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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 <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

Ctatistics					
Statistics  For all statistical and	blues confirm that the following items are present in the figure larged table larged, main taut, or Mathada section				
1	For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.				
	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				
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 descripti	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					
$\square$ Estimates of effect sizes (e.g. Cohen's $d$ , Pearson's $r$ ), indicating how they were calculated					
ı	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.				
Software and	d code				
Policy information a	bout <u>availability of computer code</u>				
Data collection	n/a				
Data analysis	n/a				
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/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					
All manuscripts mu - Accession codes - A list of figures t	bout <u>availability of data</u> ust include a <u>data availability statement</u> . This statement should provide the following information, where applicable:  unique identifiers, or web links for publicly available datasets  hat have associated raw data  any restrictions on data availability				
All the data supporting the findings of this study are available within this paper and its supplementary information.					
Field-spe	cific reporting				
Please select the on	e 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 th	ne document with all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>				

# Life sciences study design

Mycoplasma contamination

Commonly misidentified lines

(See <u>ICLAC</u> register)

n/a

All studies must dis	close on these	points even when the disclosure is negative.			
Sample size	Two settings of patient samples were tested: n=62 for line 142, n=37 for line 185. These sample sizes have the power to detect the difference between the groups.				
Data exclusions	No samples or animals were excluded from the analysis				
Replication	Cellular experiments were repeated three times; in vivo studies used animals at numbers having the power to test the difference; the mice were exposed to cigarette smoke or BaP to confirm the effects on PD-L1 expression; two AhR inhibitors were used to confirm the effects of AhR inhibitor on murine lung cancer; two settings of patient samples were tested: n=62 for line 142, n=37 for line 185. These sample sizes have the power to ensure the reproducibility.				
Randomization	The mice were numbered, intravenously or subcutaneously injected with LLC cells, randomized into groups, and treated with vehicle control or indicated regimens, for indicated time period.				
Blinding	Blinding was not used in this study, because the purpose of the clinical study was to test the efficacy of pembrolizumab in Chinese lung cancer patients.				
-		pecific materials, systems and methods			
		about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, 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 Methods					
n/a Involved in the study n/a Involved in the study					
Antibodies	Antibodies ChIP-seq				
Eukaryotic	yotic cell lines				
Palaeontolo	peontology MRI-based neuroimaging				
Animals an	d other organism	S			
Human research participants					
Clinical dat	a				
Antibodies					
	Do	hhit anti-human DD 11/H12COA Call Cignaling Taphyalagy, Dayarh, MA UCA) anti-Clasued Cornece 2 /H0CCA Call Cignaling			
Antibodies used	Te PD Ca CD	bbit anti-human PD-L1(#13684, Cell Signaling Technology, Beverly, MA, USA), anti-Cleaved Caspase-3 (#9664, Cell Signaling chnology, Beverly, MA, USA), Rabbit anti-human AhR (#83200, Cell Signaling Technology, Beverly, MA, USA), goat anti-mouse ι-L1 (#AF1019, R&D, Minneapolis, MN, USA), anti-Ki67 (#ab15580, Abcam, Cambridge, MA, USA), TTF1 (#ab76013, Abcam, mbridge, MA, USA), anti-β-Actin (#A1978, Sigma, St. Louis, MO, USA), APC anti-mouse CD3 (#100235), PE/Cy7 anti-mouse 8a (#100721), APC/Cy7 anti-mouse CD4 (#100413), PE anti-mouse CD45 (#103105), PE/Cy7 anti-mouse PD-L1 (#124313), PE ti-mouse PD-1 (#135206), FITC anti-mouse B220 (#103205, Biolegend, San Diego, CA, USA)			
Validation Documents certify that the by the manufacturers.		cuments certify that the products have met the quality control standards defined the manufacturers.			
Eukaryotic c	ell lines				
Policy information a	about <u>cell lines</u>				
Cell line source(s)	)	Cell line sources are listed in page 17.			
Authentication		The lines were authenticated by short tandem repeat (STR) profiling.			

The cell lines were not tested for mycoplasma contamination.

## Animals and other organisms

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

Laboratory animals Species: C57BL/6, C3H, A/J, NOD/SCID; sex: both; age: 4-6 weeks old.

Wild animals This study did not involve wild animal.

Field-collected samples The study did not involve samples collected from the field.

Ethics oversight The study was approved by the local research ethics committees of the Cancer Hospital, Sun Yat-Sen University, and the Third

Affiliated Hospital of Kunming Medical University (Yunnan Tumor Hospital). The animal studies were approved by the Institutional Review Board of Institute of Zoology, Chinese Academy of Sciences. All animal studies were conducted according to protocols approved by the Animal Ethics Committee of the Institute of Zoology, Chinese Academy of Sciences.

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

# Human research participants

Policy information about <u>studies involving human research participants</u>

Population characteristics See above

Recruitment 37 Chinese lung cancer patients were treated with pembrolizumab.

Ethics oversight The study was approved by the Cancer Hospital, Sun Yat-Sen University.

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

#### Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration

Tumor tissues of patients treated with pembrolizumab were tested for the expression of AhR and PD-L1. This study did not involve survival and other important information. For the trial registration number, we contacted the company to have their thoughts. However, they said that the trial is still ongoing to see the overall survival of the patients. They said that they prefer to release the trial registration number when the survival data are obtained. So I prefer not to release the number at this stage and hope you can understand this. Thanks a lot.

Study protocol

Participants receive pembrolizumab 2 mg/kg administered intravenously every 3 weeks for up to 35 administrations.

Data collection

 $The \ expression \ of \ AhR \ and \ PD-L1 \ in \ tumor \ tissues \ of \ the \ patients, \ and \ the \ responses \ of \ the \ patients \ to \ pembrolizum ab.$ 

Outcomes

The association between expression of AhR and PD-L1 in tumor tissues and the responses of the patients to pembrolizumab.

### Flow Cytometry

### Plots

Confirm that:

The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

All plots are contour plots with outliers or pseudocolor plots.

A numerical value for number of cells or percentage (with statistics) is provided.

#### Methodology

Sample preparation

Fresh tumor samples and counterpart normal lung tissues, or tumor biopsy specimens were collected. The mice were euthanized by cervical dislocation when they became moribund, lungs were isolated, and cancer tissues were harvested.

Instrument

The mice were anesthetized with mixture of oxygen/isoflurane inhalation and scanned by microscopic computed tomography cro-CT, PerkinElmer, Waltham, MA).

Software

The Summit Software v5.0 (Beckman Coulter)

Cell population abundance

n/a

Gating strategy

Cells were gated based on forward and side scatter plots, only avoiding debris and aggregates and no extensive gating strategy.

Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.