ORIGINAL RESEARCH ARTICLE

Expression of homeobox B13 gene and metabolomics study in placental tissues of gestational diabetes mellitus

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Lijuan Guo[1,2], Dan Xu[1], Jianbo Zhou[2], Yu Geng[3], Xiaoping Chen[1] and Xinping Ren[1]*

Department of Obstetrics and Gynecology, Yancheng Clinical College of Xuzhou Medical University, The First People's Hospital of Yancheng, Yancheng, 224000, Jiangsu, China[1]; Department of Obstetrics and Gynecology, Binhai County People's Hospital, Yancheng, 224500, Jiangsu, China[2]; Department of Interventional Medicine, Binhai County People's Hospital, Yancheng, 224500, Jiangsu, China[3]

***For Correspondence:** Email: *xinping_ren1011@sina.com*

Abstract

Our study aimed to investigate the expression characteristics of the homeobox B13 (HOXB13) gene in placental tissues of gestational diabetes mellitus (GDM) and its impact on placental metabolic function. Placental tissues from 30 GDM patients and normal pregnancy cases were collected. The expression of HOX family genes (including HOXB13 and HOXA2 among seven genes) was screened using quantitative polymerase chain reaction, and the protein expression of HOXB13 was validated by Western blot and immunohistochemistry. Untargeted metabolomics analysis using ultra-high-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry was performed to examine metabolic differences in placental tissues, and Kyoto Encyclopedia of Genes and Genomes pathway enrichment was applied to interpret metabolic regulation networks. The results showed that the mRNA and protein expression of HOXB13 were significantly lower in the GDM placentas compared to the normal pregnancy group. A total of 337 differential metabolites were identified, with the highest proportion being lipids and lipid-like molecules (37.96%). The levels of glucose and galactose in the GDM group were significantly reduced. Kyoto Encyclopedia of Genes and Genomes pathway analysis showed that these differential metabolites were enriched in pathways related to steroid hormone biosynthesis, retinol metabolism, and arachidonic acid metabolism. We conclude that HOXB13 is downregulated in GDM placentas, and its expression is closely associated with dysregulated glucose-lipid metabolism and abnormalities in key metabolic pathways. HOXB13 may serve as a potential biomarker and therapeutic target for GDM *(Afr J Reprod Health 2025; 29 [8]: 131-141).*

Keywords: Gestational diabetes mellitus; HOXB13; Metabolomics; Placental metabolism; KEGG pathway

Résumé

Notre étude visait à étudier les caractéristiques d'expression du gène homéobox B13 (HOXB13) dans les tissus placentaires de patients atteints de diabète gestationnel (DG) et son impact sur la fonction métabolique placentaire. Des tissus placentaires de 30 patientes atteintes de DG et de cas de grossesse normale ont été prélevés. L'expression des gènes de la famille HOX (dont HOXB13 et HOXA2 parmi sept gènes) a été criblée par réaction en chaîne par polymérase quantitative, et l'expression protéique de HOXB13 a été validée par Western blot et immunohistochimie. Une analyse métabolomique non ciblée par chromatographie liquide à ultra-haute performance couplée à une spectrométrie de masse à temps de vol quadripolaire a été réalisée afin d'examiner les différences métaboliques dans les tissus placentaires. L'enrichissement des voies de signalisation de l'Encyclopédie de Kyoto des gènes et des génomes a été appliqué pour interpréter les réseaux de régulation métabolique. Les résultats ont montré que l'expression de l'ARNm et des protéines de HOXB13 était significativement plus faible dans les placentas atteints de DG que dans le groupe de grossesse normale. Au total, 337 métabolites différentiels ont été identifiés, la proportion la plus élevée étant des lipides et des molécules de type lipidique (37,96 %). Les taux de glucose et de galactose dans le groupe GDM ont été significativement réduits. L'analyse des voies de signalisation de l'Encyclopédie des gènes et génomes de Kyoto a montré que ces métabolites différentiels étaient enrichis dans les voies liées à la biosynthèse des hormones stéroïdes, au métabolisme du rétinol et au métabolisme de l'acide arachidonique. Nous concluons que HOXB13 est sous-régulé dans les placentas du GDM, et que son expression est étroitement associée à un métabolisme glucose-lipides dérégulé et à des anomalies des principales voies métaboliques. HOXB13 pourrait servir de biomarqueur potentiel et de cible thérapeutique pour le GDM *(Afr J Reprod Health 2025; 29 87]: 131-141).*

Mots-clés: Diabète gestationnel; HOXB13; Métabolomique; Métabolisme placentaire; Voie KEGG

Introduction

Gestational diabetes mellitus (GDM) is a major complication of abnormal glucose metabolism in the middle and late stages of pregnancy, with a global incidence of 7%-18%.[1] It significantly increases the risk of adverse maternal and fetal outcomes, including preeclampsia, fetal developmental abnormalities, and long-term metabolic syndromes.[2-5] Trophoblast cells, as the core unit of maternal-fetal substance exchange, are crucial for placental metabolic balance and local inflammation. Their dysfunction is considered a key aspect of GDM pathology.[6,7] However, the molecular regulatory mechanisms underlying changes in the GDM placenta remain unclear, limiting the development of precise prevention and treatment strategies.

