

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 [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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☐ | ☒ | 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
<i>Give P values as exact values whenever suitable.</i> |
| ☐ | ☒ | 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

This study analyzed data obtained from the China National Human Biomonitoring (CNHBM)

Data analysis

-plink 1.9
-R 4.4.1
-SNPEFF 5.1
-Bedtools 2.29.1
-mediation R package
-Graphpad Prism 8 version 8.0.1
-stats R package

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 [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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

Source data are provided with this paper. The raw RNA-seq data are publicly available in the GSA-Human repository under accession code HRA014233 [<https://ngdc.cncb.ac.cn/gsa-human/s/b6tzKUuTj>] (RNA-seq of HepG2 cells exposed to BDE47 and control). The genomic, metabolomic, and exposomic data of the study population involve sensitive biomonitoring data. Due to restrictions specified in agreements with collaborating institutions (cohort initiators) and the informed consent forms signed by study participants, these data cannot be made publicly available and are subject to controlled access. The request of these individual data is suggested by sending an email to the corresponding author Professor Xiaoming Shi (shixm@chinacdc.cn) and Professor Xiaoping Miao (xpmiao@whu.edu.cn). Requests should include name, affiliation and contact details of the person requesting the data, which data are requested and the purpose of requesting the data. Requests will be subject to consideration by the management committee of the corresponding institutes and the sample collection institutes. If approved, the corresponding author will send the request data by email. Time frame for a response will be within 3 months. Data requests under agreement will be considered for purposes of reproducing the data and subject to appropriate confidentiality obligations and restrictions. Applicants must promise that these individual data applied for will only be used for scientific research and cannot be publicly released.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	We considered sex factor as a covariate in our study. Sex in the CNHBM was determined based on self-reporting data via questionnaire, and all included participants gave written informed consent for sharing of individual-level data.
Reporting on race, ethnicity, or other socially relevant groupings	The majority of CNHBM participants are Asian, and in our study, samples were not excluded or categorized based on ethnicity.
Population characteristics	The CNHBM cohort participants were Asian. In our study, 871 participants were included and more detailed information can be found in the Table1.
Recruitment	The data for this study were drawn from a subset of the CNHBM cohort, a cross-regional, longitudinal survey that enrolled a baseline population of 21,888 individuals aged 3 to 79 years. This survey is designed to explore the associations between environmental factors and the health of the Chinese population, as outlined in previous reports.
Ethics oversight	This project, initiated in 2017, received ethical approval from the Ethics Review Committee of the National Institute of Environmental Health, Chinese Centre for Disease Control and Prevention (No. 201701), with all participants providing voluntary informed consent.

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

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](https://www.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	Data for this study were derived from the 2017–2018 baseline cohort of the China National Human Biomonitoring (CNHBM) program, which covered 152 monitoring sites across 31 provinces/municipalities in China and enrolled a total of 21,888 participants. For the omics study, one sampling unit was selected from each monitoring site, with 12 residents recruited per unit, leading to the identification of 1,824 participants eligible for the omics phase. Of these, 909 individuals aged <18 years were excluded, leaving 915 adult participants aged 18–79 years. After further excluding 20 participants with missing lipid data and 24 participants with missing PBDE exposure data (due to objective factors during cohort implementation, without selective bias), 871 participants were finally included in the statistical analysis. All enrolled participants completed questionnaires and provided blood samples. For cell-based assays (e.g., gene expression, metabolite quantification), we employed $n \geq 3$ independent biological replicates, which is the standard in molecular and cellular biology to account for biological variation and enable statistical testing. This aligns with common practice in prior seminal studies of similar design.
Data exclusions	A stepwise data exclusion process was implemented according to pre-specified inclusion/exclusion criteria to guarantee the reliability of the

study dataset. First, 909 participants aged < 18 years were excluded from the 1,824 omics-phase subjects, as the lipid profiles and PBDE exposure patterns of minors are distinct from those of adults and fall outside the scope of this study. Next, 20 participants with missing lipid data were excluded; such missingness stemmed from blood sample hemolysis, suboptimal cold-chain preservation, or batch-specific instrumental detection errors. Additionally, 24 participants were excluded due to missing PBDE exposure data, which was attributed to insufficient blood sample volume, contamination or degradation during sample pretreatment, or participants' temporary physical inability to provide qualified biological samples. It is important to note that samples with PBDE levels below the limit of detection (LOD) were not excluded and were not regarded as missing data; instead, these values were assigned using the square root of the LOD, a conventional imputation method in environmental epidemiology. Following these exclusion procedures, 871 participants were ultimately included in the subsequent statistical analyses.

Replication To ensure reproducibility, key experiments included ≥ 3 biological/technical replicates, standardized protocols, validated reagents, and rigorous statistical analysis. Core phenotypes were confirmed with complementary methods. All critical experimental findings were successfully replicated; no non-replicable or irreproducible results were identified.

Randomization Given the observational nature of this study, randomization was not applicable.

Blinding This study did not require blinding as no subjective evaluation by an observer was involved.

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
 - ☒ ☐ Clinical data
 - ☒ ☐ Dual use research of concern
 - ☒ ☐ Plants

Methods

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

Antibodies

Antibodies used Primary antibody, SLC6A20 antibody, Supplier name: Proteintech. anti- β -actin, Supplier name: Proteintech. Secondary antibody: HRP-conjugated Goat Anti-Rabbit IgG, Supplier name: Proteintech.

Validation Antibodies

Primary antibody, anti-SLC6A20: Rabbit polyclonal (Proteintech, Cat# 30843-1-AP). Used at a dilution of 1:1000 for Western Blot. Validation: The antibody is validated by the manufacturer for Western Blot. Specific binding to SLC6A20 at the expected molecular weight was confirmed in our internal validation and experimental data (See Methods).

Primary antibody, anti- β -actin: Rabbit polyclonal (Proteintech, Cat# 20536-1-AP). Used at a dilution of 1:1000 for Western Blot as a loading control. Validation: The antibody is validated by the manufacturer for Western Blot and is widely cited. In our experiments, it produced a consistent and specific band pattern across all samples.

Secondary antibody: HRP-conjugated Goat Anti-Rabbit IgG (Proteintech, Cat# SA00001-2). Used at a dilution of 1:5,000.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s) The HepG2 cells were obtained from the China Center for Type Culture Collection (Wuhan, China).

Authentication The HepG2 cell lines were authenticated using short - tandem repeat (STR) profiling. The STR profiles were compared with the reference profiles in the ATCC (American Type Culture Collection) database. The results showed a high degree of similarity, confirming the authenticity of the HepG2 cell lines used in this study.

Mycoplasma contamination All HepG2 cell lines were tested for mycoplasma contamination using the PCR - based detection method. The results showed that all tested samples were negative for mycoplasma contamination, indicating that the cell lines were free from mycoplasma.

Commonly misidentified lines (See [ICLAC](#) register) In this study, no commonly misidentified cell lines were used. All cell lines were carefully selected and authenticated to ensure the reliability of the experimental results.

Plants

Seed stocks	NA
Novel plant genotypes	NA
Authentication	NA