PAI-1 DIFFERENTLY AFFECTS CYTOKINE PRODUCTION IN CANCER AND ENDOTHELIAL CELLS

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PAI-1, key component of fibrynolytic system, its synthesis is rapidly activated by cytokines and mediators driving inflammatory response, both acute and persistent low-grade as well as partakes in tumor and metastasis development in the lungs. While TNF-a and TGF-b are established potent direct stimulators of PAI-1 production in the lungs, little is known of any feed-back regulation that might be accountable for effects of PAI-1 on their synthesis. We aimed on analyzing the regulatory mechanisms between PAI-1 and its potent activator TGF-b in different types of lung cancer and endothelial cells. Dose-dependent inhibition of TGF-b production was observed in stimulated and non-stimulated endothelial cells with physiological (10mg/ml) and supraphysiological (100mg/ml) PAI-1 concentrations exerting significant suppressive effect in comparison to control (respectively $p<0.05$; $p<0.02$) as well as to cultures spiked with subphysiological PAI-1 dose of 1mg/ml ($p<0.0001$; $p<0,02$). No such regulation was demonstrated for lung cancer cell lines A549 and H1299. While no functional interplay between PAI-1 and TNF-a in the non-stimulated cell cultures was observed, dose-dependent significant inhibition of TNF production was shown in endothelial cells cultured with (100mg/ml) of PAI-1 ($p<0,02$). Present study implicates different regulatory mechanism in neoplastic and endothelial lung cells with negative feed-back regulation between PAI-1 and its potent stimulator TGF-b in endothelium.