The HOX gene family, a key regulator of embryonic development,[8] modulates organ formation and cell differentiation through spatiotemporal-specific expression.[9] Aberrant expression of HOX genes has been implicated in tumors,[10,11] preeclampsia,[12] and other diseases. Previous studies have shown that HOXC8 is downregulated in GDM placentas and contributes to trophoblast dysfunction under high-glucose conditions.[13] As a member of the same family, HOXB13 has been shown to influence tumor progression and tissue regeneration by regulating the WNT/β-catenin and FAK/Src signaling pathways.[14,15] Its abnormal methylation is also associated with placental pathology in preeclampsia.[16,17] However, the role of HOXB13 in GDM remains unexplored.

Metabolomics studies have revealed glucose-lipid metabolic reprogramming in GDM placentas, characterized by suppressed fatty acid oxidation, abnormal amino acid transport, and mitochondrial dysfunction.[18-20] These metabolic imbalances may impact HOX gene expression through epigenetic modifications, forming a "metabolism-epigenetics-functional disorder" vicious cycle. However, the regulatory role of HOX family members (e.g., HOXB13) in placental metabolic networks and GDM progression remains unclear. This study aims to elucidate the role of HOXB13 in GDM through two key approaches: (1) Collecting clinical samples and using qPCR, Western blot, and immunohistochemistry to analyze HOXB13 expression differences between GDM and normal placentas; (2) Applying untargeted metabolomics using UPLC-QTOF-MS to identify GDM-specific metabolic markers and construct metabolic interaction networks. The findings may provide new theoretical insights for early diagnosis and targeted intervention in GDM.

Methods

Placental tissues were collected from normal pregnancy (NP) women (n = 16) and gestational diabetes mellitus (GDM) patients (n = 20) who delivered at The First People's Hospital of Yancheng, Jiangsu Province between January 2024 and December 2024. Inclusion criteria: ① For the NP group, GDM was excluded based on the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. For the GDM group, the diagnostic criteria of International Association of Diabetes in Pregnancy Study Group (IADPSG)—fasting blood glucose ≥5.1 mmol/L or OGTT 1 h/2 h blood glucose ≥10.0/8.5 mmol/L—were met; ② age 18–40 years; ③ singleton pregnancy; ④ informed consent to provide placental samples.

The exclusion criteria were: ① cases lacking diagnostic evidence of gestational diabetes in the clinical data were excluded; ② cases meeting the diagnostic criteria for gestational diabetes that also had other pregnancy complications, such as diabetes complicating pregnancy, intrahepatic cholestasis of pregnancy, chronic hypertension complicating pregnancy, hyperthyroidism complicating pregnancy, or gestational idiopathic thrombocytopenic purpura; and ③ abnormal placental development (such as placental abruption, placenta previa).. The characteristics of participants were included in Table 1.

Placental tissue collection

Placental tissue samples were collected within 30 minutes after fetal delivery. To avoid calcified and infarcted areas, a 1 cm³ tissue sample was taken from the central region of the maternal side of the placenta. The tissue was rinsed with 0.9% physiological saline, snap-frozen in liquid nitrogen, and stored at -80°C for further analysis.

Table 1: Characteristics of participants

	GDM	NP	P values
Number of patients (n)	10	10	
Age (y)	32.3	31.9	<0.05
Gestational age at the time of collection (w)	36.5	35.5	>0.05
First pregnancy (n)	3	6	>0.05
Subsequent pregnancy (n)	7	4	>0.05
Pregnancy duration (w)	37	38	>0.05
Cesarean section (n)	7	5	>0.05
Birth weight (g)	3426	2895	<0.05
Hb (g/dl)	11.7	11.1	>0.05
WBC (10^3/μL)	10.2	9.8	>0.05
PLT (10^3/μL)	206	201	>0.05
Insulin level (μU/mL)	10.23	9.69	>0.05
BMI (kg/m^2)	28.42	26.13	<0.05
Preeclampsia (n)	4	2	>0.05
Preterm labour (n)	2	1	>0.05

Quantitative real-time PCR (qPCR)

Total RNA was extracted from placental tissues using the RNA-easy Isolation Kit (Vazyme, Nanjing, China). RNA was purified using isopropanol precipitation, and its quality was assessed using a NanoDrop spectrophotometer, ensuring an A260/A280 ratio greater than 1.8. Reverse transcription was performed using the HiScript II qRT SuperMix II Kit (Vazyme), and the obtained cDNA was diluted 10-fold for storage. Specific qPCR primers for HOX family genes were designed and synthesized by GenScript Biotech (Nanjing, China). qPCR reactions were performed using the ChamQ Universal SYBR qPCR Master Mix (Vazyme) in a 20 μL reaction system, including 10 μL of 2× master mix, 0.4 μL of 10 μM forward and reverse primers, and 2 μL of cDNA template. The qPCR cycling conditions were as follows: 95°C for 30 sec (pre-denaturation); 40 cycles of 95°C for 5 sec (denaturation) and 60°C for 30 sec (annealing/extension); final melting curve analysis. β-actin was used as an internal reference gene, and the $2^{-\Delta\Delta Ct}$ method was applied to calculate relative gene expression levels.

