This checklist is used to ensure good reporting standards and to improve the reproducibility of published results. For more information, please read Reporting Life Sciences Research.

Please note that in the event of publication, it is mandatory that authors include all relevant methodological and statistical information in the manuscript.

### Statistics reporting, by figure

- Please specify the following information for each panel reporting quantitative data, and where each item is reported (section, e.g. Results, & paragraph number).
- Each figure legend should ideally contain an exact sample size (n) for each experimental group/condition, where n is an exact number and not a range, a clear definition of how n is defined (for example x cells from x slices from x animals from x litters, collected over x days), a description of the statistical test used, the results of the tests, any descriptive statistics and clearly defined error bars if applicable.
- For any experiments using custom statistics, please indicate the test used and stats obtained for each experiment.
- Each figure legend should include a statement of how many times the experiment shown was replicated in the lab; the details of sample collection should be sufficiently clear so that the replicability of the experiment is obvious to the reader.
- For experiments reported in the text but not in the figures, please use the paragraph number instead of the figure number.

Note: Mean and standard deviation are not appropriate on small samples, and plotting independent data points is usually more informative. When technical replicates are reported, error and significance measures reflect the experimental variability and not the variability of the biological process; it is misleading not to state this clearly.

<table>
<thead>
<tr>
<th>TEST USED</th>
<th>n</th>
<th>DESCRIPTIVE STATS (AVERAGE, VARIANCE)</th>
<th>P VALUE</th>
<th>DEGREES OF FREEDOM &amp; F/T/Z/R/ETC VALUE</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>FIGURE NUMBER</td>
<td>WHICH TEST?</td>
<td>SECTION &amp; PARAGRAPH #</td>
<td>EXACT VALUE</td>
<td>DEFINED?</td>
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<tr>
<td>1a</td>
<td>one-way ANOVA</td>
<td>Fig legend</td>
<td>9, 9, 10, 15</td>
<td>mice from at least 3 litters/group</td>
</tr>
<tr>
<td>results para 6</td>
<td>unpaired t-test</td>
<td>Results para 6</td>
<td>15</td>
<td>slices from 10 mice</td>
</tr>
<tr>
<td>Figure Number</td>
<td>Test Used</td>
<td>n</td>
<td>Descriptive Stats (Average, Variance)</td>
<td>P Value</td>
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<tr>
<td>1a</td>
<td>regression additive genetic model/weighted z meta-analysis</td>
<td>Online Mthds stats.</td>
<td>226=115 +61+50</td>
<td>unique people rs6910730/TREM1</td>
</tr>
<tr>
<td>1b</td>
<td>regression additive genetic model/weighted z meta-analysis</td>
<td>Online Mthds stats.</td>
<td>226=115 +61+50</td>
<td>unique people rs2627567/TREM1</td>
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<td>1c</td>
<td>regression additive genetic model/weighted z meta-analysis</td>
<td>Online Mthds stats.</td>
<td>165=115 +50</td>
<td>PGP unique people rs6910730/TREM2</td>
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<td>Online Mthds stats.</td>
<td>165=115 +50</td>
<td>PGP unique people rs2627567/TREM2</td>
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<td>Online Mthds stats.</td>
<td>226=115 +61+50</td>
<td>unique people rs3865444/TREM2</td>
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<td>paired t-test</td>
<td>Online Mthds stats.</td>
<td>43=24 +19</td>
<td>unique people CD33 blocking</td>
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<td>linear regression</td>
<td>Online Mthds stats.</td>
<td>489</td>
<td>unique people amyloid/TREM2</td>
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<td>SF 2</td>
<td>pearson correlations</td>
<td>Online Mthds stats.</td>
<td>CD33/TREM2 (n=226) PTK2B/ TYROBP (n=177)</td>
<td>unique people</td>
</tr>
</tbody>
</table>
### Representative figures

1. Are any representative images shown (including Western blots and immunohistochemistry/staining) in the paper?
   
   If so, what figure(s)?

   Yes. Figure 2b and Supplementary Figure 1a.

2. For each representative image, is there a clear statement of how many times this experiment was successfully repeated and a discussion of any limitations in repeatability?
   
   If so, where is this reported (section, paragraph #)?

   Yes. For Figure 2a, Figure 2c is a graph showing results from all samples tested (n=43), and the repeatability of this experiment is discussed in paragraph 8 of the main text.

   For the representative histograms in Supplementary Figure 1a, paragraph 2 of the main text and Supplementary Table 1 indicate the n used in each cohort for discovery and validation phases.

### Statistics and general methods

1. Is there a justification of the sample size?
   
   If so, how was it justified?

   Where (section, paragraph #)?

   Even if no sample size calculation was performed, authors should report why the sample size is adequate to measure their effect size.

   Not formally justified.


2. Are statistical tests justified as appropriate for every figure?
   
   Where (section, paragraph #)?

   Yes

   a. If there is a section summarizing the statistical methods in the methods, is the statistical test for each experiment clearly defined?

