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SOMATOSTATIN EFFECT ON TNFA RECEPTORS IN KUPFFER CELLS

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Introduction Somatostatin is a mediator of immune functions and has been used as an antineoplastic agent in animal

models and human neoplasias. We have demonstrated that octreotide-a somatostatin analogue- inhibits only LPS-induced secretion of pro-inflammatory cytokines including tumour necrosis factor (TNF) α by Kupffer cells.[1 2] We therefore tested the hypothesis that somatostatin modulates the expression of TNFα receptors and apoptosis of Kupffer cells.

Methods Rat Kupffer cells were isolated by centrifugal elutriation. TNFR1 and TNFR2 expression was studied by RT-PCR, quantitative PCR, Western Blot and immunofluorescence before and after octreotide pre-incubation. Apoptosis was assessed by quantitative measurement of cytoplasmic histone-associated DNA fragments (Roche). TNFα mRNa expression was assessed by a semiquantitative PCR and TNFα was measured in cell supernatants by ELISA.

Results TNFR1 and TNFR2 m RNA are constitutively expressed in Kupffer cells. Octreotide incubation increased both receptors expression with a peak at 6 h and return to basal levels at 24 h. TNFR1 was mostly influenced. However only TNFR2 protein increase was identified by Western blot, while a band at 90 kD was present instead of a band at 55 kD as expected for TNFR1. TNFa mRNA expression and protein secretion was not influenced by octreotide at 24 h. However a significant inhibition was observed at 48 h. TNF had no effect on Kupffer cell apoptosis while octreotide significantly increased their apoptosis and this effect was not influenced by co-incubation with TNFα.

Conclusion TNFR1 and TNFR2 are constitutively expressed in Kupffer cells and their expression is strongly increased by somatostatin. Moreover somatostatin increases Kupffer cell apoptosis. These findings may in part explain the antineoplasmatic effect of somatostatin.

Competing interests None.

Keywords Kupffer cells, somatostatin, TNF Receptors, TNF-alpha.

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