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Data Article

DATA in BRIEF of: Adaptative mechanisms indicated by placental protein expression changes in high-altitude Tibetan women during vaginal delivery

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ABSTRACT

Over a period of 30,000 to 40,000 years, high-altitude Tibetans have physiologically and genetically adapted to conditions such as hypoxia, low temperature, and high-intensity ultraviolet radiation. Based on the unique physiological and morphological characteristics of the Tibetan people, they have outstanding hypoxia adaptation skills and can continue to thrive in plateau hypoxia. The placenta of high-altitude Tibetans is protected from oxidative stress during delivery; however, little is known about changes in placental protein expression during vaginal delivery. In this study, we aimed to reveal these adaptive mechanisms by studying changes in placental protein expression during vaginal delivery in high-altitude Tibetans, low-altitude Tibetans, and low-altitude Han populations. Studying the changing mechanisms of maternal responses to hypoxia at high altitudes can reveal the molecular mechanisms of maternal and fetal adaptation to hypoxia at high altitudes and provide theories for preventing and

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treating maternal hypoxia and intrauterine growth and development restriction caused by other diseases.

Specifications Table

Subject	High-altitude medicine
Specific subject area	High-altitude adaptation
Type of data	Table and Figure
Data collection	Maternal and neonatal information will be obtained from obstetric registration books and medical records. Placental tissue will be obtained immediately after delivery and stored in liquid nitrogen at −80 °C for subsequent protein extraction, enzymatic digestion, liquid chromatography-tandem mass spectrometry analysis, and bioinformatics analysis.
Data source location	Sample: Pregnant women at full term with vaginal delivery of Tibetan ethnicity at high altitude (3780 m), low altitude Tibetan population (2200 m), and low altitude Han Chinese population (2200 m), excluding pregnancy complications. Data to be collected for both pregnant women and newborns include age, parity, height, pre-pregnancy weight, weight gain during pregnancy, systolic blood pressure, diastolic blood pressure, fetal weight, ratio of fetal weight to placental weight, Apgar score, and liquid chromatography-mass spectrometry analysis of placental proteins post-delivery.
Data accessibility	In the ARTICLE as well as in the iProX integrated proteome resources (URL:https://www.iprox.cn/page/project.html?id=IPX0008402000; Project ID: IPX0008402000).
Related research article	Liu H, Tenzing N, van Patot MT, Qile M, Ge RL, Wuren T. Enhanced Placental Mitochondrial Respiration in Tibetan Women at High Altitude. Front Physiol. 2021 Jul 14; 12:697022. doi: 10.3389/fphys.2021.697022.

1. Value of the Data

- Reproductive adaptation in high-altitude hypoxia has always been a research hotspot, and currently, there is still a lack of data on protein expression during natural delivery in high-altitude hypoxia-adapted populations.
- Current research suggests that high-altitude hypoxia has no effect on the growth and development of fetuses in the indigenous Tibetan population, which may contribute to their successful reproduction in high-altitude hypoxic environments. Therefore, exploring the molecular mechanisms of placental changes during natural delivery under acute ischemic-hypoxic stress conditions in high-altitude Tibetan populations not only provides a theoretical basis for understanding how the Tibetan population successfully reproduces in high-altitude hypoxic environments but also offers new prediction and treatment targets for numerous hypoxia-related metabolic diseases and severe pregnancy complications such as preeclampsia.

2. Background

Living at high altitudes is extremely challenging due to exposure to hypoxia, low temperatures, and high levels of ultraviolet radiation [1]. However, the Tibetan population has adapted to these conditions both physiologically and genetically over a period of 30,000 to 40,000 years [2]. It has long been speculated that fetal growth restriction and preeclampsia are caused by abnormal placental development [3]. Compared to Europeans, the placentas of high-altitude Ti-

Table 1
Maternal and neonatal information.

