PLACENTAL CONTRIBUTION TO FETAL NEUROLOGICAL DEVELOPMENT: ROLE OF PLACENTA-DERIVED MESENCHYMAL STROMAL CELLS (PDMSCS) IN PHYSIOLOGICAL AND PREECLAMPTIC PREGNANCIES

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

Rossella Barrile, Cristian Zenerino, Domenica Giuffrida, Anna Maria Nuzzo, Edoardo Terzolo, Tullia Todros, Alessandro Rolfo

Dept. of Surgical Sciences, University of Turin, Turin, Italy

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.

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