Exploration of specific immunohistochemical markers for a partial hydatidiform mole

1) Chiba University Hospital, Japan 2) Ciba Cancer Center, Japan

Hirokazu Usui[1,2)], Matsuko Nakamura[1)], Eri Katayama[1)], Asuka Sato[1)], Kaori Koga[1)]

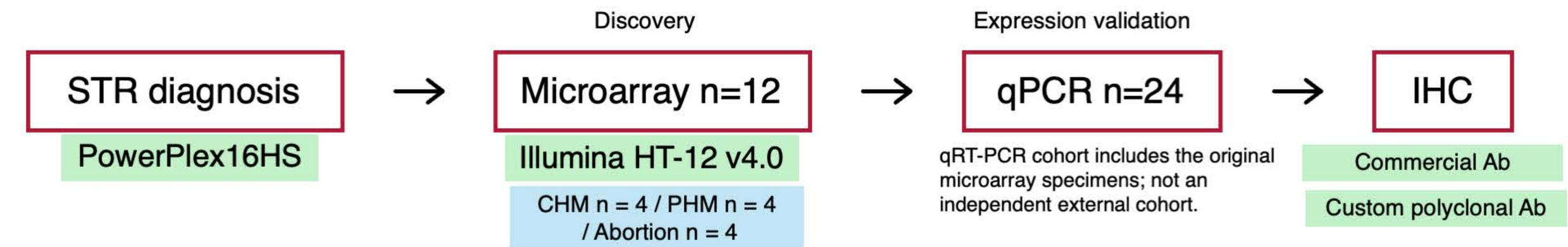
ABSTRACT

[Objective] Accurate histopathological diagnosis of partial hydatidiform mole (PHM) remains challenging. Although p57KIP2 immunohistochemistry helps distinguish complete hydatidiform mole (CHM) from PHM, reliable immunohistochemical markers for differentiating PHM from biparental abortion (AB) are lacking. This study aimed to identify candidate immunohistochemical markers for PHM.
[Methods] Diagnoses were confirmed by short tandem repeat (STR) genotyping. Gene expression profiles of CHM (n = 4), PHM (n = 4), and AB (n = 4) were analyzed using Illumina HumanHT-12 v4 microarrays. Candidate genes were evaluated by quantitative real-time PCR (qPCR) in 24 samples (8 per group, including the 12 microarray samples). Commercial and custom-generated, peptide-affinity-purified antibodies were subsequently evaluated by immunohistochemistry (IHC).
[Results] Transcriptomic profiling identified candidate molecular markers for PHM diagnosis, but reliable IHC assays for HBZ, HBE1, and CD209 could not be established. However, all evaluated antibodies targeting HBE1, HBZ, and CD209 exhibited strong nonspecific decidual staining, preventing the establishment of reliable IHC assays. In contrast, anti-HBG successfully stained fetal erythrocytes in AB and placental mesenchymal dysplasia tissues.
[Conclusion] Transcriptomic profiling identified candidate molecular markers for PHM diagnosis, but reliable HBE1/HBZ immunostaining could not be established. Further evaluation of alternative targets and antibody specificity is required to develop clinically applicable IHC markers.

BACLGROUND & OBJECTIVE

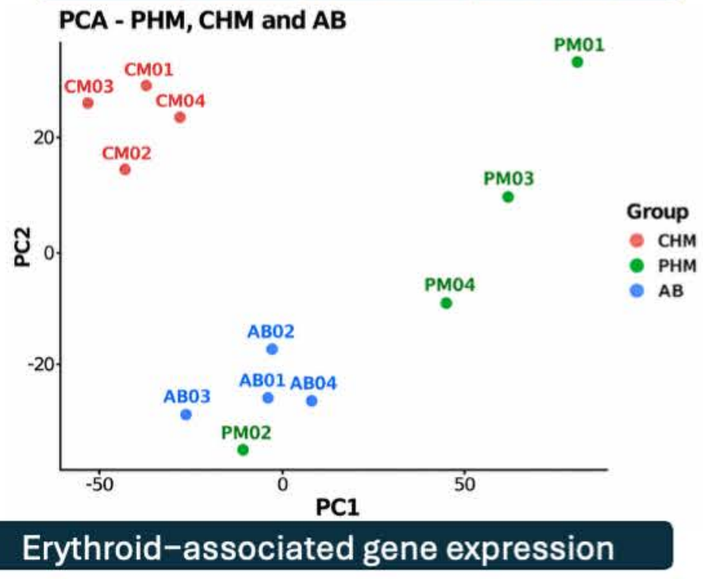
- The distinction of PHM from atypical (hydropic) abortus villi remains challenging.
- No effective auxiliary immunohistochemical procedure currently exists to distinguish PHM from biparental abortion.
- The aim of this study was to identify specific immunohistochemical markers for the diagnosis of PHM.

