Sweetening placentation: hyperglycosylated hCG facilitates trophoblast invasion

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Embryo implantation and placental development

- Deferred implantation
  - Placenta accreta
  - Placenta previa
- Placental insufficiency
  - IUGR
  - Preeclampsia
  - Spontaneous abortion
  - Miscarriage
  - Recurrent pregnancy loss
  - Preterm birth
  - Fetal death
- Premature decidual senescence
  - Shallow invasion
  - Preeclampsia
- Receptivity
  - Implantation
  - Decidualization
  - Implantation failure
  - Decidualization failure
  - Infertility
- Umbilical artery and vein
- Trophoblast
- Chorionic villi
- Intervillous space
- Maternal vessels
- Decidua
- Myo
- Uterine artery and vein
- Radial artery and vein
- Full-term birth
Pre-eclampsia: when placentation goes wrong

- Myometrium
- Chorion
- Amnion
- Amniotic cavity
- Uterine artery
- Placenta vascularized by allantoic vessels
- Decidua basalis
- Radial artery
- Arcuate artery
- Allantoic vessels in umbilical cord
- Remnants of yolk sac

b. Normal pregnancy
- Placenta
- Villous trophoblast cell
- Spiral arterial wall replaced by trophoblast cells (endovascular)
- Decidua basalis
- Basal artery
- Media
- Endothelium
- Radi artery
- Arcuate artery

E. Pre-eclampsia and fetal growth restriction
- Placenta
- Placental villous tree has fewer branches because of altered blood flow characteristics
- Extravillous trophoblast cells (interstitial)
- Placental bed giant cells
- Decidua basalis
- Spiral artery remains narrowed in this segment
- Media
- Endothelium
- Radi artery
- Arcuate artery
Factors involved in placentation

- Proteases
- Chemokines/cytokines
- TGF’s
- Hyperglycosylated hCG?

Dynamic maternal-fetal communication
Why hyperglycosylated hCG?
Hypothesis: hyperglycosylated hCG (hCG-H) is expressed by the invasive trophoblast in facilitates placentation

Aims: Determine localization and function of hyperglycosylated hCG in first trimester pregnancies
hCG-H immunolocalization throughout the first trimester of pregnancy
hCG-H production is highest in the early first trimester placenta

![Image of Western blot showing hCG-H and B-actin expression over gestational weeks 6 to 12]

Relative abundance of hCG-H (normalized to betacatenin)

<table>
<thead>
<tr>
<th>Week of Gestation</th>
<th>Relative Abundance</th>
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<tbody>
<tr>
<td>6</td>
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<td>12</td>
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N=3 placentae per gestational week
hCG-H localizes to the anchoring villi within the maternal endometrium
Invasive trophoblasts and endovascular trophoblasts in maternal decidua express hCG-H
Neutralizing hCG-H inhibits placental villous outgrowth
Neutralizing hCG-H inhibits trophoblast invasion but not migration

xCelligence migration/invasion assay

Migration

Invasion

Cell index

Time (hours)

Time (hours)
Conclusions

- hCG-H is expressed by the invasive trophoblast within the placental villous

- Invasive trophoblasts within the maternal decidua and those remodelling the maternal blood vessels express hCG-H

- Neutralizing hCG-H inhibits outgrowth of first trimester placental villous explants

- Functionally, hCG-H facilitates invasions, but not migration or proliferation, of trophoblasts