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COMPARATIVE ANALYSIS OF INTEGRIN ALPHA 8 EXPRESSION AND ITS LIGANDS FIBRONECTIN AND OSTEOPONTIN IN HUMAN, RAT AND MOUSE PLACENTA

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Objectives: Integrins exert important regulatory functions in placentogenesis. Null-mutation of certain integrin α-subunits leads to placental defects with subsequent fetal growth restriction or embryonic lethality in mice. The α8-integrin regulates cell survival, proliferation, adhesion and migration of renal and vascular cells. The placental role of α8-integrin has not been investigated so far. We hypothesized that α8-integrin is expressed in placental compartments as well.
Methods: The localization of α8-integrin and its ligands fibronectin (FN) and osteopontin (OPN) was studied by immunohistochemistry in the placentas of humans, rats and mice. The vascularisation of mouse labyrinth layer was analyzed after staining for the endothelial marker CD31 in placentas of α8-integrin-deficient mice. In humans, expression of α8 integrin was assessed via RT-PCR in healthy placenta and the placental pathologies intrauterine growth restriction (IUGR), preeclampsia (PE) and HELLP-syndrome, as well as in immunomagnetic bead-separated extravillous and villous trophoblasts at term.
Results: In human first and third trimester placenta α8-integrin was expressed in syncytiotrophoblast and extravillous trophoblasts, where it co-localized with OPN. Co-expression of FN was observed in extravillous trophoblasts only. No expressional changes of α8 integrin were detected in the placental pathologies studied. In analogy to human placenta, rodent placenta showed α8-integrin expression in giant cells and the labyrinth layer. Colocalization of OPN and FN however showed species-specific differences. Knockout of α8-integrin in mice did not cause intrauterine growth restriction, despite a reduction of vascularisation in the labyrinth layer.
Conclusion: The α8-integrin chain is expressed in functional compartments of both rodent and human placentas colocalizing with its ligands OPN and/or FN. It is conceivable that α8-integrin contributes to the regulation of cellular functions in trophoblasts, although our data from α8-integrin-deficient mice suggest that a lack of α8-integrin only results in a mild placental pathology. Thus, the lack of α8-integrin in placenta can largely be compensated.