	Tibetan		Chinese Han	*P*-values	Nationality
	3780 m	2200 m	2200 m	Altitude	
Maternal characteristics					
N	10	10	10		
Age (years)	27.8 ± 1.1	27.7 ± 1.1	28.6 ± 1.9	NS	NS
Parity	2.3 ± 0.3	1.5 ± 0.2	1.9 ± 0.2	NS	NS
Height (cm)	161 ± 1.2	162 ± 1.2	162 ± 1.1	<0.05	NS
Non-pregnancy weight (kg)	58 ± 1.1	59 ± 0.9	58 ± 1.2	NS	NS
Weight gain with pregnancy (kg)	12 ± 2	10 ± 0.8	11 ± 0.9	NS	NS
Systolic BP (mmHg)	120 ± 2	121 ± 1	122 ± 2	NS	NS
Diastolic BP (mmHg)	80 ± 2	81 ± 1	80 ± 2	NS	NS
Infant characterictics					
Birth weight (g)	3160 ± 129	3070 ± 178	3140 ± 147	NS	NS
Birth/Placental weight ratio	4.9 ± 0.3	4.7 ± 0.2	4.7 ± 0.3	NS	NS
Apgar score	8.8 ± 0.249	8.9 ± 0.276	9.2 ± 0.249	NS	NS

All values are mean ± standard error.

betans are protected from oxidative stress during delivery. However, little is known about the changes in placental protein expression during natural delivery. Previous studies have found that the respiratory function of mitochondria in high-altitude Tibetan placentas is enhanced, the mitochondria in the placenta are less, the content of complexes is high, and the efficiency of placental mitochondria in utilizing oxygen is improved [4]. In this study, we aimed to reveal these adaptation mechanisms by studying the changes in placental protein expression during natural delivery in high-altitude Tibetans, low-altitude Tibetans, and low-altitude Han Chinese.

3. Data Description

This dataset (see also the SUPPPLEMENTARY FILE section) provides basic information about pregnant women and their newborns, as well as comparisons of differences in placental protein expression following vaginal delivery. These data are presented in the form of figures and tables as well as in form of RAW DATA in the SUPPPLEMENTARY FILE section. The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium (https://proteomecentral.proteomexchange.org) via the iProX partner repository [5,6] with the dataset identifier **PXD050881**.

Table 1 describes the basic characteristics of mothers and newborns.

Fig. 1 is an overview of protein identification.

Fig. 2 is a statistical chart and heatmap of differential proteins.

Fig. 3 is the functional classification of differential proteins.

Fig. 4 is functional enrichment analysis of differential proteins.

Fig. 5 is the cluster analysis after functional enrichment analysis of differential proteins.

Previous studies conducted by our research group at the proteomics and transcriptomics levels have demonstrated that the placentas of women delivering vaginally at low altitudes exhibit significant characteristics of acute ischemia and hypoxia compared to those delivered via cesarean section. Conversely, there were no differences observed in the gene expression profiles of placentas from high-altitude Tibetan women delivered vaginally versus those delivered via cesarean section, indicating a blunted response to acute ischemia and hypoxia among the high-altitude Tibetan population [7,8]. it was found that pregnant Tibetan women living at high altitudes exhibit enhanced mitochondrial respiratory function and improved efficiency of placental oxidative phosphorylation [4]. In this experimental study, we discovered that the protein expression patterns in the placentas of the low-altitude Tibetan group were similar to those of the