STUDY DESIGN

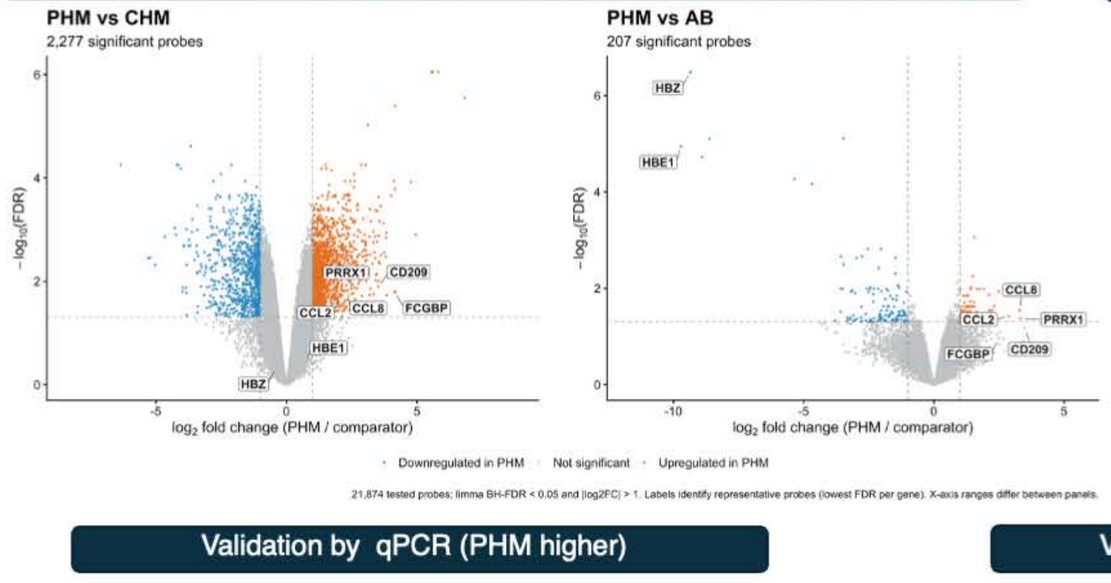


RESULTS

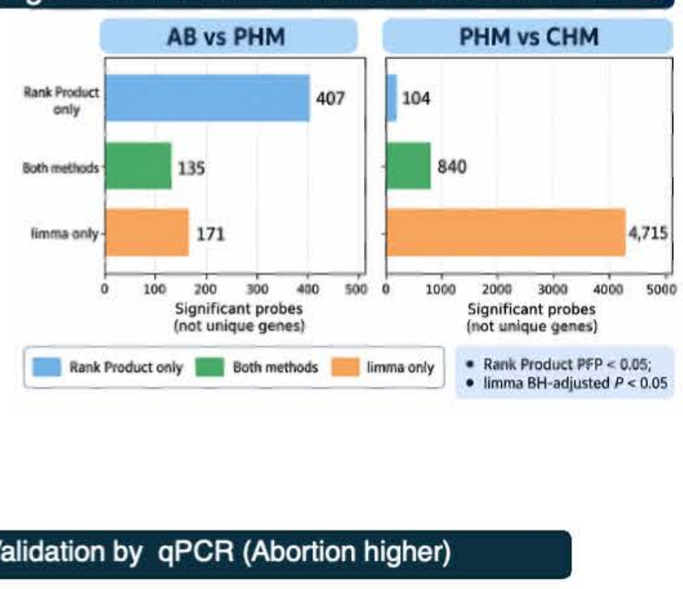
Principal Component Analysis (PCA)



