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Dissertations-Kurzfassung

Tumor induced endothelial differentiation in vitro

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Introduction: Endothelial cells compose the inner part of every blood vessel. The vascular endothelium plays the role of barrier between the vessel lumen and the surrounding tissue, controlling the transit of substances solved in the blood as well as the movement of leukocytes into and out of the blood stream. Endothelial cells are involved in many aspects of vascular biology as control of blood pressure, haemostasis, and angiogenesis which is the neoformation of blood vessels from a pre-existing one and a crucial event in metastatic development. According to their localisation, endothelial cells display great differences in shape and also in function. In the present work, we focused on lung microvascular endothelial cells (LMECs).

Results: LMECs treated with TS/A (a murine breast cancer strain) -conditioned medium presented a change in their morphology and underwent an increase of tube formation *in vitro*. Affymetrix gene profiling of LMECs treated with TS/A-conditioned medium was performed and several gene families were found to be over expressed. Different matrix metalloproteinases (MMPs); CC and CXC inflammatory cytokines; as well as Ptges1, coding for the enzyme responsible of the production of the prostaglandin E_2 (PGE_2), displayed an increase in their transcription after treatment. PGE_2 is a lipid principally implicated in inflammation but also in metastasis spread and angiogenesis, and it was chosen as a candidate for TS/A-conditioned medium effects. LMECs treated with PGE_2 showed the same morphologic change than that produced by TS/A-conditioned medium. However the cells did not display any stimulation in the set of genes induced by TS/A-conditioned medium, and on functional level the tube formation *in vitro* was increased but did not reach significance.

Conclusion: The data exposed in this dissertation show that ECs isolated *ex vivo* from preferential target organ of metastasis can undergo transdifferentiation and angiogenic activation induced by tumor-derived soluble factors, *in vitro*. TS/A-conditioned medium can trigger a kind of “edothelial-mesenchymal transition” morphological change in LMECs, comparable to epithelial-mesenchymal transition, and enhance their angiogenic potential in tube forming assay *in vitro*. Moreover, in response to this stimulus, LMECs can over-express molecules which could be relevant for promotion and treatment of tumor metastases *in vivo*.