Features of PLAP expression in placental structures during allogeneic pregnancy (surrogate maternity, oocyte donation) on the background of pre-eclampsia, as an indicator of exosomal trophoblast activity

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Allogeneic pregnancy

**surrogate maternity**

Age 29.4 ± 3.19

A history of successful pregnancies

Somatically HEALTHY

Threats and preterm birth (43.3% 54.3%)

HIP and PE (15.4%)

**egg donation**

Age 42.7 ± 3.91

First birth or and first pregnancy

Somatic history (including autoimmune and cardiovascular diseases)

Threats and preterm birth (11.3% 45.4%)

HIP and PE (24%)
The theory of pathogenesis of PE associated with exosomes

Placental exosomes in normal and complicated pregnancy

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The understanding of how cells communicate has undergone a paradigm shift with the recognition of the role of exosomes in intercellular signaling (Table 1). Exosomes are a subpopulation of extracellular vesicles that are distinct in size (~40-120 nm), density (1.13-1.19 g/mL⁻¹), content, and biogenesis. Exosomes are of endosomal origin, formed by the inward budding multivesicular bodies (MVB) (Figure 1). As such, they are enriched with late endosomal membrane markers, including Tsg101, CD63, CD9, and CD81. Exosomes are released into extracellular compartments by exocytosis, following the fusion of MVB with the plasma membrane.

While there is considerable contemporary interest in elucidating the role of placenta-derived extracellular vesicles in normal and complicated pregnancies and their utility as biomarkers and therapeutic interventions, progress in the field is hindered by a lack of standardized extracellular vesicle taxonomy and isolation protocols. The term “extracellular vesicle” is nonspecific and refers to all membrane-bound vesicles from nanometer to micrometer diameters and of different biogenic origins. To meaningfully ascribe biological function and/or diagnostic and therapeutic utility to extracellular vesicles, and in particular exosomes, greater specificity and vesicle characterization is required. The current literature relating to exosome biology must be interpreted in this context. Exosomes are a subtype of extracellular vesicle that are specifically defined by an endosomal biogenesis and particle size (40-120 nm) and density (1.13-1.19 g/mL⁻¹). Exosomes are specifically package with signaling molecules (including protein, messenger RNA, microRNA, and noncoding RNA) and are released by exocytosis into biofluid compartments. Exosomes regulate the activity of both proximal and distal target cells, including translational activity, angiogenesis, proliferation, metabolism, and apoptosis. As such, exosomal signaling represents an integral pathway mediating intercellular communication. During pregnancy, the placenta releases exosomes into the maternal circulation from as early as 6 weeks of gestation. Release is regulated by factors that include both oxygen tension and glucose concentration and correlates with...
Exosomes

https://doi.org/10.3390/cells8060558
Aim of study

To Investigate the exosomal activity of trophoblast in the norm and with the preeclampsia in allogeneic pregnancy
Inclusion criteria
• IVF with a donor egg
• Single pregnancy
• Gestational age > 20 weeks
• Clinically confirmed development of pre-eclampsia (all degrees of severity)

Exclusion criteria:
• Multiple pregnancy
• Severe extragenital pathology
• Gestational age < 20 weeks
• Complications of pregnancy with well-studied pathogenesis (APS, hereditary forms of thrombophilia, etc.)

Material
Methods

1. Clinical and laboratory analysis (HLA II detection)
2. Morphological verification
   - Histological study paraffin sections of placenta and placental bed, staining PAS, Orcein, hematoxylin and eosin.
   - Immunohistochemical study of placenta and placental bed paraffin sections
     - monoclonal mouse anti-human PLAP (Dako)
     - monoclonal mouse anti-human CD9 (Dako)
     - mouse anti-human CD81 (Dako)
   - Morphometric analysis of optical density (ImageM 2.0)
   - Electron microscopy
Results. Somatic history and obstetric complications

- Premature birth
- Premature placental abruption
- PE
- HIP
- GDM
- The threat in the III trimester
- The threat in the II trimester
- The threat in the I trimester
- Diseases of the hepatobiliary system
- Endocrine diseases
- Respiratory diseases
- Urinary system diseases
- Cardiovascular disease

OE (n=21)
SM (n=47)
OD (n=42)
Results. Morphological changes in placenta in AP with PE

Perivillous fibrioniod with LGI, H&E, x200
Lymphoplasmacytic deciduitis, H&E, x400

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Histological image showing lymphoplasmacytic deciduitis with H&E staining.
Results. Morphological changes in placental bed in AP with PE

Massive deposits of fibrinoid in the uteroplacental region, HE, x400
Perivascular infiltration in placental bed, H&E, x400
Complete remodeling of the spiral arteries (%)
Partial remodeling of the spiral arteries (%)
Lack of remodeling (%)
Expression of exosome markers in villous trophoblast

The diagram shows the expression levels of exosome markers in different stages of villous trophoblast development. The markers CD81, CD9, and PLAP are highlighted with different colors and error bars indicating variability. The stages are labeled as OE (early), OD (mid), and SM (late). The x-axis represents the expression levels, ranging from 0 to 0.9.
## Expression of exosome markers in placental bed

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**Markers:**
- **CD81**
- **CD9**
- **PLAP**

### Figures

- **CD81**
- **CD9**
- **PLAP**
Syncytiotrophoblast, brush border
↓ PLAP ↓ CD9 ↓ CD81
relate to ↓ exosome secretion, containing miRNA-127-5p and etc.

↑ Th1 ↓ Th2
↑ cytotoxic NK
↓ apoptosis of maternal T cells through FasL and TRAIL
↓ activation tTreg

disruption of immunological tolerance

damage to the trophoblast by the mother’s immune system

↓ PIGF

↑ proinflammatory cytokines

↓ sFLT
↓ sEng

Preeclampsia

Conclusions

• Placentas and placental beds in the allogeneic pregnancy are characterized by pronounced signs of immune alteration of the placenta. The pathology of the placental bed consists in chronic inflammation in the perivascular region and a violation of the remodeling of the spiral arteries.

• PLAP, CD9 and CD81 were found in the cells of the syncytiotrophoblast villi, parietal trophoblast and single cells of the extravillous trophoblast of the placental bed.

• The development of PE during allogeneic pregnancy is accompanied by a decrease in the content of exosome components in syncytiotrophoblast cells
Thank you for attention!