   Yes, there is a Statistical analysis section in the Online Methods, and the statistical tests for each analysis are clearly defined.

   b. Do the data meet the assumptions of the specific statistical test you chose (e.g. normality for a parametric test)?

   Yes, protein data was rank-based normalized prior to analysis to reduce influence of outliers. This is discussed in the Statistical analysis section of the Online Methods.
c. Is there any estimate of variance within each group of data? Is the variance similar between groups that are being statistically compared? Where is this described (section, paragraph #)?

Variance is not estimated or presented because data was rank-based normalized within each group and then meta-analyzed using the weighted z method. This analysis makes no assumptions about equal variances.

d. Are tests specified as one- or two-sided?

two sided

e. Are there adjustments for multiple comparisons?

Two of the four trans associations detected in the discovery phase (p<0.01) were validated in the replication phase at a Bonferroni cut-off of p<0.013. Additionally, FDR q-values were reported for permutations of trans-eQTLs.

3. Are criteria for excluding data points reported? Was this criterion established prior to data collection? Where is this described (section, paragraph #)?

Not reported.

Samples failing monocyte gating due to poor cell viability were excluded from analysis. Failure was assessed on a case by case basis prior to analysis. 14 Samples were excluded.

4. Define the method of randomization used to assign subjects (or samples) to the experimental groups and to collect and process data. If no randomization was used, state so. Where does this appear (section, paragraph #)?

There was no formal randomization method. European subjects were chosen randomly from available samples and analyzed together in one experimental group.

This is stated in paragraph 1 of the Statistical analysis section in the Online Methods.

5. Is a statement of the extent to which investigator knew the group allocation during the experiment and in assessing outcome included? If no blinding was done, state so. Where (section, paragraph #)?

N/A

6. For experiments in live vertebrates, is a statement of compliance with ethical guidelines/regulations included? Where (section, paragraph #)?

Yes. A statement of compliance is included in the first paragraph of the Online Methods.

7. Is the species of the animals used reported? Where (section, paragraph #)?

Yes. The use of human subjects is stated in the first paragraph of the Online Methods.

8. Is the strain of the animals (including background strains of KO/transgenic animals used) reported? Where (section, paragraph #)?

N/A
9. Is the sex of the animals/subjects used reported?
   Where (section, paragraph #)?
   Yes. Supplementary Table 1.

10. Is the age of the animals/subjects reported?
    Where (section, paragraph #)?
    Yes. Supplementary Table 1.

11. For animals housed in a vivarium, is the light/dark cycle reported?
    Where (section, paragraph #)?
    N/A

12. For animals housed in a vivarium, is the housing group (i.e. number of animals per cage) reported?
    Where (section, paragraph #)?
    N/A

13. For behavioral experiments, is the time of day reported (e.g. light or dark cycle)?
    Where (section, paragraph #)?
    N/A

14. Is the previous history of the animals/subjects (e.g. prior drug administration, surgery, behavioral testing) reported?
    Where (section, paragraph #)?
    Details of the cohorts used in the study are reported in paragraphs 2-4 of the Online Methods.

   a. If multiple behavioral tests were conducted in the same group of animals, is this reported?
      Where (section, paragraph #)?
      N/A

15. If any animals/subjects were excluded from analysis, is this reported?
    Where (section, paragraph #)?
    Not reported.

   a. How were the criteria for exclusion defined?
      Where is this described (section, paragraph #)?
      Not reported.

   b. Specify reasons for any discrepancy between the number of animals at the beginning and end of the study.
      Where is this described (section, paragraph #)?
      Not reported.

**Reagents**

1. Have antibodies been validated for use in the system under study (assay and species)?
   Yes. All antibodies were purchased commercially and have been validated for flow cytometry/human cells by the vendors.
a. Is antibody catalog number given?
   Where does this appear (section, paragraph #)?

   For APC TREM2 antibody, the catalogue number is provided in the "Flow Cytometry" section of the Online Methods. Clone numbers are provided for the other antibodies.

b. Where were the validation data reported (citation, supplementary information, Antibodypedia)?
   Where does this appear (section, paragraph #)?

   The validation of APC TREM2 specificity can be found on the R&D website and by Jay et al. Both the link to the website and citation are reported in the "Flow Cytometry" section of the Online Methods. For the other antibodies, validation data can be found on the vendor websites.

2. If cell lines were used to reflect the properties of a particular tissue or disease state, is their source identified?
   Where (section, paragraph #)?

   N/A

   a. Were they recently authenticated?
      Where is this information reported (section, paragraph #)?

      N/A

Data deposition

Data deposition in a public repository is mandatory for:
   a. Protein, DNA and RNA sequences
   b. Macromolecular structures
   c. Crystallographic data for small molecules
   d. Microarray data

Deposition is strongly recommended for many other datasets for which structured public repositories exist; more details on our data policy are available here. We encourage the provision of other source data in supplementary information or in unstructured repositories such as Figshare and Dryad.

We encourage publication of Data Descriptors (see Scientific Data) to maximize data reuse.

