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Reporting Summary

Nature Research 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 Research 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	Thermo Scientific Xcalibur (Version 4.2.47, Thermo Fisher Scientific)
Data analysis	Java, version 8 (www.java.com/en/); SIEVE, 2.2.58 SP2. (Thermo Fisher Scientific) Please contact Thermo Fisher Scientific for a complimentary SIEVE license for use with IonStar; MS-GF+ (https://omics.pnl.gov/software/ms-gf); IDPicker, 3.1.643.0 64-bit (http://proteowizard.sourceforge.net/idpicker/); R 4.0.5 or higher (https://www.r-project.org/) and R Studio 2021.09.0-351 or higher (https://www.rstudio.com/products/rstudio/download/); R Shiny interactive web application package "UHR.IonStar" (https://github.com/JunQu-Lab/UHRIonStarApp).

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 Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

The mass spectrometry proteomics data for 25-sample technical evaluation sample set that associated with Fig. 4-6 have been deposited to the ProteomeXchange Consortium (http://proteomecentral.proteomexchange.org) via the PRIDE partner repository with the dataset identifier PXD030780. The data that support the anticipated results of rat brain samples (Fig. 7) are available through the original publication. The data that support the anticipated results of ARDS patients (Fig. 8) are available from the corresponding author upon reasonable request.

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	No sample size calculations were performed in the example studies shown in anticipated results. However, sample sizes were informed by prior literature using similar experimental paradigms that yields interpretable results and the lab's previous experience.
Data exclusions	No data were excluded.
Replication	Attempts at replication were successful.
Randomization	LC-MS measurement were randomized.
Blinding	The investigator was not blinded to group allocation during data collection or analysis.

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
☐	☒ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Human colon cancer cell line SW620 (RPID: CVCL_0547) was obtained from the American Type Culture Collection.
Authentication	The cell line used were authenticated by American Type Culture Collection using STR analysis.
Mycoplasma contamination	All cell lines used were free of mycoplasma.
Commonly misidentified lines (See ICLAC register)	Not applicable.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	Male Wistar rats (350–500 g)
Wild animals	Not applicable.
Field-collected samples	Not applicable.
Ethics oversight	The experimental procedures related with animal in this protocol were approved by the Institutional Animal Care and Use Committee of University at Buffalo.

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	The ARDS patient serum samples were a subset of serum samples from a larger group of patients diagnosed with chronic obstructive pulmonary disease (COPD). Other population characteristics were irrelevant with the manuscript.
Recruitment	For the example of ARDS patients in the Anticipated Results part, we randomly select a subset of samples from subjects that had been recruited.
Ethics oversight	The study was approved by the Institutional Review Boards of the Veterans Affairs Western New York Healthcare System and University at Buffalo. The participants gave the written consent to the study via an IRB approved consent form.

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