Materials Design Analysis Reporting (MDAR) Checklist for Authors

The MDAR framework establishes a minimum set of requirements in transparent reporting applicable to studies in the life sciences (see Statement of Task: doi:10.31222/osf.io/9sm4x.). The MDAR checklist is a tool for authors, editors and others seeking to adopt the MDAR framework for transparent reporting in manuscripts and other outputs. Please refer to the MDAR Elaboration Document for additional context for the MDAR framework.

Materials

Antibodies	Yes (indicate where provided: page no/section/legend)	n/a
For commercial reagents, provide supplier name, catalogue number and RRID, if available.	Supplemental Materials, Supplementary Table 3	

Cell materials	Yes (indicate where provided: page no/section/legend)	n/a
Cell lines: Provide species information, strain. Provide accession number in repository **OR** supplier name, catalog number, clone number, **OR** RRID	Materials and Methods, "FRET Biosensor Experiment" subsection. RRID: CVCL_DA04	
Primary cultures: Provide species, strain, sex of origin, genetic modification status.		x

Experimental animals	Yes (indicate where provided: page no/section/legend)	n/a
Laboratory animals: Provide species, strain, sex, age, genetic modification status. Provide accession number in repository **OR** supplier name, catalog number, clone number, **OR** RRID	Materials and Methods, "Mice" subsection; and Supplemental Materials and methods, "Mice" subsection. RRID: IMSR_JAX:000664	
Animal observed in or captured from the field: Provide species, sex and age where possible		x
Model organisms: Provide Accession number in repository (where relevant) **OR** RRID		x

Plants and microbes	Yes (indicate where provided: page no/section/legend)	n/a
Plants: provide species and strain, unique accession number if available, and source (including location for collected wild specimens)		x
Microbes: provide species and strain, unique accession number if available, and source		x

Human research participants	Yes (indicate where provided: page no/section/legend)	n/a
Identify authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	Supplemental Materials, "Human Subjects Research" subsection. Approval was obtained from the Attikon University General Hospital's Bioethics Committee and the University of Pennsylvania IRB (702681, 298201, 824867).	
Provide statement confirming informed consent obtained from study participants.	Supplemental Materials, "Human Subjects Research" subsection. Informed consent was obtained from all participants or their next of kin surrogate. Consents did not include language permitting public sharing of genomic data.	
Report on age and sex for all study participants.	Approximate age of study participants are included in Supplemental Materials, Supplemental Table 1. Sex of study participants are not reported to ensure anonymity.	

Design

Study protocol	Yes (indicate where provided: page no/section/legend)	n/a
For clinical trials, provide the trial registration number **OR** cite DOI in manuscript.		x

Laboratory protocol	Yes (indicate where provided: page no/section/legend)	n/a
Provide DOI or other citation details if detailed step-by-step protocols are available.		x

Experimental study design (statistics details)	Yes (indicate where provided: page no/section/legend)	n/a
State whether and how the following have been done**, or** if they were not carried out.		
Sample size determination	For mouse studies, power analyses were performed to estimate the number of mice per genotype to adequately detect differences in pathologic outcomes which showed that n=4 had a power of ~0.8 to detect a moderate difference with an alpha of 0.05; and that an n=6 had a power of >0.9. In addition, prior studies have shown that a minimum of n=3 is required for group level differences.	
Randomisation	Mice were randomly assigned to AD lysate versus control lysate versus immunodepleted lysate injections (simple randomization; supplemental fig. 5D)	
Blinding	Electron microscopy fibril experiments were analyzed blinded to group (Fig. 6A and B). Mouse experiments were analyzed blinded to genotype (Fig. 7).	
Inclusion/exclusion criteria	Inclusion criteria for mice were based on the *VCP* genotype and age of littermates as described. No mice were excluded from analysis.	

