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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	/a Confirmed				
☐ ☐ The exact s	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement				
A statemer	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly				
The statisti Only commo	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	A description of all covariates tested				
A description	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons				
A full descr	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 hyp	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 <i>Give P values as exact values whenever suitable.</i>				
For Bayesia	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings				
For hierarc	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes				
\square 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 a	bout <u>availability of computer code</u>				
Data collection	ata collection There were no computer codes used in the analyses related to this manuscript				
Data analysis	nta analysis Data analysis was all done using JJ GraphPad Prism software version 7				
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 <u>data availability statement</u> . 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					

De-identified data from both in vitro and ex vivo samples from human participants will be available on request.

Research involving human participants, their data, or biological material

Policy information about studies with <u>human participants or human data</u>. See also policy information about <u>sex, gender (identity/presentation)</u>, <u>and sexual orientation</u> and <u>race, ethnicity and racism</u>.

Reporting on sex and gender

For in vitro experiments, typically with 3-6 samples from individual human participants, neither the biologic sex nor the societal gender were reported. For those sample sizes, seeing differences would be extraordinary. Please see Table 1 and 2 which includes biologic sex related to the ex vivo studies.

Reporting on race, ethnicity, or other socially relevant groupings

We report race as Black, White or other in Table 2 (for the ex vivo study of ciliated cell phenotype). As is apparent only one participant was enrolled as "other"

Population characteristics

We report asthma as severe or mild-moderate. These definitions are based on the European Respiratory Society and American Thoracic Society definitions of severe asthma from 2013 (Chung, K.F., Wenzel, S. & European Respiratory Society/American Thoracic Society Severe Asthma International Guidelines Task, F. From the authors: International European Respiratory Society/American Thoracic Society guidelines on severe asthma. Eur Respir J 44, 1378-1379 (2014). This definition is based on clinical symptoms (asthma control), exacerbations, lung function changes and amount of medications used. Lung function (FEV1) data are also included in the figures. Healthy individuals were those without any evidence of respiratory disease (or other chronic disease) and normal lung function.

Recruitment

Participants were recruited through the University of Pittsburgh Clinical and Translational Science Institute registry, the University of Pittsburgh Asthma and Environmental Lung Health registry, as well as through the pulmonary clinics. Social media ads (Facebook) were occasionally utilized.

Ethics oversight

University of Pittsburgh Institutional Review Board

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

Field-specific reporting

Please select the or	ne below th	at is the best fit for your research.	If yo	ou are not sure	, read the appropriate s	sections before ma	king your selection.
X Life sciences		Behavioural & social sciences		Ecological, e	volutionary & environm	ental 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

For in vitro experiments, typically 3-6 samples from individual human participants were evaluated. This is relatively standard for in vitro studies and no sample size calculations were performed. The ex vivo studies of specific proteins of interest (by immunofluorescence) in freshly brushed human airway epithelial cells, sample size was limited by availability of bronchoscopic specimens, and also not by sample size calculations. For the ex vivo studies comparing 15LO1 protein expression with ciliated cell phenotype, a pilot analysis supported that using a standard deviation of 7-8% for ciliated cell percentages, a sample size of 35-40 participants would be sufficient with 90% power and an alpha of 0.05.

Data exclusions

No data were excluded.

Replication

The ex vivo studies of ciliary length were not replicated using another center's data. This would be very difficult as few centers do bronchoscopies on asthmatic participants and very few collect samples for western blot/protein analysis.

Randomization

This was not a clinical trial, so there was no randomization

Blinding

This was not a clinical trial so there was no blinding

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 & experime	ntal 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 of	organisms			
Clinical data				
Dual use research o	f concern			
Plants				
·				
Antibodies				
CA). PINK1 (rabbit IgG), LC3E (rabbit IgG) was from Protei GPX4 (rabbit IgG), MTCO2 (r		oit IgG) was purchased from Sigma-Aldrich (St. Louis, MO). 15LO1 (rabbit IgG) was from Abnova (Walnut, B (rabbit IgG) and GAPDH (goat IgG) was from NOVUS (Littleton, CO). pParkin (rabbit IgG) and OPTN intech (Rosemont, IL) PEBP1 (mouse IgG) and OPTN (mouse IgG) was from Santa Cruz (Santa Cruz, CA). mouse IgG) and Total OXHPOS (mouse IgG) was from Abcam (Cambridge, MA). ATP synthase (Mouse IgG) ad, CA). The anti-GAPDH antibody was from Novus Biologicals (Littleton, CO).		
		been validated and applied in our previous publications. PINK1, pPARKIN, OPTN and ATP synthase have curers with multiple publication references.		
Clinical data				
Policy information about <u>cl</u>				
All manuscripts should comply	with the ICMJE guidelines for	r <u>publication of clinical research</u> and a completed <u>CONSORT checklist</u> must be included with all submissions		
Clinical trial registration	Since this is not a clinical trial, there is no registration			
Study protocol	The study protocol can be provided on request. This is an observational study which focuses on collection of lung-specific biologic samples (Immune Mechanisms of Severe Asthma/NIAID and Protein-Oxidized Phospholipid Interactions Determine Epithelial Cell Fate and Asthma Control/NIAID)			
Data collection	Samples were all collected as part of IRB approved research bronchoscopies with associated clinical visits where asthma contro questionnaires, spirometry and asthma related clinical history was obtained.			

As this is an exploratory study of mechanisms of severe asthma, there is no primary outcome

Outcomes