Epithelial Membrane Protein 2 (EMP2) deficiency alters placental angiogenesis

Alison Chu, Carmen J. Williams, Carla Janzen, Madhuri Wadehra

Division of Neonatology and Developmental Biology, Departments of Pediatrics, Pathology and Obstetrics & Gynecology
Placental blood vessel development

<table>
<thead>
<tr>
<th>Maternal Side</th>
<th>Fetal Side</th>
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<tbody>
<tr>
<td>Myometrium</td>
<td>Decidua</td>
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<td>Maternal spiral artery</td>
<td>Syncytial knot</td>
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<tr>
<td>Smooth muscle</td>
<td>Extravillous invading trophoblast</td>
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<td>Maternal blood flow</td>
<td>Villous trophoblast</td>
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<tr>
<td>Myometrium</td>
<td>Cytotrophoblasts</td>
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<td>Myometrium</td>
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- ✓ HIF1α
- ✓ VEGF
- ? Epithelial membrane protein 2

NK CELLS

DECIDUA

- Normal pregnancy
- Non-physiological change
Epithelial membrane protein 2 (EMP2)

- EMP2 is a transmembrane protein that modulates cell surface expression of MHC class I molecules, integrins, and caveolins.
- In endometrial cell lines, EMP2 expression regulates angiogenesis via alterations of HIF-1α and VEGF.
- In the mouse, EMP2 is expressed on the uterine epithelial cell surface and in trophoectoderm cells of the implanting embryo. **Knock-down of EMP2 reduces integrin expression, and impairs implantation in vivo.**
Objectives

(1) To utilize a murine EMP2 knock-out model to understand mechanisms of altered placental vascularization

(2) To characterize EMP2 expression in the human placenta
EMP2 is detected in the maternal decidua and embryonic trophoblast-derived tissues throughout gestation in wild type mouse placentas.
Hypovascularity (decreased CD34+ endothelial staining) in EMP-2 deficient placentas

EMP2-deficient placentas demonstrated reduced vascular development at E9.5, as confirmed by CD34 staining for endothelial cells (below), and confirmed by tomato lectin staining (above).
HIF1α expression by uterine NK cells is increased in EMP2−/− mice

(A) HIF1α expression is increased in EMP2−/− placentas, in decidual leukocytes.

(B) Characterization of leukocyte population revealed an increase in uNK cell populations in both number and persistence over gestation.

![Graph showing HIF1α expression over days with EMP2+/+ and EMP2−/− groups, indicating increased expression in EMP2−/−.](image)

n=5/group *p=0.02
EMP2 is expressed in human placenta and reduced in IUGR pregnancies

Placentas complicated by IUGR showed lower EMP2 expression in both placental villi and in interstitial trophoblasts, and by Western immunoblotting, compared to AGA placentas.
Conclusions

1. In a murine model, deletion of EMP2 reduces litter sizes by 20%, and this may be due to reduced and aberrant placental angiogenesis, but does not alter pup viability, possibly through a compensatory increase in uterine NK cell populations.

2. EMP2 expression is altered in human placentas with IUGR, with decreased expression in both villous and extravillous trophoblasts.
THANK YOU

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