Sample definition and in-laboratory replication	Yes (indicate where provided: page no/section/legend)	n/a
State number of times the experiment was replicated in laboratory	All replicates documented in figure legends. Michaelis-Menten kinetic ATPase analysis, n=3; VCP ATPase activity across NaCl concentration, n=5; VCP ATPase activity across temperature, n=3. (Fig. 4). Tau disaggregase assays, n=5 (Fig. 5D and E). Disaggregase reactions of recombinant tau n=3, α-synuclein n=3, or TDP-43 n=5 (Fig. 5F). Disaggregase blocking experiments, n=5. (Figure 5G). VCP ATPase activity of wild type (WT) and D2 mutant VCP (D2) across NaCl concentration n=5, and temperature n=3. (Supplemental Fig. 3C). Electron microscopy images of fibrils, n=3 (Fig. 6A and B). FRET tau biosensor experiments, n=5. (Fig 6D and E) Heterozygous breeding of D395G of PAM mouse lines--D395G n=54 litters; PAM n=38 litters (Supplemental Fig. 4A and B). RNA sequencing of mice, n=4-6 mice per genotype (Supplemental Fig. E to G). Immunoblot and immunohistochemical staining of mice, n=4-6 mice per genotype (Supplemental Fig. 4H and I) Mice injected with AD lysates, n=6-7 per genotype. (Fig. 7, Supplemental Fig. 5C). Mice injected with AD, control and immunodepleted lysatess, n=4-5 mice per group (Supplemental Fig. 5D).	
Define whether data describe technical or biological replicates	Technical replicates were analyzed for all in vitro studies (Michaelis-Menten kinetic ATPase analysis, disaggregase assays, FRET biosensor cells). Biological replicates were analyzed for mouse studies including immunoblotting and immunohistochemical staining.	

Ethics	Yes (indicate where provided: page no/section/legend)	n/a
Studies involving human participants: State details of authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	Approval was obtained from the Attikon University General Hospital's Bioethics Committee and the University of Pennsylvania IRB (702681, 298201, 824867).	
Studies involving experimental animals: State details of authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	Supplemental Materials, Materials and Methods, Mice Subsection, Page 7. Protocol #806075 was reviewed and approved by the Institutional Animal Care and Use Committee (IACUC). Experiments were completed in accordance to the IACUC of the University of Pennsylvania.	
Studies involving specimen and field samples: State if relevant permits obtained, provide details of authority approving study; if none were required, explain why.		x

Dual Use Research of Concern (DURC)	Yes (indicate where provided: page no/section/legend)	n/a
If study is subject to dual use research of concern, state the authority granting approval and reference number for the regulatory approval		x

Analysis

Attrition	Yes (indicate where provided: page no/section/legend)	n/a
State if sample or data point from the analysis is excluded, and whether the criteria for exclusion were determined and specified in advance.		x

Statistics	Yes (indicate where provided: page no/section/legend)	n/a
Describe statistical tests used and justify choice of tests.	Materials and Methods, "RNA-sequencing" and "Statistics" subsections. Two-tailed t-test, one-way ANOVA with Bonferroni post-hoc, or two-way ANOVA with Bonferroni post-hoc were used to make comparisons between groups. Linear mixed effects regression models were performed to account for fixed and random effects of independent variables.	

Data Availability	Yes (indicate where provided: page no/section/legend)	n/a
State whether newly created datasets are available, including protocols for access or restriction on access.	RNA sequencing of the mouse samples are available in NCBI's Gene Expression Omnibus (GEO) database and will be made public upon publication. The informed consents for research participants did not include language permitting release of genomic data in public databases. Therefore, human genomics data is available upon request to Edward B. Lee (edward.lee@pennmedicine.upenn.edu) subject to a data use agreement to ensure maintenance of personal privacy.	
If data are publicly available, provide accession number in repository or DOI or URL.	GSE156831	
If publicly available data are reused, provide accession number in repository or DOI or URL, where possible.		x

Code Availability	Yes (indicate where provided: page no/section/legend)	n/a
For all newly generated code and software essential for replicating the main findings of the study:		
State whether the code or software is available.		x
If code is publicly available, provide accession number in repository, or DOI or URL.		x

Reporting

Adherence to community standards	Yes (indicate where provided: page no/section/legend)	n/a
MDAR framework recommends adoption of discipline-specific guidelines, established and endorsed through community initiatives. Journals have their own policy about requiring specific guidelines and recommendations to complement MDAR.		
State if relevant guidelines (eg., ICMJE, MIBBI, ARRIVE) have been followed, and whether a checklist (eg., CONSORT, PRISMA, ARRIVE) is provided with the manuscript.	This manuscript has been written in accordance with established guidelines (ICMJE, ARRIVE) and a MDAR checklist is provided with the manuscript.	