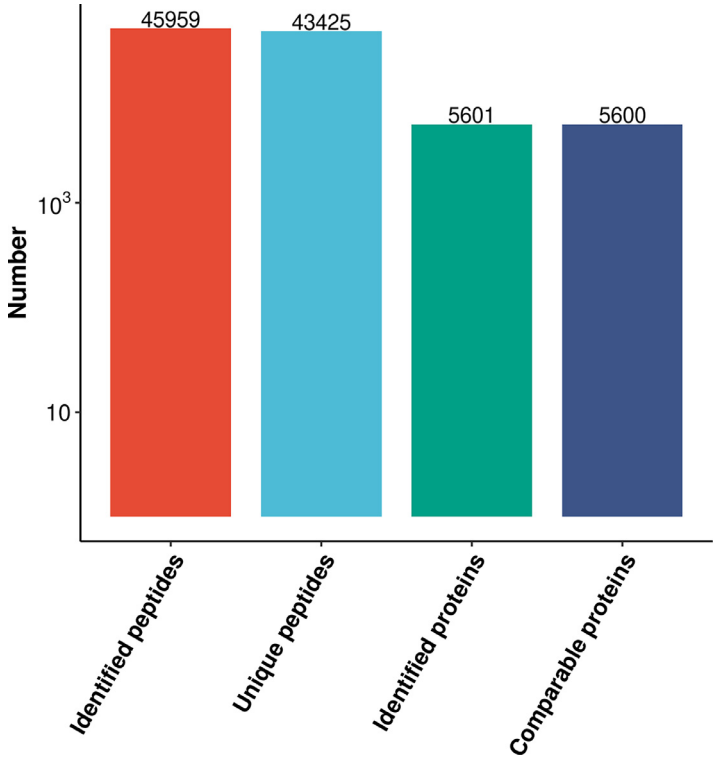

Fig. 1. Protein Identification Overview. identified peptides: The number of identified peptide segments, the number of columns of peptide segments parsed from the matching results. Identified proteins: The number of identified proteins, the number of proteins parsed from specific peptide segments. comparable proteins: The number of proteins available for quantitative comparison, the number of proteins quantified from specific peptide segments.

low-altitude Han Chinese group. However, in the high-altitude Tibetan group, when experiencing ischemia and hypoxia during vaginal delivery, the biological processes within the placenta were richer compared to the low-altitude Tibetan group, involving numerous transcription and translation processes. We speculate that these biological processes are closely associated with adaptation to high-altitude hypoxia.

4. Experimental Design, Materials and Methods

This study was approved by the Qinghai University Affiliated Hospital Ethics Committee. In total, 30 human full term (37–40 weeks) placentas were collected after laboring vaginal delivery, with the written consent of donors after receiving an explanation from local doctors in their native language. Placental tissues from high-altitude Tibetan women ($n = 10$) were collected at Yushu Bayi Hospital (3780 m); those from lower-altitude Tibetan ($n = 10$) and Han ($n = 10$) woman were collected at the Guide County Hospital (2200 m) and Qinghai University Affiliated Hospital (2261 m). The general characteristics of the pregnancies are provided in Table 1. All neonates had Apgar scores between 8 and 9. Each placenta was weighed immediately after delivery and divided into six sections for random sampling. Samples from the fetal side of the placenta were biopsied within 15 min, placed on ice and in PBS and delivered to the laboratory.

