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COMBINED EFFECT OF EXTRACELLULAR HSP70 AND LYPOPOLYSACCHARIDE OR LYPOTEICHOIC ACID ON CYTOKINE SECRETION IN CELLULAR MODELS OF COPD

Hulina A.¹, Grdić Rajković M.¹, Popović-Grle S.², VUKIĆ DUGAC A.², Samaržija M.², Rumora L.¹

¹ Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb, Croatia
Department of Medical Biochemistry and Haematology

² University Hospital Centre Zagreb, School of Medicine, University of Zagreb, Zagreb, Croatia
Clinical Department for Lung Diseases Jordanovac

Aims: Extracellular Hsp70 (eHsp70) can act as damage-associated molecular pattern (DAMP) via Toll-like receptors TLR2 and TLR4, and stimulate immune and inflammatory responses leading to sterile inflammation and propagation of already existing inflammation. It was found elevated in sera of patients with chronic obstructive pulmonary disease (COPD), who also have frequent bacterial colonisations and infections. We used tracheo-bronchial epithelial NCI-H292 and macrophage-like THP-1 cell lines as models of pulmonary and systemic compartments of COPD to assess inflammatory effects of combination of eHsp70 with bacterial products lipopolysaccharide (LPS), a TLR4 agonist, and lypoteichoic acid (LTA), a TLR2 agonist.

Methods: NCI-H292 and THP-1 cells were treated with combinations of recombinant human Hsp70 protein (rhHsp70) and LPS or LTA for 4, 12, 24 and 48 h. Concentrations of IL-6 and IL-8 were determined by ELISA method in cell supernatants.

Results: Combination of rhHsp70 and LPS had synergistic effect on IL-6 secretion in both cell lines (after 24 h treatment for THP-1 cells, and after 12 h for NCI-H292 cells). Its effect on IL-8 secretion was synergistic in NCI-H292 cells (for 12 and 48 h), while it was synergistic for shorter treatments in THP-1 cells (4 and 12 h), and turns antagonistic after 48 h treatment. Combination of rhHsp70 and LTA had antagonistic effect on IL-6 in THP-1 cells after 4 and 12 h treatment, while it was synergistic after 48 h. In NCI-H292 cells, effect was antagonistic after 12

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h treatment. Effect on IL-8 secretion was antagonistic in THP-1 cells (4h), and synergistic in NCI-H292 cells (12 and 48 h).

Conclusion: In conclusion, we suggest that eHsp70 might significantly influence pro-inflammatory effects of bacterial products LTA and LPS. This might alter sensitivity of TLR2 and TLR4 receptors leading to desensitization or inappropriate activation which in turn might contribute to the worsening of the COPD patient's condition.