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IMMUNOTARGETING OF THE PULMONARY ENDOTHELIUM VIA ANGIOTENSIN-CONVERTING-ENZYME IN ISOLATED VENTILATED AND PERFUSED HUMAN LUNG

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OBJECTIVES: Vascular immunotargeting of catalase via Angiotensin-Converting-Enzyme (ACE) attenuated lung ischemia reperfusion injury in the rat. As this might be a promising modality for extension of the viability of human lung grafts for transplantation we tested the hypothesis whether anti-ACE antibodies are suitable for human lung protection within the model of isolated perfused and ventilated human lung resections.
METHODS: Right after surgery for lung cancer, human lung specimens were isolated, ventilated and perfused under physiological conditions with 500 ?g of either mouse monoclonal antibodies (mAb) to human ACE (9B9, I2H5, 3G8) or non-immune mouse IgG (as a negative control) followed by wash-out perfusion. Perfusion pressure, pH and lung weight gain were measured before and during perfusion. After mAb perfusion and wash-out perfusion period lung tissue was tested for the uptake of mAbs by immunohistochemistry and by enzyme-capture technique. Furthermore antibody concentration and ACE shedding were measured within the perfusate.
RESULTS: ACE activity in tumor and normal lung tissue did not differ between the groups perfused with different mAbs. However ACE activity in normal lung tissue (17?6 U/g) was significantly higher compared to tumor tissue (6.0?3.0; $p<0.01$). Absolute retaining of mAbs was with 1.3?1.1 % of injected dose per gram of tissue in normal lung tissue, 0.7?0.7% of injected dose per gram of tumor tissue and was significantly higher compared to non-immune mouse IgG (0.1?0.1%/g; $p<0.01$). Anti-ACE mAbs concentration in the perfusate dropped significantly to 47?11% ($p<0.001$) at 40 min of perfusion. No significant difference between different anti-ACE mAbs in the depletion from perfusate has been observed. mAb 9B9 showed the most intense immunostaining (i.e. most significant lung uptake) after each experiment in normal and tumor lung tissue compared to mAbs i2H5 and 3G8 ($p<0.01$).
CONCLUSION: These results validate a possibility of immunotargeting of pulmonary endothelium in the human lung tissue by anti-ACE mAbs under in vivo conditions. Furthermore the model might be useful to investigate targeted therapies in lung cancer without side effects for the patient.