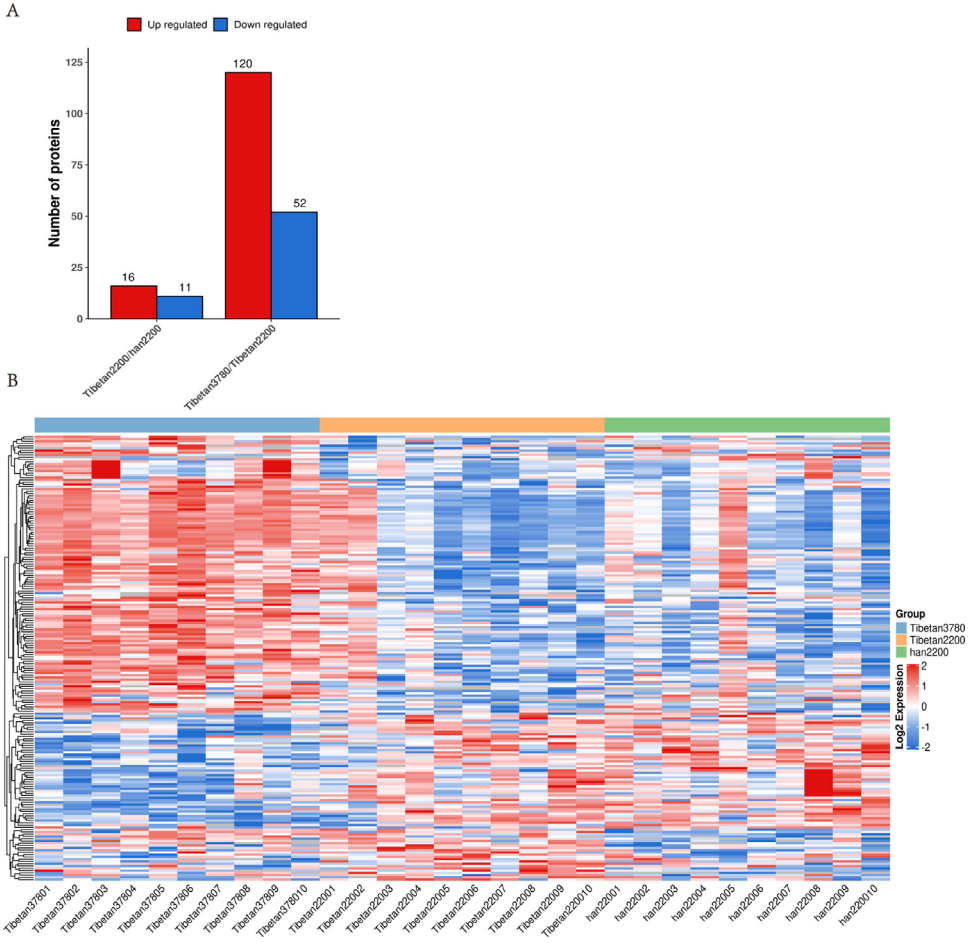

Fig. 2. Differential protein screening. (A) Differential protein statistics chart. (B) Differential protein heatmap.

This experiment involves 30 individuals (with 10 individuals per group) and utilizes 4D-SmartDIA quantitative proteomic analysis of placental tissue samples (3 groups with 10 replicates each). Through the organic integration of a series of cutting-edge technologies including protein extraction, enzymatic digestion, liquid chromatography-mass spectrometry (LC-MS/MS) analysis, and bioinformatics analysis, quantitative proteomic analysis of the samples is conducted. The specific analysis workflow is as follows: 1) Raw files obtained from mass spectrometry detection are used to construct sample-specific protein databases based on the source of the samples. Database searching is then performed using analysis software. 2) Quality control analysis is conducted at the peptide and protein levels based on the results of the database search. 3) Quantitative analysis of proteins is performed, including analysis of quantitative distribution and repeatability. 4) Identified proteins are annotated with common functional annotations, including GO, KEGG, Protein domain, COG/KOG, and STRING database annotations. 5) Based on the quantitative results, differential multiples (Fold Change, FC) between the two groups and significance P-values of T-tests are calculated. Differential screening is conducted according to preset thresholds, and differential analysis-related statistical graphs are plotted. 6) Functional classification and statistical analysis of differential proteins between the two groups are performed, including GO secondary classification, subcellular localization classification, COG/KOG classifica-

