

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



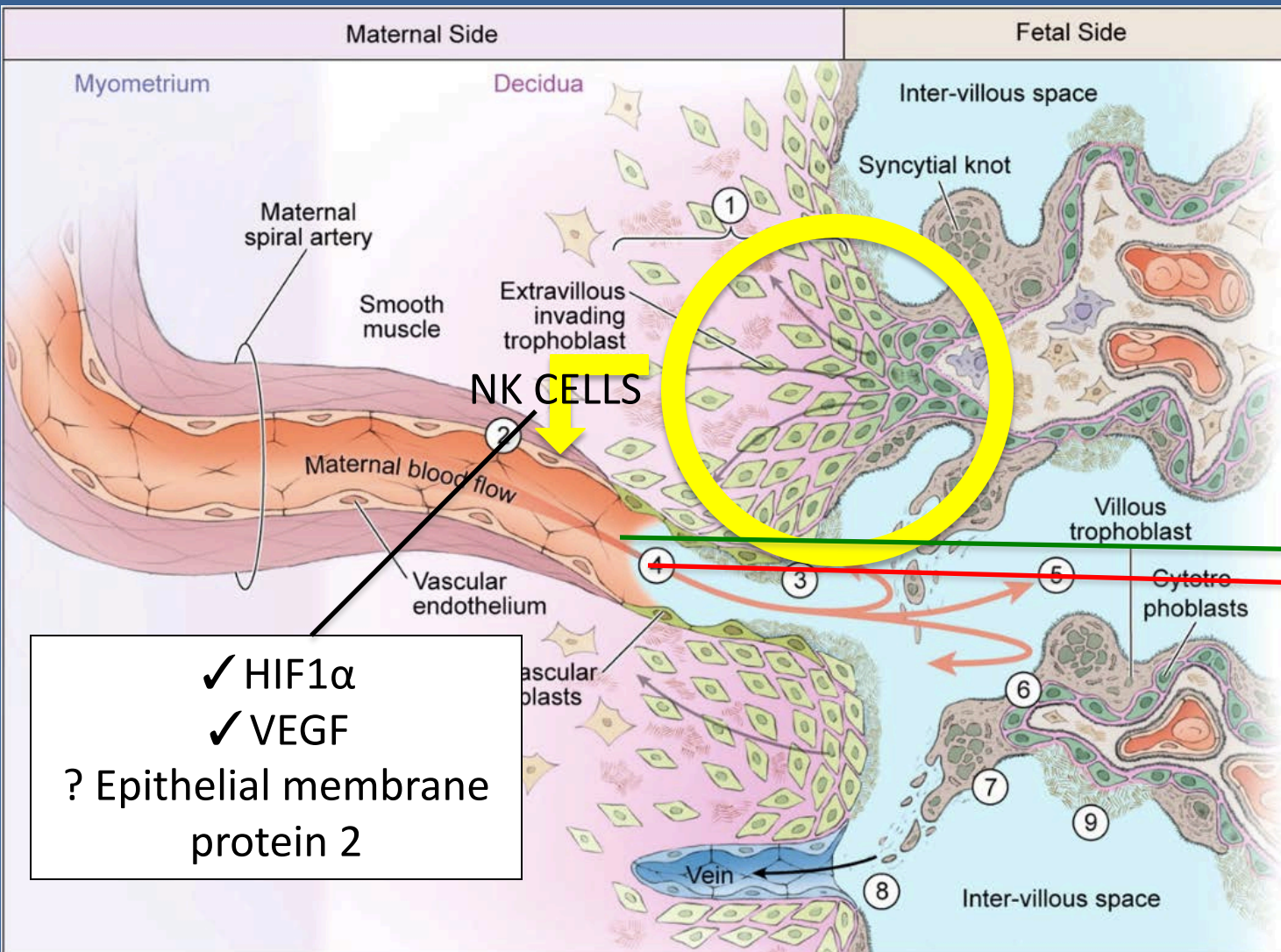
David Geffen
School of Medicine

Mattel Children's Hospital **UCLA**



UCLA Children's Discovery
and Innovation Institute

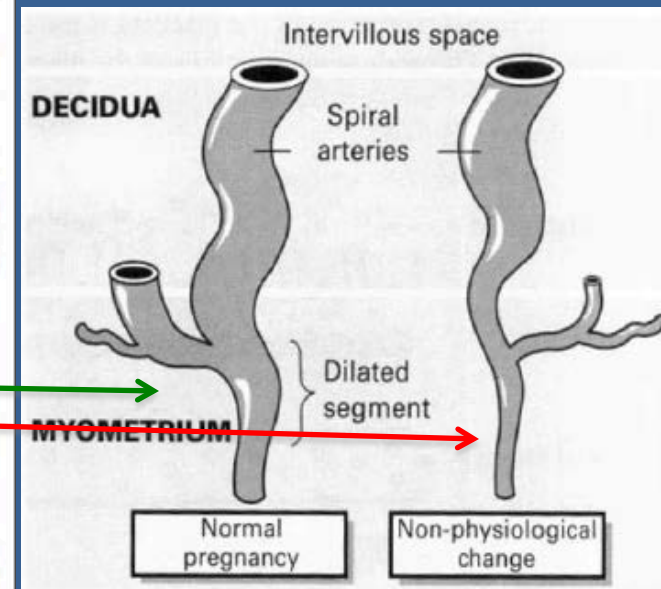
Placental blood vessel development



✓ HIF1 α

✓ VEGF

? Epithelial membrane protein 2



Epithelial membrane protein 2 (EMP2)