Western blot analysis

A 100 mg placental tissue sample was homogenized in RIPA lysis buffer (Servicebio, G2002) for total protein extraction. Protein concentration was determined using the BCA method (Thermo Scientific). A total of 30 μg of protein was loaded onto a 10% SDS-PAGE gel (Vazyme) and transferred to a PVDF membrane. The membrane was blocked with 5% skim milk for 1 hour, followed by overnight incubation at 4°C with primary antibodies: HOXB13 (1:1000, Proteintech, 26384-1-AP), β-actin (1:1000, Proteintech, HRP-66009). The membrane was then washed with TBST and incubated with HRP-conjugated secondary antibody (1:10,000, Proteintech, SA00001-2) for 1 hour. Protein bands were detected using ECL detection reagent (Abbkin, BMU102-CN).

Immunohistochemistry (IHC) staining

Placental tissue paraffin sections (3 μm thick) were deparaffinized and subjected to antigen retrieval. Endogenous peroxidase activity was blocked with 3% hydrogen peroxide (H2O2), and 5% bovine serum albumin (BSA) was used to block non-specific binding. Sections were incubated overnight at 4°C with primary antibody HOXB13 (1:200, Proteintech, 26384-1-AP), followed by PBS washing and incubation with an HRP-conjugated secondary antibody (1:100, Proteintech, SA00001-2) for 30 minutes. Detection was performed using a DAB chromogenic reagent (Servicebio, G1212), and cell nuclei were counterstained with hematoxylin. The staining results were independently evaluated by two blinded pathologists.

ELISA

ELISA was conducted using a HOXB13 ELISA kit (BY-EH111390, BoYabscience, Nanjing, Jiangsu, China). All samples were diluted appropriately using the sample dilution buffer provided in the kit. If sample concentrations exceeded the standard curve range, additional dilution was performed. The pre-coated ELISA plate was prepared by setting up standard, blank, and sample wells. Into the standard wells, 50μL of calibration standards at different concentrations were added, while 50μL of sample dilution buffer was pipetted into the blank wells. For sample wells, 50μL of the prepared sample was added. To each well (except the blank), 100 μL of HRP-labeled detection antibody was introduced. The plate was then sealed and incubated at 37°C for 60 minutes. Following incubation, the liquid was discarded, and the plate was patted dry on absorbent paper. Each well was filled with wash buffer and left for 20 seconds before being discarded. This step was repeated five times to ensure thorough removal of unbound components. After washing, substrate solutions A and B were mixed at a 1:1 ratio, and 100 μL of the resulting solution was added to each well. The plate was covered and incubated in the dark at 37°C for 15 minutes. Subsequently, 50μL of stop solution was added to terminate the reaction, and absorbance was measured at 450nm using a microplate reader. To determine sample concentrations, a standard curve was generated using the absorbance values of the calibration standards. A four-parameter logistic (4-PL) fitting model was applied to calculate sample concentrations from OD values. If dilution was performed, the calculated concentration was multiplied by the dilution factor to obtain the final concentration.

Metabolomics analysis

Based on Western blot and immunohistochemistry results, three NP placental tissues with high HOXB13 expression and three GDM placental tissues with low HOXB13 expression were selected for untargeted metabolomics sequencing analysis (conducted by Novogene Co., Ltd., Beijing, China). Placental tissues were ground in liquid nitrogen, and metabolites were extracted using 80% methanol (20:1 v/w ratio). The samples were centrifuged at 16,000 × g at 4°C for 15 minutes, and the supernatant was collected. After nitrogen blow-drying, samples were analyzed using a UHPLC-QTOF-MS system (Agilent 6545XT). The chromatographic column used was ACQUITY UPLC HSS T3 (2.1 × 100 mm, 1.8 μm). The mobile phases were 0.1% formic acid in water (A) and acetonitrile (B), with a gradient elution program of 5%-95% B over 15 minutes. The mass spectrometry scan range was m/z 50-1500 in both positive and negative ion modes.

Statistical analysis

Raw data were processed using Progenesis QI software for peak alignment, normalization, and metabolite annotation (HMDB and KEGG databases). Differential metabolites were selected based on the criteria: VIP > 1.0, Fold Change (FC) > 1.5 or < 0.667, $P < 0.05$. Pathway enrichment analysis was conducted using MetaboAnalyst 5.0, with KEGG pathway analysis ($P < 0.05$) performed to explore potential metabolic networks.

Ethical consideration

This study was approved by the Ethics Committee of The First People's Hospital of Yancheng (2023-YC-123), and all participants signed informed consent forms.