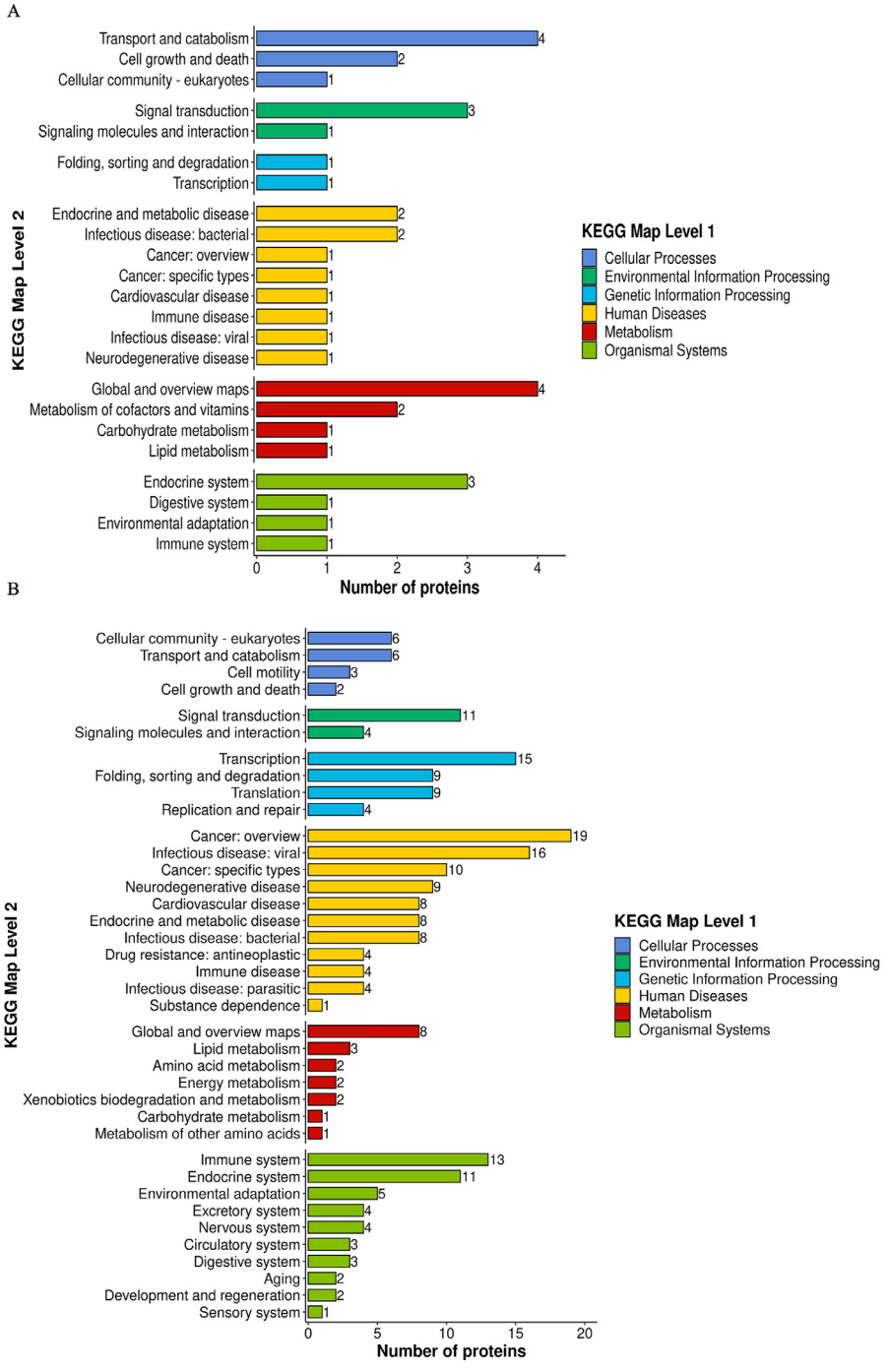

Fig. 3. Differential Protein Functional Classification. The horizontal axis represents the number of differential proteins in each classification, while the vertical axis represents the secondary functional classification within KEGG's primary categories (Metabolism, Genetic Information Processing, Environmental Information Processing, Cellular Processes, Organismal Systems, Human Diseases, Drug Development). (A) Tibetan 2200 vs. Han 2200. (B) Tibetan 3780 vs. Tibetan 2200.