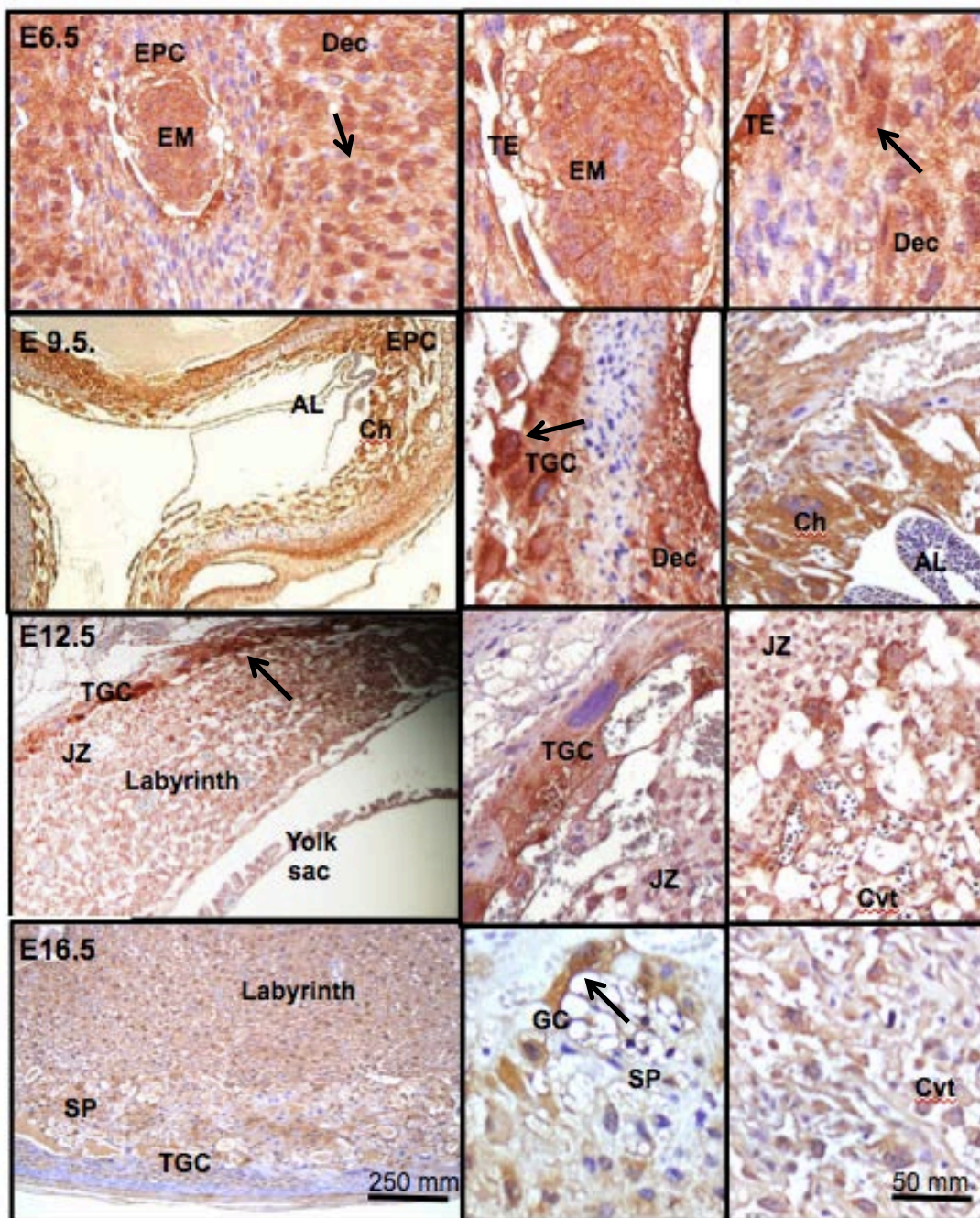
- EMP2 is a transmembrane protein that modulates cell surface expression of MHC class I molecules, integrins, and caveolins.
- In endometrial cell lines, EMP2 expression regulates angiogenesis via alterations of HIF-1 α and VEGF
- In the mouse, EMP2 is expressed on the uterine epithelial cell surface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