1. Are accession codes for deposit dates provided?
   Where (section, paragraph #)?

   N/A

Computer code/software

Any custom algorithm/software that is central to the methods must be supplied by the authors in a usable and readable form for readers at the time of publication. However, referees may ask for this information at any time during the review process.

1. Identify all custom software or scripts that were required to conduct the study and where in the procedures each was used.

   All analyses were completed using publicly available R packages including: base, sva, pamr, and limma.

2. If computer code was used to generate results that are central to the paper’s conclusions, include a statement in the Methods section under “Code availability” to indicate whether and how the code can be accessed. Include version information as necessary and any restrictions on availability.

   N/A

Human subjects
1. Which IRB approved the protocol?
   Where is this stated (section, paragraph #)?
   The Partners and Rush University IRBs approved the protocols used in this study. This is stated in the first paragraph of the Online Methods.

2. Is demographic information on all subjects provided?
   Where (section, paragraph #)?
   Yes. Demographic information on all cohorts can be found in paragraphs 2-4 of the Online Methods. Demographic information of subjects specifically used in the study is provided in Supplementary Table 1.

3. Is the number of human subjects, their age and sex clearly defined?
   Where (section, paragraph #)?
   Yes. The number of subjects, their age and sex are provided in Supplementary Table 1.

4. Are the inclusion and exclusion criteria (if any) clearly specified?
   Where (section, paragraph #)?
   For all experiments and analyses (with the exception of the CD33 suppression experiments) subjects were limited to those of European descent. This is stated in paragraphs 2-4 of the Online Methods.

5. How well were the groups matched?
   Where is this information described (section, paragraph #)?
   N/A

6. Is a statement included confirming that informed consent was obtained from all subjects?
   Where (section, paragraph #)?
   Yes. This statement is included in the first paragraph of the Online Methods.

7. For publication of patient photos, is a statement included confirming that consent to publish was obtained?
   Where (section, paragraph #)?
   N/A

fMRI studies

For papers reporting functional imaging (fMRI) results please ensure that these minimal reporting guidelines are met and that all this information is clearly provided in the methods:

1. Were any subjects scanned but then rejected for the analysis after the data was collected?
   N/A
   a. If yes, is the number rejected and reasons for rejection described?
      N/A
      Where (section, paragraph #)?

2. Is the number of blocks, trials or experimental units per session and/or subjects specified?
   N/A
   Where (section, paragraph #)?

3. Is the length of each trial and interval between trials specified?
   N/A
4. Is a blocked, event-related, or mixed design being used? If applicable, please specify the block length or how the event-related or mixed design was optimized. 

| 4. | N/A |

5. Is the task design clearly described?

| 5. | N/A |

6. How was behavioral performance measured?

| 6. | N/A |

7. Is an ANOVA or factorial design being used?

| 7. | N/A |

8. For data acquisition, is a whole brain scan used?

| 8. | N/A |

   a. How was this region determined?

| 8. | N/A |

9. Is the field strength (in Tesla) of the MRI system stated?

| 9. | N/A |

   a. Is the pulse sequence type (gradient/spin echo, EPI/spiral) stated?

| 9. | N/A |

   b. Are the field-of-view, matrix size, slice thickness, and TE/TR/flip angle clearly stated?

| 9. | N/A |

10. Are the software and specific parameters (model/functions, smoothing kernel size if applicable, etc.) used for data processing and pre-processing clearly stated?

| 10. | N/A |

11. Is the coordinate space for the anatomical/functional imaging data clearly defined as subject/native space or standardized stereotaxic space, e.g., original Talairach, MNI305, ICBM152, etc? Where (section, paragraph #)?

| 11. | N/A |

12. If there was data normalization/standardization to a specific space template, are the type of transformation (linear vs. nonlinear) used and image types being transformed clearly described? Where (section, paragraph #)?

| 12. | N/A |

13. How were anatomical locations determined, e.g., via an automated labeling algorithm (AAL), standardized coordinate database (Talairach daemon), probabilistic atlases, etc.?

| 13. | N/A |

14. Were any additional regressors (behavioral covariates, motion etc) used?

| 14. | N/A |

15. Is the contrast construction clearly defined?

| 15. | N/A |

16. Is a mixed/random effects or fixed inference used?

| 16. | N/A |
a. If fixed effects inference used, is this justified?  
N/A

17. Were repeated measures used (multiple measurements per subject)?  
N/A

  a. If so, are the method to account for within subject correlation and the assumptions made about variance clearly stated?  
N/A

18. If the threshold used for inference and visualization in figures varies, is this clearly stated?  
N/A

19. Are statistical inferences corrected for multiple comparisons?  
N/A

  a. If not, is this labeled as uncorrected?  
N/A

20. Are the results based on an ROI (region of interest) analysis?  
N/A

  a. If so, is the rationale clearly described?  
N/A

  b. How were the ROI’s defined (functional vs anatomical localization)?  
N/A

21. Is there correction for multiple comparisons within each voxel?  
N/A

22. For cluster-wise significance, is the cluster-defining threshold and the corrected significance level defined?  
N/A

Additional comments

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