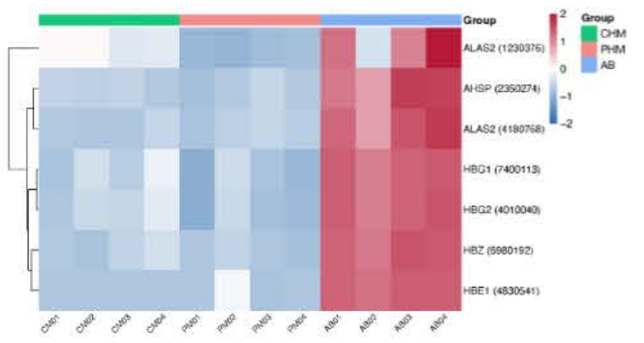
Differential gene expression in PHM, CHM and biparental abortion



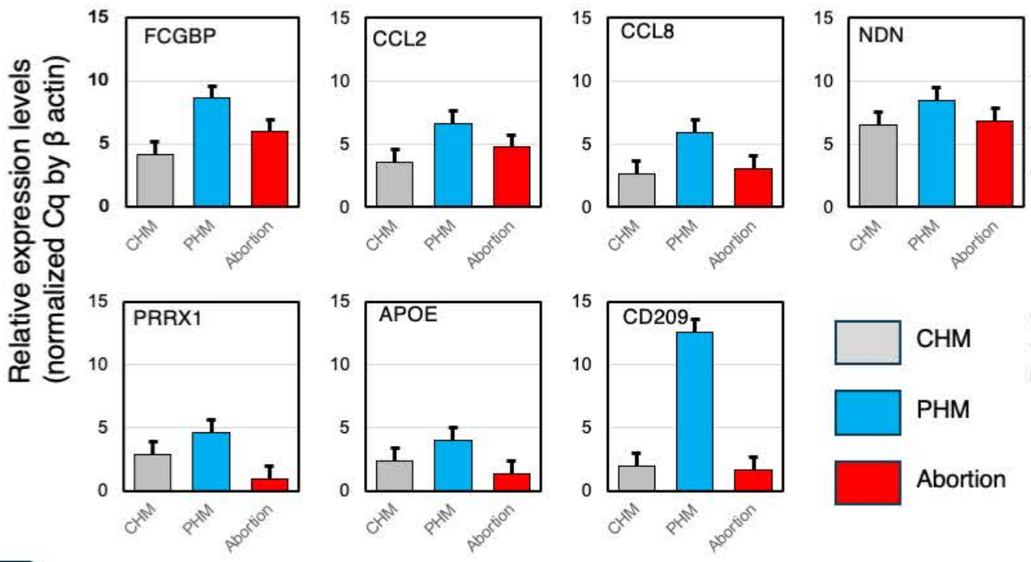
Agreement between Rank Product and limma



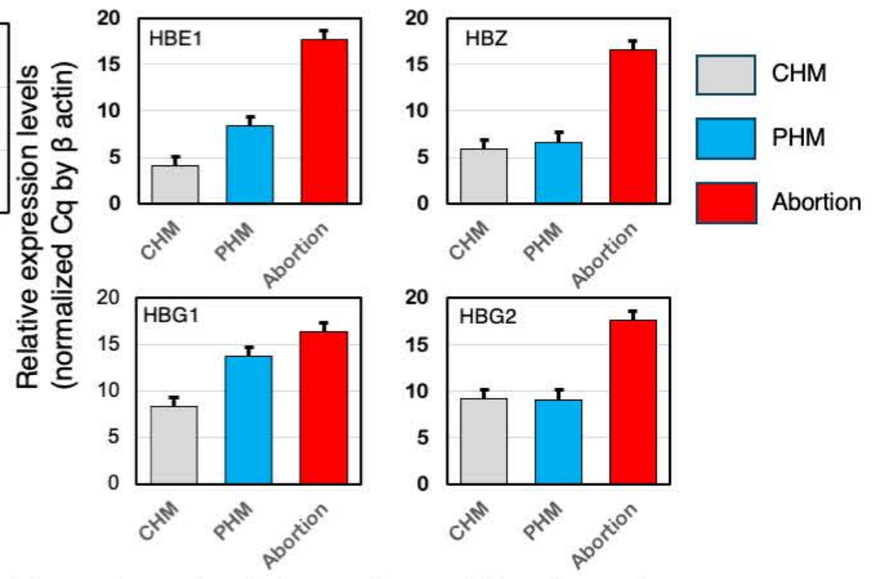
Erythroid-associated gene expression



Validation by qPCR (PHM higher)