Objectives

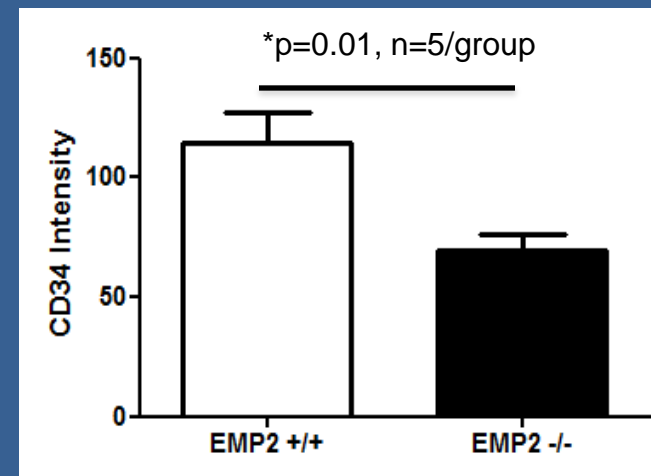
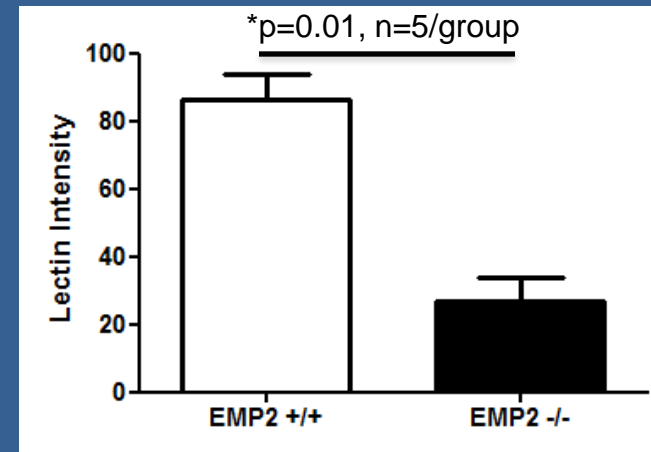
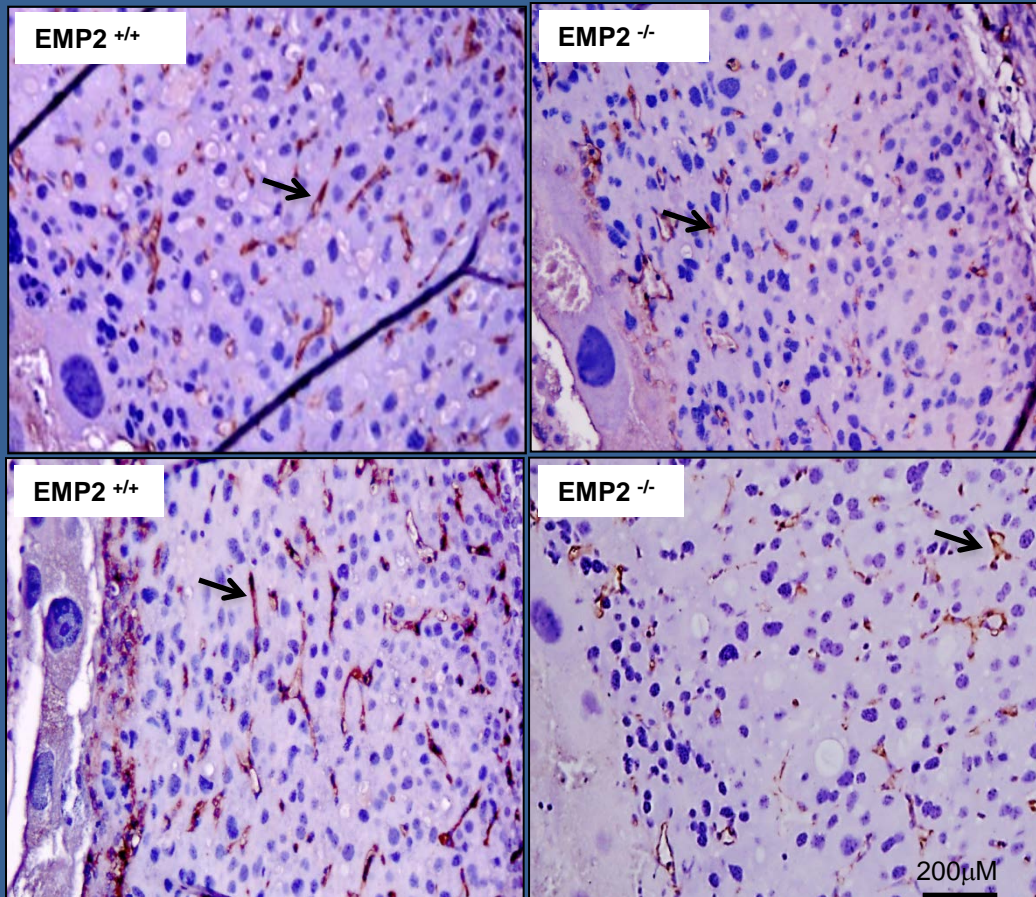
- (1) To utilize a murine EMP2 knock-out model to understand mechanisms of altered placental vascularization
- (2) To characterize EMP2 expression in the human placenta

EMP2 is expressed
in the wild-type
mouse placenta

EMP2 is detected in the
maternal decidua and
embryonic trophoblast-
derived tissues throughout
gestation in wild type
mouse placentas.