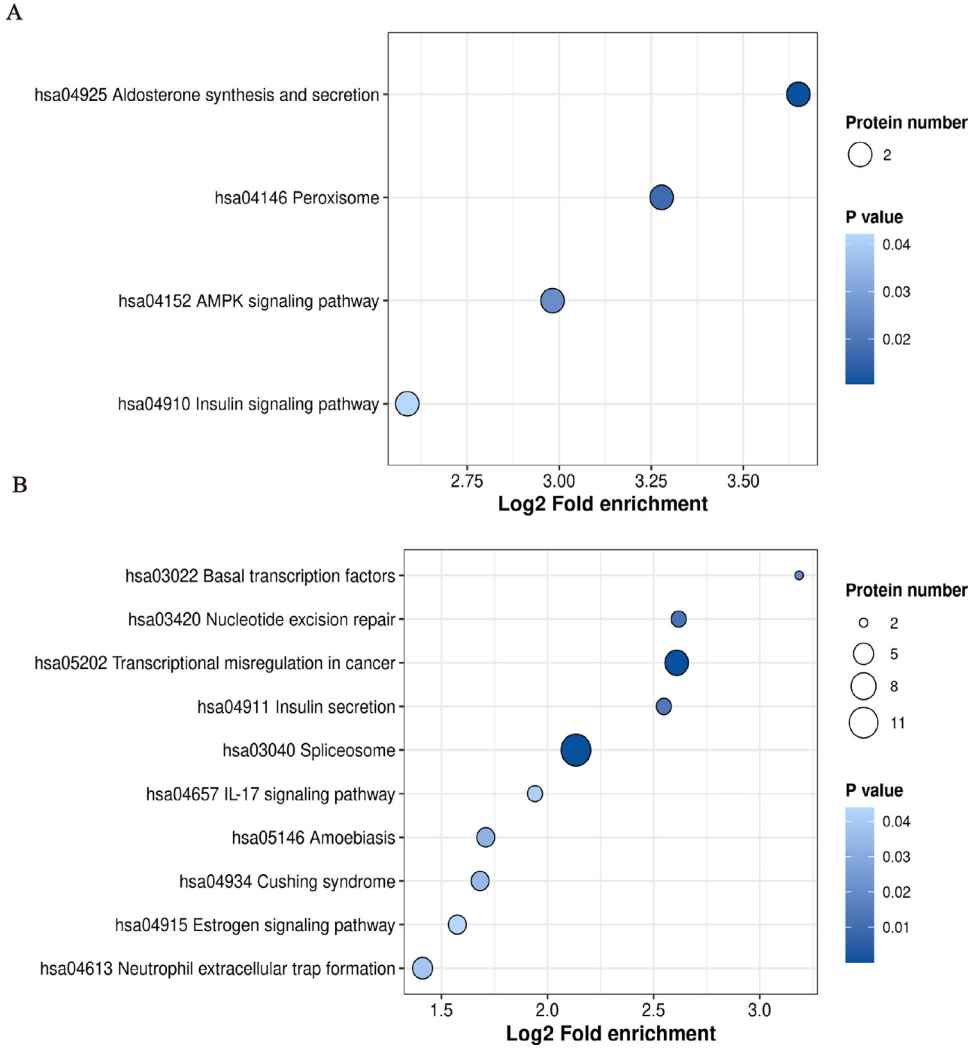

Fig. 4. Differential protein functional enrichment analysis. The results of the top 20 most significantly enriched functions are given in the significantly enriched bubble chart. The vertical axis is the KEGG pathway description information, and the horizontal axis is the enrichment degree of differential proteins in this function after Log2 transformation (Fold enrichment), the larger the value, the higher the degree of enrichment; the color of the dot represents the significance of enrichment P value, the bluer the color, the stronger the significance of enrichment; the size of the dot represents the number of differential proteins in the KEGG pathway, and the dot The larger the value, the greater the number of differential proteins. (A) Tibetan 2200 vs. Han 2200. (B) Tibetan 3780 vs. Tibetan 2200.

tion, and KEGG pathway classification statistics. 7) Enrichment analysis of differential proteins between the two groups is performed using Fisher's exact test method, involving GO, KEGG, and Protein domain functions. 8) When there are multiple experimental groups in the project, enrichment clustering analysis is conducted to compare the functional connections of differential proteins under different experimental conditions.