Results

Screening of HOX Gene Family: qPCR Validation

qPCR was used to detect the expression levels of seven HOX family members (HOXB13, HOXA2, HOXC8, HOXA10, HOXB6, HOXD10, HOXD9) in placental tissues from GDM and normal pregnancy (NP) groups. The results showed that placental (0.28 ± 0.05 vs. 1.00 ± 0.12, $P < 0.001$) and serum HOXB13 expression (0.34 ± 0.09 vs. 1.00 ± 0.14, $P < 0.001$) in the GDM group was significantly lower than in the NP group, with the greatest degree of difference among all tested genes. Among the remaining genes, only HOXC8 showed a slight decrease, while HOXA2, HOXA10, and others showed no statistically significant differences ($P > 0.05$, Figure 1A).

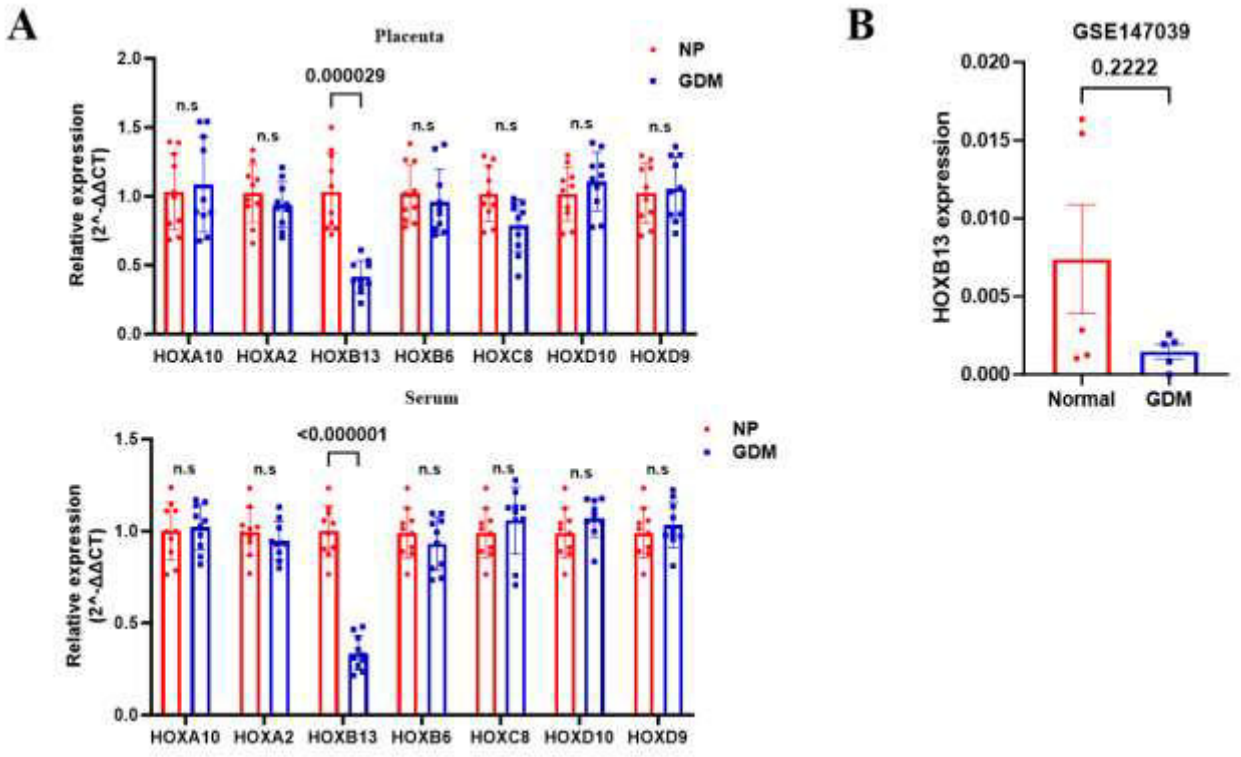

Figure 1: HOX family expression in NP and GDM tissues. A. Placental and serum HOXB13, HOXA2, HOXC8, HOXA10, HOXB6, HOXD10, and HOXD9 expression in NP and GDM tissues were assessed by qPCR. B. HOXB13 expression in offspring of a mouse model of GDM and normal mice according to GSE147039 dataset.

Based on these results, the subsequent study focused on functional validation of HOXB13.

In the GSE147039 dataset, HOXB13 exhibits a trend of downregulation in the offspring of a mouse model of GDM compared to normal mice (Figure 1B). However, due to substantial individual variability among the mice, the difference did not reach statistical significance. Nevertheless, this trend suggests the potential heritable downregulation of HOXB13 in GDM.

Validation of HOXB13 protein expression by western blot

Western blot analysis showed that HOXB13 protein expression in GM placental tissues was reduced by 65.2% compared to the NP group (0.34 ± 0.07 vs. 0.98 ± 0.11, $P < 0.001$, Figure 2). This trend was consistent with the qPCR results. β-actin was used as a loading control, and its band intensity showed no significant difference between groups ($P = 0.876$).