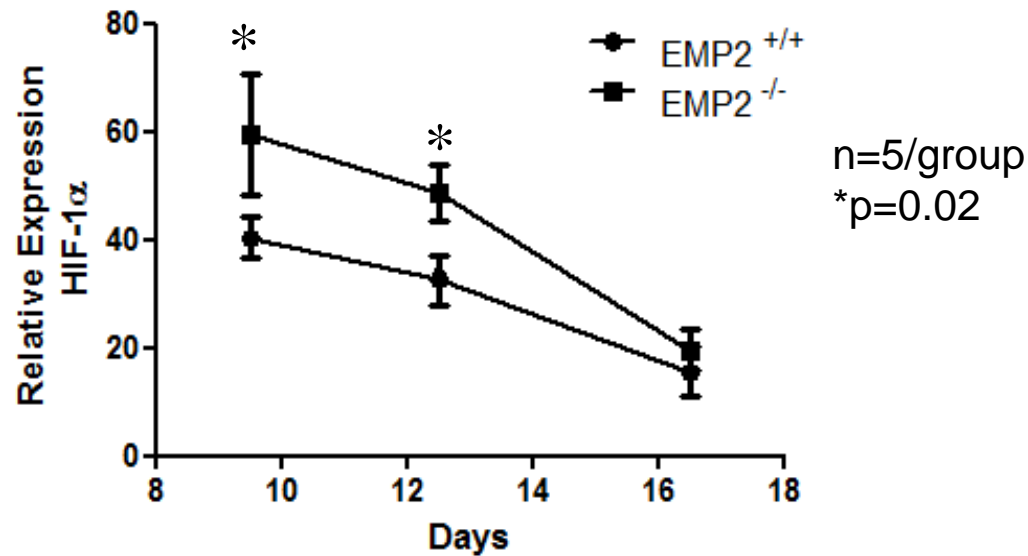


Hypovascularity (decreased CD34+ endothelial staining) in EMP-2 deficient placentas



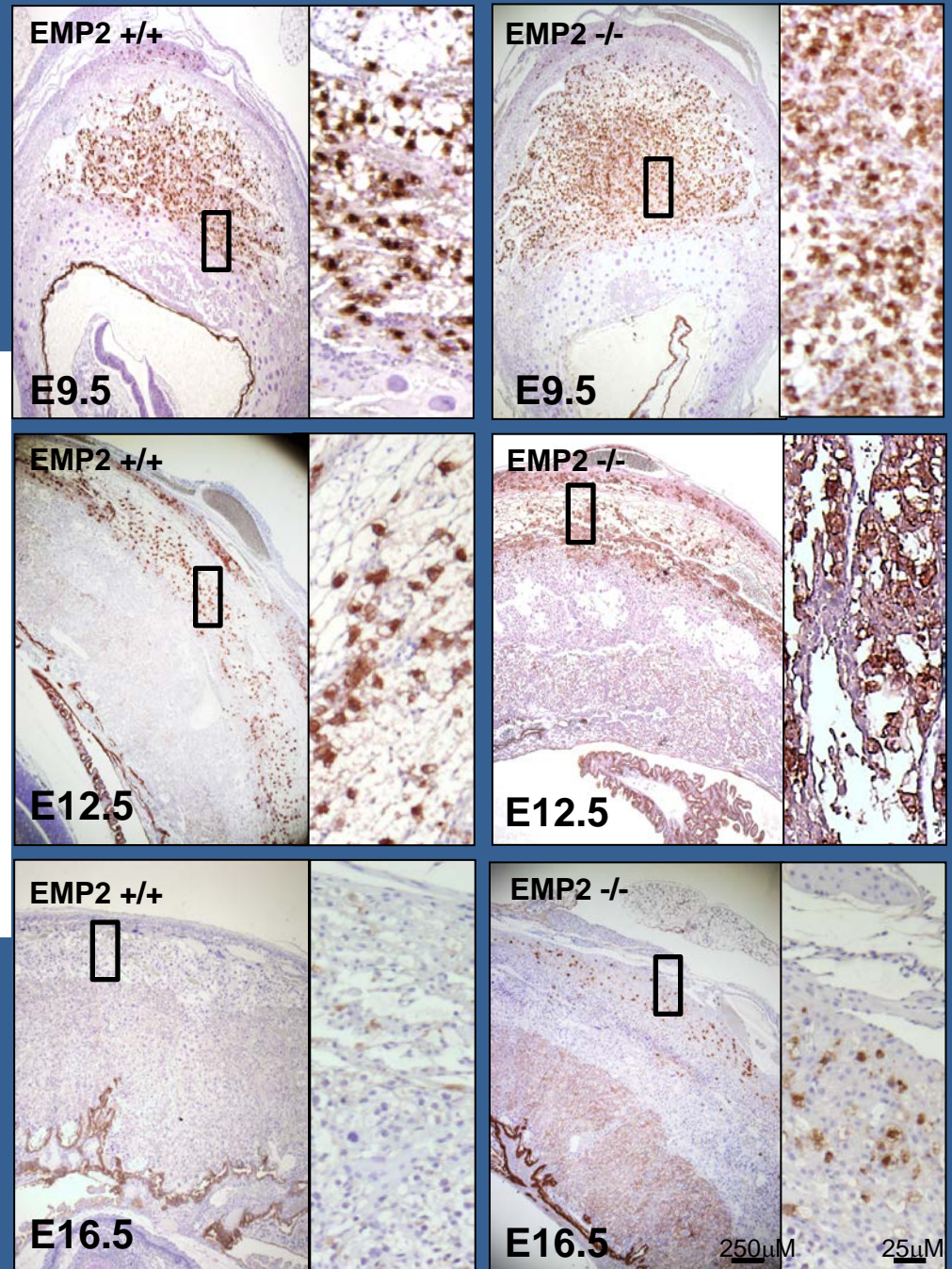
EMP2-deficient placentas demonstrated reduced vascular development at E9.5, as confirmed by CD34 staining for endothelial cells (below), and confirmed by tomato lectin staining (above).

