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(Abstracts)

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Freie Vorträge – Parallelsitzungen

LUNGE/HERZ

V01.
Intragraft Activation of Indoleamine (2,3)-Dioxygenase Is Not Able to Prevent Murine Cardiac Allograft Rejection

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Background: Indoleamine (2,3)-dioxygenase (IDO) via tryptophan depletion inhibits T cell proliferation and leads to T cell anergy. IDO is activated by INF-gamma and has been demonstrated to play an essential role in maternal tolerance. The role of IDO in transplantation however remains unclear.

Methods: Hearts of C57BL/10 (H-2b) mice were transplanted heterotopically to C3H/He (H-2k) recipients. Syngeneic transplants and allograft recipients treated with CsA (15 mg/kg) served as controls. Serum concentrations of kynurenine and tryptophan were analysed by high performance liquid chromatography (HPLC) on reversed phase 2, 4, 6 and 8 days following transplantation. Kynurenine per tryptophan quotients (kyn/trp ratio) were calculated as an indirect estimate of IDO activity. Intragraft IDO mRNA expression was assessed by quantitative RT-PCR (Taqman technology).

Results: Untreated allografts were rejected after 7.3 ± 0.6 days as confirmed by H & E histology. There was an increase of serum kynurenine and a decrease of tryptophan concentrations as reflected by a significant increase of kyn/trp ratios (day 2 post transplant: 18 ± 10 ; day 4: 21 ± 8; day 6: 43 ± 23; day 8: 37 ± 14) $P < 0.05$ at each timepoint. Intragraft expression of IDO mRNA was induced up to 100-fold on postoperative days 6 and 8. Animals receiving a syngeneic heart or allograft recipients treated with CsA however did not show changes in kyn/trp ratios (21 ± 5 and 19 ± 3 respectively) and expression profiles of IDO mRNA remained unchanged (syngeneic), or were attenuated 2.6 ± 0.6 fold (CsA).

Conclusions: Despite its tolerogenic effect in maternal immunity strong expression of IDO in cardiac allografts could not prevent rejection. IDO activity however may serve as a new marker of immune activation and via its regulation by INF-gamma offer a potential tool of modulating the alloimmune response.

V02.
SLPI and Extracellular Protease Inhibitor Gene Expression Is Associated with Decreased Expression of Macrophage Activators in Postischemic Inflammation of Murine Cardiac Isografts

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Background: Secretory leukocyte protease inhibitor (SLPI) functions as potent inhibitor of enzymes with serine protease activity and is crucially involved in wound healing and inflammatory cell activation. Recently, it has been shown that administration of SLPI had protective effects in hepatic ischemia/reperfusion injury. We have investigated expression of SLPI, macrophage activation 2 protein (MA2) and extracellular protease inhibitor (PI) in an isogeneic cardiac transplant model in mice.

Methods: Hearts from C57BL/6 mice were transplanted heterotopically without cold ischemia (group 1) or after 10 hours of cold ischemia (group 2). Grafts were harvested after 2 min., 2 h, 12 h and 24 h of reperfusion (n = 5 per group and timepoint) and mRNA extracts were pooled per group. After reverse transcription of poly-