Validation of HOXB13 protein expression by immunohistochemistry staining

According to immunohistochemistry (IHC) staining, in the NP group, HOXB13 was strongly expressed in the cytoplasm of trophoblast cells, appearing as brown-yellow granules, whereas the staining intensity in the GDM group was significantly reduced (Figure 3). Additionally, we examined two early pregnancy miscarriage samples (gestational days 50 and 42) and found that HOXB13 was also positively expressed in early villous tissues.

ELISA detection of HOXB13 expression and their association with fasting glucose level

According to ELISA results, placental (8.79 ± 2.63 vs. 14.65 ± 2.99, $P = 0.0007$) and serum (13.63 ± 2.20 vs. 16.48 ± 1.64, $P = 0.0007$) HOXB13 expression levels were lower in GDM tissues than NP tissues (Figure 4A).

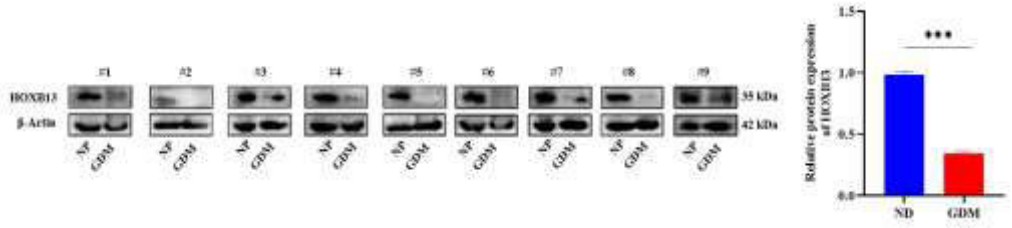

Figure 2: Western blot analysis of HOXB13 protein expression in paired NP and GDM placental tissues (n = 9 pairs).

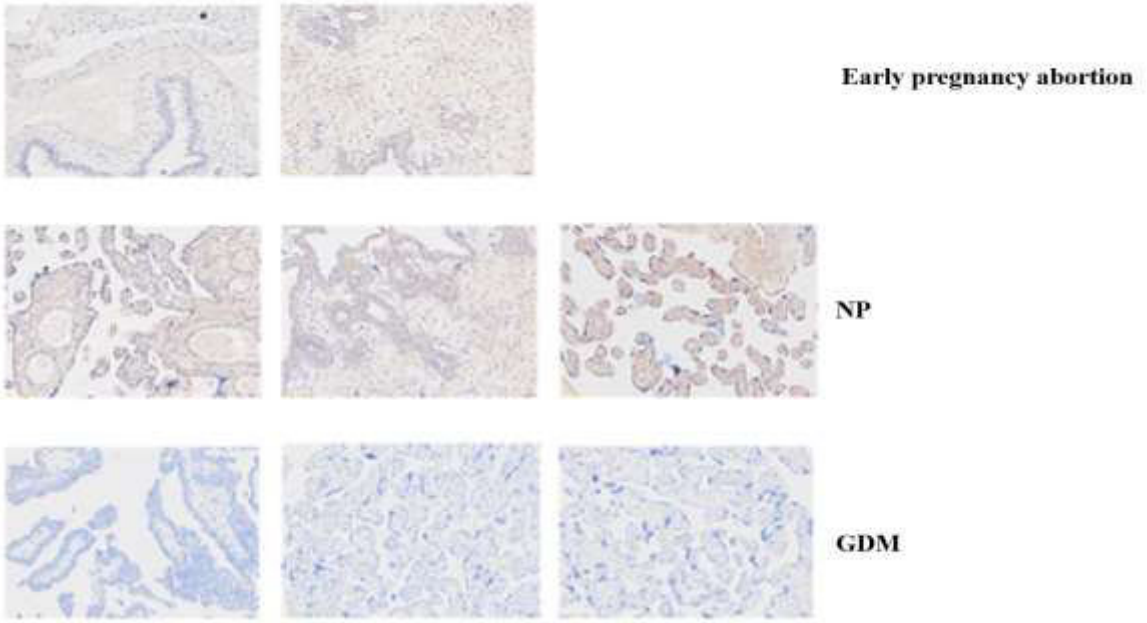

Figure 3: Immunohistochemistry detection of HOXB13 expression in villous tissue of early pregnancy abortion, NP, and GDM placental tissues.

Next, Pearson correlation analysis was performed to reveal the correlation between HOXB13 expression and fasting glucose level, and the results showed significant positive correlation between placental/serum HOXB13 expression and fasting glucose level (Figure 4B).

Association of HOXB13 with placental metabolic function

A total of 1,704 positive ion mode metabolites and 1,203 negative ion mode metabolites were identified in this study. Differential metabolite screening was conducted based on VIP > 1.0, FC > 1.5 or < 0.667, and P < 0.05.