HIF1 α expression by uterine NK cells is increased in *EMP2*^{-/-} mice

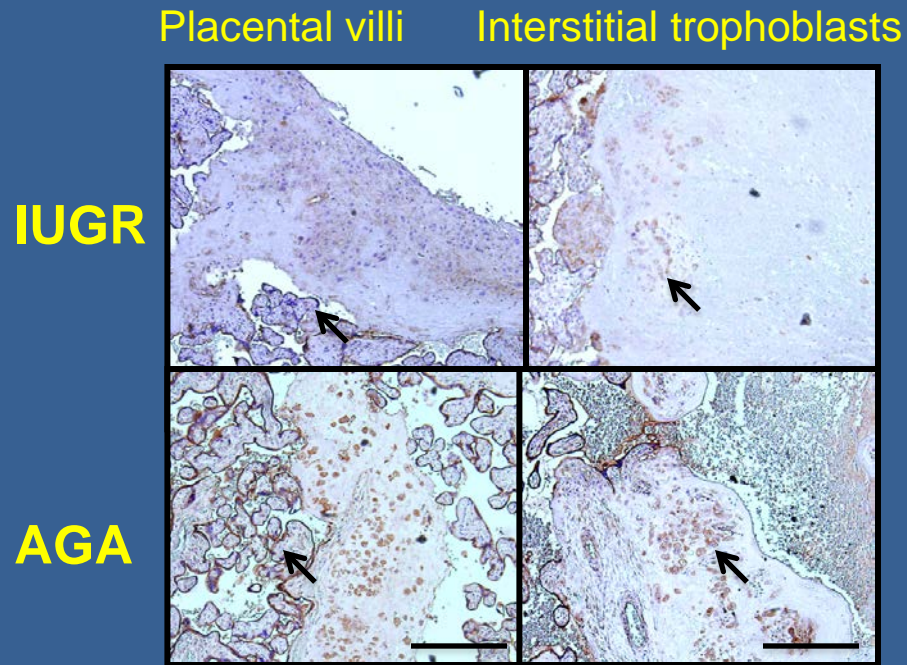


(A) HIF1 α expression is increased in *EMP2*^{-/-} placentas, in decidual leukocytes.

