Trophoblast and vascular organoid cultures recapitulate the role of WNT2B in promoting intravillous vascularization in human ruptured ectopic pregnancy

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Abstract (300 word limit)

Statement of the Problem: Ectopic pregnancy is a critical pregnancy complication and a major cause of pregnancy-related death during the first trimester. We revealed the importance of intravillous vascularization as one of the etiological factors for human ruptured ectopic pregnancy, and demonstrated the WNT2B is, at least, one of important factors for intravillous angiogenesis. Methodology & Theoretical Orientation: Clinical placental samples obtained from pregnant women at the International Peace Maternity and Child Health Hospital (IPMCH) from October 2019 to November 2021 and divided into intrauterine pregnancy (IP) (n=46), abortive ectopic pregnancy (AEP) (n=38) and ruptured ectopic pregnancy (REP) (n=33) groups for histological analyses, explant culture, RT-qPCR, and ELISA. Maternal-fetal interfaces (IP=2, AEP=2, REP=3) were collected for single-cell RNA sequencing. HUVECs, trophoblast stem cells, trophoblast organoids and vessel organoids were applied to mechanism research. Findings: Compared with AEP, the size of REP placental villi and the depth of trophoblast invasion are correlated with the extent of intravillous vascularization. Single-cell transcriptomic analysis demonstrates that they exhibited fundamental differences in angiogenic and WNT signaling pathways. Organoid models were used to investigate the crosstalk between trophoblast and intravillous vascularization. We identified a key pro-angiogenic factor secreted by human trophoblasts, WNT2B, that promotes villous vasculogenesis, angiogenesis, and vascular network expansion in REP condition. Conclusion & Significance: Our results revealed the important role of WNT-mediated angiogenesis and built an organoid co-culture model for investigating intricate communications between trophoblasts and endothelial/endothelial progenitor cells.

Image

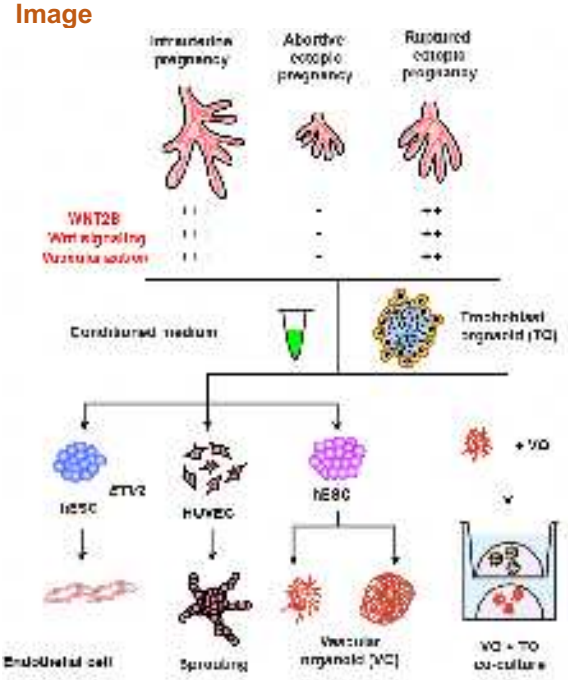


Figure 1. Schematic illustration and summary of the experiments design and WNT2B promoting the vascular sprouting.

Recent Publications (minimum 5)

1. Zhang, D., Shi, W., Li, C., Yuan, J.J., Xia, W., Xue, R.H., Sun, J., and Zhang, J. (2016). Risk factors for recurrent ectopic pregnancy: a case-control study. Bjog 123 Suppl 3, 82-89. 10.1111/1471-0528.14011
2. Fukami, T., Tsujioka, H., Matsuoka, S., Sorano, S., Tohyama, A., Yamamoto, H., Nakamura, S., Goto, M., Matsuoka, R., and Eguchi, F. (2016). Rupture risk factors of fallopian tubal pregnancy. Clin Exp Obstet Gynecol 43, 800-802.
3. Wang, Y., and Zhao, S. (2010). Chapter6, Vasculogenesis and Angiogenesis of Human Placenta. In Vascular Biology of the Placenta., (San Rafael (CA): Morgan & Claypool Life Sciences).
4. Verlohren, S., and Dröge, L.A. (2022). The diagnostic value of angiogenic and antiangiogenic factors in differential diagnosis of preeclampsia. Am J Obstet Gynecol 226, S1048-s1058. 10.1016/j.ajog.2020.09.046.
5. Foulquier, S., Daskalopoulos, E.P., Lluri, G., Hermans, K.C.M., Deb, A., and Blankesteijn, W.M. (2018). WNT Signaling in Cardiac and Vascular Disease. Pharmacol Rev 70, 68-141. 10.1124/pr.117.013896.

Photograph



Biography (150 word limit)

Mrs. Zhao majors in Obstetrics and Gynecology at Shanghai Jiaotong University of Medicine and is currently a second-year Ph.D. student. Mrs. Zhao is aimed at investigating the molecular mechanisms involved in placental development, particularly in pathological pregnancy. Considering the lack of EP phenotypes in rodents, as well as fundamental differences in placental structures between mice and humans, we established human endometrium organoids, placental organoids, and fallopian tubal organoids to investigate the pathogenesis of ectopic pregnancy.

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Notes/Comments:

We are pleased to submit our abstract entitled "**Trophoblast and vascular organoid cultures recapitulate the role of WNT2B in promoting intravillous vascularization in human ruptured ectopic pregnancy",** for consideration to be accepted as a poster**.** We are very grateful for your consideration and careful handling of our abstract, and we look forward to your reply.