Medical University of Graz

The role of platelet-derived factors on epithelial-to-mesenchymal transition of trophoblasts

Summary

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Supervisor:	PD Dr. Martin Gauster
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between August 18, 2021 00:00 and October 04, 2021 23:59 (Europe/Zurich)

Description

Background:

Differentiation of cytotrophoblasts into the invasive extravillous phenotype is an essential process in early human pregnancy. The differentiation process is suggested to have several factors in common with the epithelial-to-mesenchymal transition (EMT) observed in embryonic development, wound healing and cancer metastasis. When the epithelial cytotrophoblasts leave the terminal ends of the anchoring placental villi, molecular changes take place to enable trophoblasts to migrate into the maternal uterine wall. Among these changes are increased secretion of metalloproteinases and upregulation of EMT-associated genes, whereas junction proteins are downregulated. However, the EMT in invasive trophoblasts is not fully accomplished since the hallmark marker of epithelial trophoblasts, cytokeratin 7, is not downregulated and contrary the classical mesenchymal marker vimentin, is not induced during the differentiation into the invasive phenotype.

Recently, we showed maternal platelets in intercellular gaps of distal areas of trophoblast columns, indicating that maternal plasma components, including particles such as platelets and multivesicular cargos with only 2-3 µm in diameter, can leak into the intercellular gaps of distal trophoblast column areas. Our ultrastructural observations showed an amoeboid shape of the platelets as well as appearance of fine-grained material in the open canalicular system (OCS) and cell surface invaginations of platelets, suggesting their activation and extrusion of granules content to the platelet exterior.

Hypothesis and objectives:

The presence of maternal platelets and the release of their granules content into the intercellular space of distal parts of trophoblast columns tempts to speculate on a role of platelet-derived factors in influencing trophoblast differentiation into the invasive phenotype. This project will test whether or not platelet-derived factors induce partial EMT of trophoblasts and will evaluate whether this process differs when platelets are activated by different agonists.

Methodology:

Beside standard molecular biology techniques and conventional cell culture, the candidate will perform placental explant- and outgrowth cultures, isolation of human platelets and preparation of platelet releasates, as well as histological surveys.

References:

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