# Placental contribution to fetal neurological development: Role of placenta-derived mesenchymal stromal cells (PDMSCs) in physiological and preeclamptic pregnancies

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Introduction: Preeclampsia (PE), severe placenta-related syndrome, is often associated with Fetal Growth Restriction (FGR). Even though PE-FGR resolves with placental removal, it causes severe long-term complications such as neurological disorders for the newborn. The syncithiotrophoblast plays a key role in fetal neurodevelopment by providing serotonin to the fetus through maternal tryptophan conversion. We recently demonstrated that PDMSCs, a unique cell type with stem cell-like features resident in the placental villi, express BDNF, NT3 and NT4 neurotrophins, key modulators of fetal neurogenesis and that these molecules are over-expressed in PE-PDMSCs. PDMSCs contribution to fetal neurodevelopment has never been investigated.

In the present study, we evaluated the expression of neurogenesis markers Doublecortin (DCX) and NCAM, of indolamine-2,3-dioxygenase (IDO), responsible for

tryptophan metabolism and accumulation of neurotoxic metabolites, in normal and PE-PDMSCs in order to understand their role in physiological and pathological fetal neurodevelopment.

Methods: PDMSCs were isolated from healthy (n=7) and PE-FGR (n=7) placentae. DCX, NCAM and IDO mRNA levels were determined by Real Time PCR. Western blot assay was used to determine “NCAM polysialic acid-modified” (PSA-NCAM) protein levels. PSA-NCAM are inversely correlated to those of NCAM, acting as a negative modulator of neurodevelopment.

Results: DCX and NCAM mRNA levels were over-expressed ($p<0.05$), while IDO mRNA expression was significantly decreased ($p<0.05$) in PE-FGR vs normal PDMSCs. In contrast, PSA-NCAM protein levels were down-regulated ($p<0.05$) in PE-FGR vs normal PDMSCs.

Conclusions: Herein, we characterized, for the first time to our knowledge, the expression of neurogenesis-related molecules in normal and PE-FGR PDMSCs. DCX and NCAM mRNA increase together with PSA-NCAM and IDO down-regulation suggest that PE-PDMSCs try to counteract impaired fetal neurodevelopment by promoting pro-neurogenic factors expression and avoiding neurotoxic metabolites placental accumulation. Further investigation is required.

***The definitive version is available at:***

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