Validation by qPCR (Abortion higher)

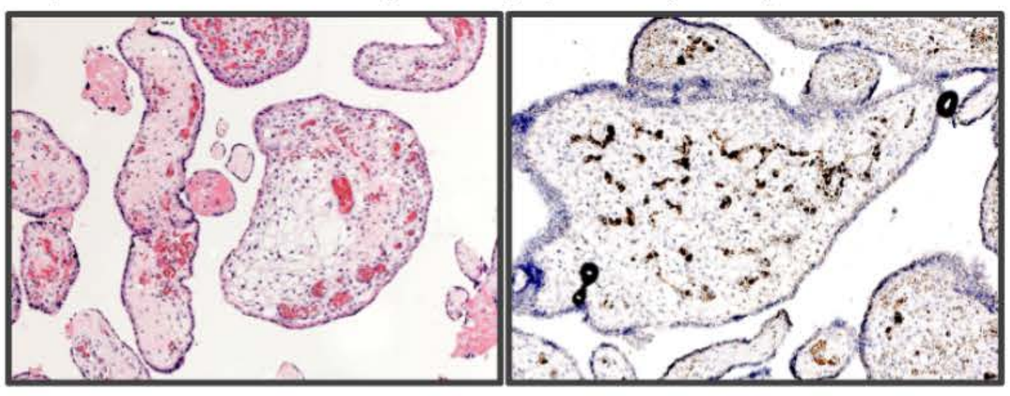


Immunohistochemical evaluation

Target	Vendor	Antibody type	Catalog No.	IHC findings
HBZ	Bioss	Rabbit polyclonal	bs-9883R	Strong nonspecific decidual staining
HBZ	Santa Cruz	Mouse monoclonal	sc-101272	Strong nonspecific decidual staining
HBZ	GeneTex	Mouse monoclonal	GTX633545	Strong nonspecific decidual staining
HBZ	Custom	Rabbit polyclonal; peptide-affinity-purified		Strong nonspecific decidual staining
HBE1	Abcam	Rabbit polyclonal	ab228709	Strong nonspecific decidual staining
HBE1	GeneTex	Rabbit polyclonal	GTX108396	Strong nonspecific decidual staining
HBE1	Custom	Rabbit polyclonal; peptide-affinity-purified		Strong nonspecific decidual staining
HBG	Santa Cruz	Mouse monoclonal	sc-21756	Fetal erythrocyte staining in AB and PMD
CD209	BD Pharmingen	Mouse monoclonal	551249	Strong nonspecific decidual staining

All evaluated antibodies targeting HBZ, HBE1, and CD209 showed strong nonspecific decidual staining. In contrast, anti-HBG successfully stained fetal erythrocytes in AB and PMD tissues.

Immunohistochemical detection of fetal erythrocytes in placental mesenchymal dysplasia (PMD).



H&E (left) and anti-HBG IHC (right) from different sections of the same PMD case. Anti-HBG (Santa Cruz Biotechnology, sc-21756) highlighted fetal erythrocytes within chorionic villous vessels.

DISCUSSION

- Molecular differences: PHM differed markedly from CHM but showed fewer differentially expressed probes compared with biparental abortion (AB).
- Erythroid-associated genes: Higher expression of HBE1, HBZ, HBG1, and HBG2 in AB may reflect differences in gestational age or tissue composition rather than PHM-specific alterations.
- IHC limitations: Antibodies targeting HBZ, HBE1, and CD209 showed strong nonspecific decidual staining, including peptide-affinity-purified custom antibodies against HBZ and HBE1. These findings highlight the difficulty of translating transcriptomic candidates into reliable diagnostic IHC markers.

CONCLUSION

- Transcriptomic profiling identified candidate PHM biomarkers, but reliable IHC assays for HBZ, HBE1, and CD209 could not be established. Further validation of alternative markers is required.