Experimental design			
Design type	Indicate task or resting state; event-related or block design.		
Design specifications	Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.		
Behavioral performance r	State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).		
Acquisition			
Imaging type(s)	Specify: functional, structural, diffusion, perfusion.		
Field strength	Specify in Tesla		
Sequence & imaging para	Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.		

State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.

Area of acquisition

Used

Not used

Diffusion MRI

Preprocessing	
Preprocessing software	Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).
Normalization	If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.
Normalization template	Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.
Noise and artifact removal	Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).
Volume censoring	Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.
Statistical modeling & infe	erence
Model type and settings	Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).

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	second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).		
Effect(s) tested	Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.		
Specify type of analysis: W	hole brain ROI-based Both		
Statistic type for inference (See Eklund et al. 2016)	Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.		
Correction	Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).		

Models & analysis					
n/a Involved in the study Functional and/or effective connectivity					
Graph analysis					
Multivariate modeling or predictive analysis					
Functional and/or effective connectivity	Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).				
Graph analysis	Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).				

Multivariate modeling and predictive analysis | Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.