In the GDM vs. NP comparison group, a total of 189 significantly altered metabolites were identified in the positive ion mode, including 166 upregulated and 23 downregulated metabolites. In the negative ion mode, 148 significantly altered metabolites were identified, with 105 upregulated and 43 downregulated.

To classify the detected metabolites, Table 2 was drawn to reflect their chemical categories and proportions.

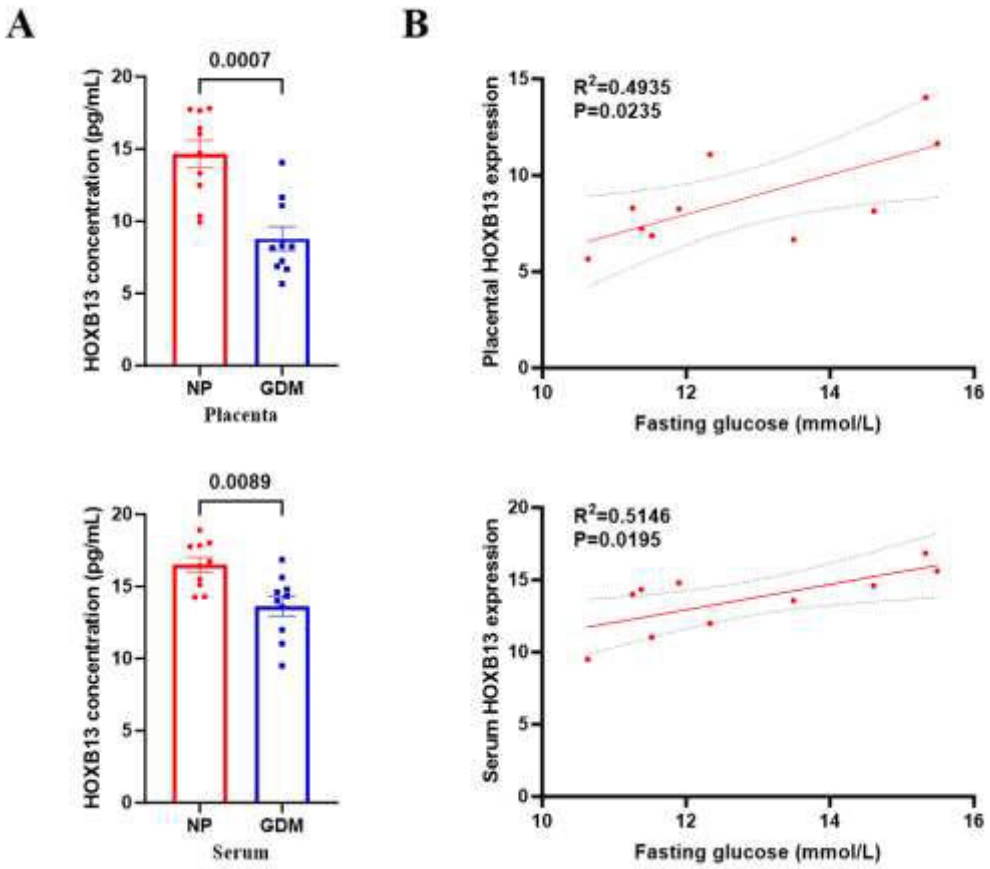

Figure 4: ELISA detection of HOXB13 expression and their association with fasting glucose level. A. Placental and serum HOXB13 expression levels in NP and GDM tissues were assessed by ELISA. B. Correlation of placental/serum HOXB13 expression and fasting glucose level was assessed using Pearson correlation analysis

The major metabolic categories included: lipids and lipid-like molecules (37.96%), organic acids and derivatives (19.06%), organoheterocyclic compounds (15.80%), benzenoids (9.78%), organic oxygen compounds (6.44%), phenylpropanoids and polyketides (5.77%), nucleosides, nucleotides, and analogues (2.42%), alkaloids and derivatives (1.00%).

Screening of differential metabolites

A univariate analysis was performed on all detected metabolites, including unidentified metabolites, based on the screening criteria FC > 1.5 or < 0.67 and P < 0.05. A volcano plot was used to illustrate the top 10 most significantly altered metabolites (Figure 5).In the positive ion mode, the most significantly upregulated metabolites included: Octaethyleneglycol monododecyl ether, Heptaethylene glycol monododecyl ether, 19-Hydroxyconopharyngine, L-2-amino-8-hydroxyoctanoate, Capsaicin beta-D-glucopyranoside. The most significantly downregulated metabolites included: Enniatin B1, Arenarine B, Ro 20-1724, N-Methyldioctylamine, Guanadrel.

In the negative ion mode, the most significantly upregulated metabolites included: Xeniolide F, Androsta-1,4,6-triene-3,17-dione, Grevillol, Phosphatidic acid (20:3(5Z,8Z,14Z)-O(11S,12R)/12:0), 1beta-Hydroxyalantolactone. The most significantly downregulated metabolites included: 3-hydroxy-O,5-dimethyl-L-tyrosine, Pizotifen, 3-oxo-C14 homoserine lactone, 3beta,5alpha,6beta-Cholestanetriol, Mescaline.