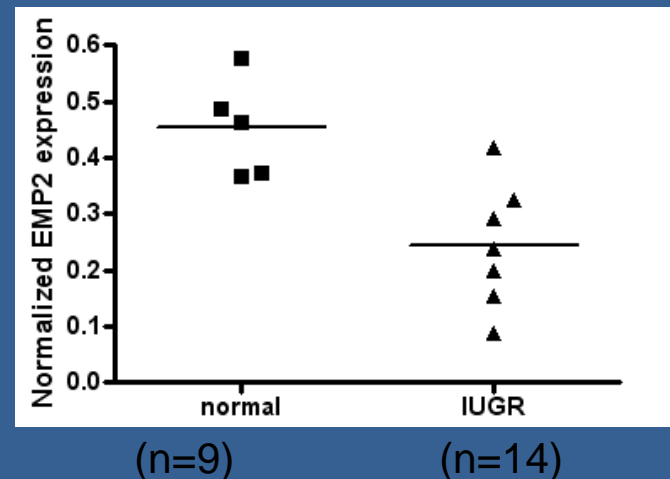
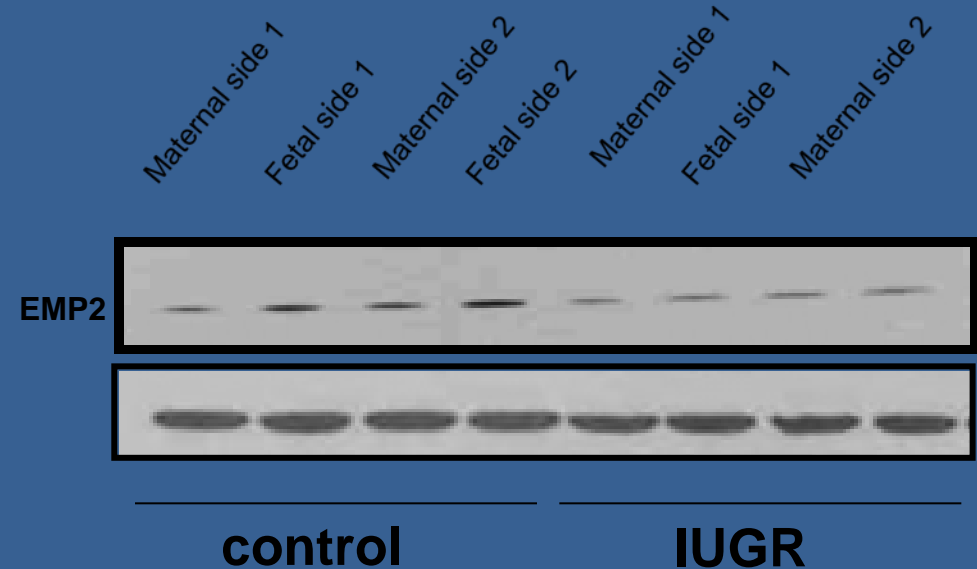
(B) Characterization of leukocyte population revealed an increase in uNK cell populations in both number and persistence over gestation.



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

Sherin U. Devaskar, MD

Shanthie Thamotharan

Amit Ganguly

Carla Janzen, MD

Madhuri Wadehra, PhD

Ann Chan

Peggy Sullivan, MD

Uday Devaskar, MD

AC is supported in part by the NIH UCLA Child Health Research Center Development Award 5K12HD034610, the UCLA Children's Discovery and Innovation Institute (CDI) Seed Grant, and the American Heart Association Beginning Grant-in-Aid Western Affiliate States 15BGIA25710060.