

POSTER PRESENTATION

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# 0104. Modulatory effects of heat shock with or without glutamine compared to LPS on peripheral blood mononuclear cells heat-shock-protein 90 $\alpha$ expression in severe sepsis and trauma

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## Introduction

Inflammatory stimuli cause posttranslational modifications of inducible 90 $\alpha$ -kDa-heat-shock-protein (HSP90 $\alpha$ ) that are Hsp90-inhibitor sensitive and may be important to the pro-inflammatory actions of Hsp90 $\alpha$ .

## Objectives

We investigated the heat-shock (HS) and lipopolysaccharide (LPS)-stress response effect on HSP90 $\alpha$  in cultured peripheral blood mononuclear cells (PBMCs) from patients with severe sepsis (SS) or trauma-related systemic inflammatory response syndrome (SIRS) compared to healthy-controls (H) and any possible modulating Glutamine (Gln)-effect.

## Methods

PBMCs of 16/H, 11/SS, and 7/SIRS were incubated with 1 $\mu$ g/ml LPS or 43 $^{\circ}$ HS vs.no stimulation for 4h. In each group 3 experiments involved L-Ala-Gln10mM incubation 1h before (Gln-b) or after (Gln-a) induction, or no glutamine (1088 measurements). Intracellular Mean Fluorescence Intensity (MFI) levels of monocytes (mHSP90 $\alpha$ ) or lymphocytes (lHSP90 $\alpha$ ) determined using Flow Cytometry.

## Results

Baseline mHSP90 $\alpha$  was higher in SIRS (187 $\pm$ 30 vs. 112 $\pm$ 10,  $p$ < 0.01) and lHSP90 $\alpha$  in SS (91 $\pm$ 19 vs. 47 $\pm$ 3,

$p$ < 0.001) compared to H. LPS induced H-mHSP90 $\alpha$  (141 $\pm$ 12 vs. 112 $\pm$ 10,  $p$ < 0.001) and HS H-lHSP90 $\alpha$  (66 $\pm$ 7 vs. 47 $\pm$ 3,  $p$ < 0.0001). Neither LPS nor HS exhibit any significant effect in SIRS- or SS-mHSP90 $\alpha$  or lHSP90 $\alpha$ . Glutamine given before LPS suppressed SS-lHSP90 $\alpha$  (Gln-b 61 $\pm$ 5 vs. 91 $\pm$ 19,  $p$ < 0.004). Similarly, when glutamine was given before or after HS suppressed SS-lHSP90 $\alpha$  (Gln-a 73 $\pm$ 5 vs. 91 $\pm$ 19,  $p$ < 0.001; Gln-b 78 $\pm$ 4 vs. 91 $\pm$ 19,  $p$ < 0.05), respectively.

## Conclusions

PBMCs express higher baseline mHSP90 $\alpha$  in SIRS and lHSP90 $\alpha$  in SS, not further induced by LPS or HS, contrasting their induction effects in H. Gln pre-treatment may attenuate the LPS or HS-induced lHSP90 $\alpha$  in SS.

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