Table 2: Classification and proportion of detected metabolites

Metabolic category	Percentage (%)
Lipids and lipid-like molecules	37.96
Organic acids and derivatives	19.06
Organoheterocyclic compounds	15.80
Benzenoids	9.78
Organic oxygen compounds	6.44
Phenylpropanoids and polyketides	5.77
Nucleosides, nucleotides, and analogues	2.42
Alkaloids and derivatives	1.00
Organic nitrogen compounds	0.59
Lignans, neolignans and related compounds	0.50
Organohalogen compounds	0.50
Organosulfur compounds	0.08
Organophosphorus compounds	0.08

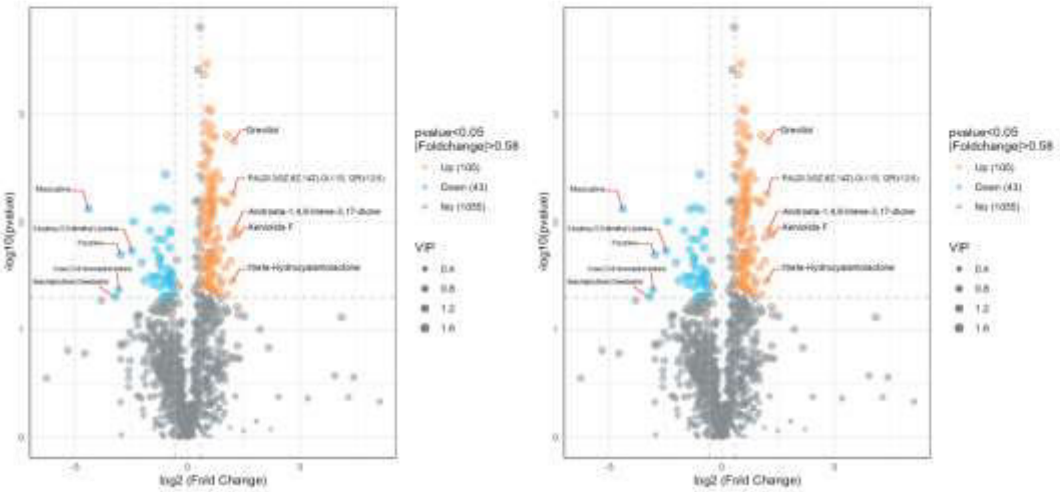

Figure 5: Volcano plot of differential metabolites (Left: Positive ion mode; Right: Negative ion mode).

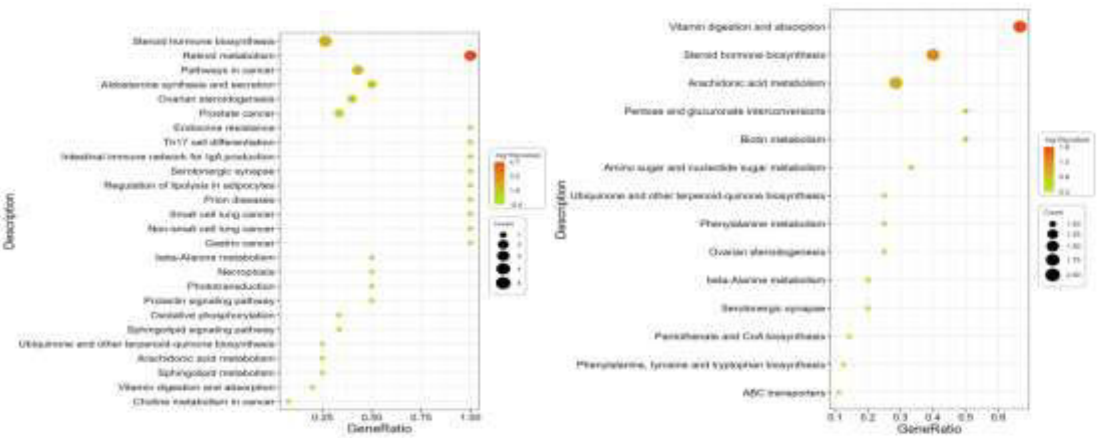

Figure 6: KEGG pathway enrichment analysis of significantly altered metabolites (Left: Positive ion mode; Right: Negative ion mode).

Bioinformatics analysis of differential metabolites

Cluster analysis was performed to determine the metabolic patterns under different experimental conditions. Metabolites with similar metabolic patterns may have similar functions or participate in the same metabolic processes or pathways. Therefore, clustering metabolites with similar or related patterns allows for functional inference.
Significantly altered metabolites (VIP > 1.0, P < 0.05, FC > 1.5 or < 0.67, and with identified names) were subjected to KEGG pathway enrichment analysis. The results of the pathway enrichment analysis are shown in Figure 6.

