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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 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	NanoString nSolver software
Data analysis	Graphpad Prism 9, ade4 software

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

The authors declare that all data supporting the findings of this study are available within the paper and its supplementary information files. The transcriptomic data generated in this study have been deposited in the GEO (Gene Expression Omnibus database) under accession GSE272505 (https://www.ncbi.nlm.nih.gov/geo/info/linking.html)

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 specifically used the term "sex" rather than "gender" because we focused on biological characteristics relevant to pregnancy.
Reporting on race, ethnicity, or other socially relevant groupings	We restricted our characterization of patients' race to physical traits, categorizing them as Black, Caucasian, and Asian individuals. We deliberately refrained from associating these categorizations with socioeconomic status.
Population characteristics	Patients were chategorized according to age, race, body mass index, smoking status, hypertension disorder history, diabetes mellitus history, CHI history, number of live births, ongoing treatment and obstetrical outcomes.
Recruitment	First, transcriptomic data were obtained from 18 placental samples presenting with grade 2 or grade 3 CHI, sourced from a retrospective analysis of 122 cases with CHI from the fetal and placental pathology archives predating the SARS-CoV-2 pandemic, to exclude cases of CHI attributed to SARS-CoV-2 infection. Eighteen samples were matched in a 3:1 ratio with placental controls based on gestational age, maternal age, and fetal sex. Second, the three participants in the study were consecutively selected if they had a history of severe recurrent CHI, defined by at least two pregnancy losses attributed to grade 3 CHI.
Ethics oversight	BORDEAUX local ethics committee (CNIL number: CER-BDX-2022-34)

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

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No sample size calculation was performed for this study. For the transcriptomic analysis, our objective was to conduct the analysis in a single run, which necessitated limiting the number of samples to 24. As for the clinical study, given the remarkable results observed, we opted to publish the findings from the initial three patients.
Data exclusions	We excluded the placental samples after the SARS-CoV-2 pandemic, to avoid cases of CHI due to SARS-Cov2-infection.
Replication	Placental analyses were conducted by two different fetopathologists to enhance the accuracy of the diagnosis. Transcriptomic analyses were independently replicated by two different biostatisticians.
Randomization	No randomization was performed for this study. The objective was to administer the experimental treatment to three consecutive patients who met the specified criteria.
Blinding	The analysis of placenta samples used for transcriptomic analysis was conducted in a blinded manner to enhance the accuracy of diagnosis. Blinding was deemed unnecessary for the clinical study, as all patients received the treatment.

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

Plants

Seed stocks	not applicable
Novel plant genotypes	not applicable
Authentication	not applicable