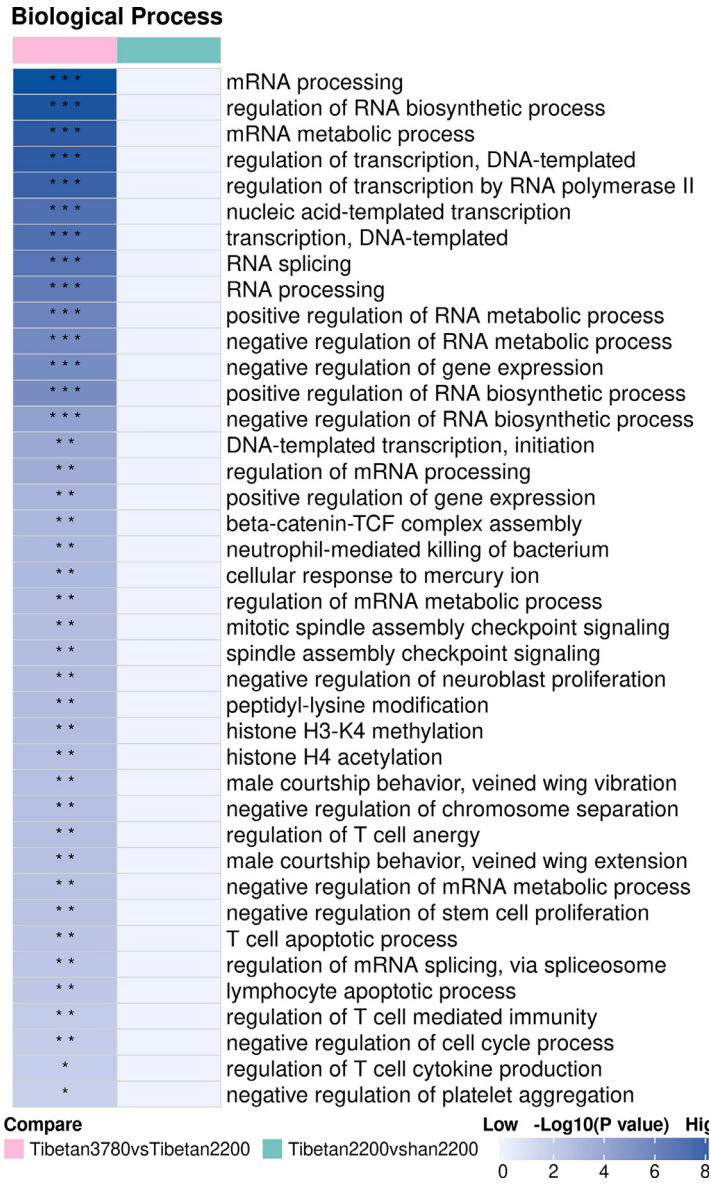

Fig. 5. Cluster analysis of differential proteins in different comparison groups. Based on the Fisher's exact test P value obtained from enrichment analysis, the hierarchical clustering method is used to cluster related functions in different comparison groups together and draw a heatmap. The horizontal direction of the heat map represents different comparison groups, and the vertical direction represents the enriched related functions of differentially expressed proteins in different comparison groups. Blue represents high enrichment significance, blue and white represents low enrichment significance, The Fisher exact probability test was used for comparison between groups. * $P < 0.05$, ** $P < 0.01$, * * * $P < 0.0001$.

Limitations

Due to the common practice among Han Chinese females, where the majority relocates from high-altitude regions to low-altitude areas for perinatal care until childbirth during pregnancy, our study lacks data on pregnant Han Chinese women who have migrated to high-altitude areas. Although 2200 m is not generally considered low altitude, altitude-induced illness is not induced at altitudes less than 2500 m, unless another pathology is present. At 2200 m, atmospheric oxygen pressure is about 80% of that at sea level, while at 3700 m it is 71 %, Thus, subjects residing at 3780 m experience a significantly more hypoxic environment than those at 2200 m.

Ethics Statement

The studies involving human participants were reviewed and approved by Qinghai University Affiliated Hospital Ethics Committee. The patients/participants provided their written informed consent to participate in this study. The approved ethics protocol number is AF-RHEC-0018–01.

Data Availability

4D-SmartDIA quantitative protein set of 30 different altitudehuman placental tissue samples (Original data) (iprox).

CRediT Author Statement

Huifang Liu: Data curation, Formal analysis, Writing – original draft; **Tana Wuren:** Conceptualization; **Ri-li Ge:** Funding acquisition, Project administration.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary Materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dib.2024.110542.

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