In the positive ion mode, differential metabolites were mainly enriched in pathways such as: , Retinol metabolism, Steroid hormone biosynthesis, Pathways in cancer, Metabolic pathways, Aldosterone synthesis and secretion, Ovarian steroidogenesis, Prostate cancer, Endocrine resistance, Th17 cell differentiation, Intestinal immune network for IgA production, Serotonergic synapse, Regulation of lipolysis in adipocytes, Prion diseases, Small cell lung cancer, Non-small cell lung cancer, Gastric cancer, Beta-alanine metabolism, Necroptosis, Phototransduction, Prolactin signaling pathway, Oxidative phosphorylation, Sphingolipid signaling pathway, Sphingolipid metabolism.
In the negative ion mode, differential metabolites were significantly enriched in pathways such as: Vitamin digestion and absorption, Steroid hormone biosynthesis, Arachidonic acid metabolism, Pentose and glucuronate interconversions, Biotin metabolism, Amino sugar and nucleotide sugar metabolism, Ubiquinone and other terpenoid-quinone biosynthesis, Phenylalanine metabolism, Ovarian steroidogenesis, Beta-alanine metabolism, Serotonergic synapse, Pantothenate and CoA biosynthesis, Phenylalanine, tyrosine, and tryptophan biosynthesis, ABC transporters.

Discussion

Gestational diabetes mellitus (GDM) is a pregnancy complication characterized by placental metabolic dysfunction, and its molecular mechanisms remain incompletely understood. This study integrates HOX gene family screening, protein expression validation, and metabolomics analysis to reveal, for the first time, the critical regulatory role of HOXB13 in the GDM placenta.

qPCR screening showed that HOXB13 expression was significantly lower in GDM placentas compared to normal pregnancies, whereas other HOX family members (such as HOXA2 and HOXC8) exhibited smaller or statistically insignificant differences. This suggests that HOXB13 may be a key regulatory factor in placental metabolic imbalance in GDM. Western blot and immunohistochemistry further confirmed that HOXB13 protein expression was reduced in trophoblast cells of GDM placentas, and its low expression was closely associated with abnormal glucose metabolism in the placenta.

The HOX gene family, known as a key regulator of embryonic development, has recently been linked to metabolic diseases[21]. For instance, HOXA10 influences energy metabolism homeostasis by regulating adipocyte differentiation[22], while HOXC8 is involved in hepatic lipid metabolism regulation[23]. This study is the first to demonstrate that HOXB13 downregulation in the placenta is significantly associated with glucose-lipid metabolic reprogramming. Untargeted metabolomics analysis identified 337 differential metabolites in GDM placentas, with the highest proportion belonging to lipids and lipid-like molecules (37.96%). This includes the accumulation of palmitic acid, sphingosine, and other lipotoxic metabolites, suggesting that fatty acid oxidation and glycolytic imbalance may be key mechanisms of placental dysfunction in GDM. Additionally, targeted quantification of sugars revealed that glucose (47.8% decrease) and galactose (46.7% decrease) levels were significantly lower in GDM placentas and positively correlated with HOXB13 expression. These findings indicate that HOXB13 may be involved in GDM pathology by regulating placental energy substrate utilization.

KEGG pathway enrichment analysis further revealed that differential metabolites in both positive and negative ion modes were enriched in pathways such as steroid hormone biosynthesis, retinol metabolism, arachidonic acid metabolism, and vitamin digestion and absorption. For example,

in the negative ion mode, enrichment in vitamin absorption pathways may reflect abnormal placental transport of fat-soluble vitamins, while in the positive ion mode, disruptions in retinol metabolism may be linked to enhanced oxidative stress and inflammation in the placenta. Notably, the consistent enrichment of the steroid hormone biosynthesis pathway ($P < 0.05$ in both ion modes) suggests that HOXB13 may influence maternal insulin sensitivity through regulation of placental hormone secretion. These findings provide new insights into the metabolic networks underlying GDM.

Study strengths and limitations

The main advantage of our study lies in that we for the first time reveal the expression characteristics of HOXB13 in the placenta of pregnant women with gestational diabetes and its potential role in metabolic regulation, which may provide a potential biomarker and therapeutic target for GDM. The main limitations of this study include: (1) The samples were obtained from a single region, which may affect the statistical power. (2) Further molecular biology experiments, such as overexpression or knockdown models of HOXB13, are needed to directly confirm its causal effect. (3) Since metabolomics analysis is mainly based on correlations, future studies should combine transcriptomics and protein interaction studies to clarify the specific regulatory mechanisms.

Conclusions

HOXB13 is downregulated in GDM placentas, and its expression is closely associated with dysregulated glucose-lipid metabolism and abnormalities in key metabolic pathways. HOXB13 may serve as a potential biomarker and therapeutic target for GDM.

Funding

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Conflicts of interest

All authors declare that there are no conflicts of interest.

Data availability statement

Original data generated in this study were available from the corresponding author on reasonable request.

Authors contribution

Lijuan Guo, Dan Xu: conceived and designed the study. Jianbo Zhou, Yu Geng: collected and analysed the data. Xiaoping Chen, Xinping Ren: prepared the manuscript. All authors mentioned in the article approved the manuscript.

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