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HSP90 IN AXIAL SPONDYLOARTHRITIS, PSORIATIC ARTHRITIS AND RHEUMATOID ARTHRITIS

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Career situation of first and presenting author Student for a master or a PhD.

Introduction Hsp90 is a highly conserved molecular chaperone that regulates activation of innate immunity, antigen presentation, and the induction of proinflammatory cytokines and chemokines. These properties predispose Hsp90 to its potential role in the pathogenesis of autoimmune inflammatory rheumatic diseases.

Objectives The aim of this study was to assess plasma Hsp90 in patients with axial spondyloarthritis (axSpA), psoriatic arthritis (PsA), rheumatoid arthritis (RA) and healthy controls (HC) and to determine its potential association with disease activity and clinical features.

Methods A total of 136 patients, that were divided into groups according to the type of a rheumatic disease (SpA, RA, PsA), and age-/sex- matched healthy individuals were included. Plasma Hsp90 levels were measured by ELISA (eBioscience, Vienna, Austria). Data are presented as median (IQR).

Results Plasma Hsp90 levels were significantly increased in axSpA and in RA patients compared to HC. The increased plasma levels of Hsp90 in PsA compared to HC did not reach statistical significance. Hsp90 concentrations were higher in RA patients with an altered serum lipid profile: low-density lipoprotein (LDL: $r=0.352$, $p=0.048$), high-density lipoprotein (HDL: $r=-0.349$, $p=0.046$) and atherogenic index (calculated as $\log(\text{triglycerides}/\text{HDL})$) (AI: $r=0.454$, $p=0.009$). Furthermore, Hsp90 levels in r-axSpA patients positively correlated with the MRI presence of active inflammatory lesions in sacroiliac joints (SPARCC MRI score for SI joints: $r=0.594$, $p=0.020$). Increased Hsp90 levels in PsA patients were associated with the count of joint deformities ($r=0.526$, $p=0.025$). No further statistically significant associations were found between Hsp90 plasma levels and RA-, axSpA- or PsA-specific clinical features.

Conclusions We demonstrated elevated plasma concentrations of Hsp90 in RA and in axSpA patients compared to healthy controls. Hsp90 could be associated with early alterations of serum lipids and development of atherosclerosis in RA. Furthermore, in r-axSpA, Hsp90 may represent an independent marker of SI joint inflammation, whereas in PsA, plasma Hsp90 correlates with joint deformities. These data suggest that Hsp90 could become a potential biomarker of structural changes in SpA.

REFERENCE

None.

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Disclosure of Interest None declared.

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NLRP3 INFLAMMASOME-MEDIATED PYROPTOSIS AGGRAVATES THE AIRWAY INFLAMMATION IN TOLUENE DIISOCYANATE-INDUCED ASTHMATIC MICE

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Career situation of first and presenting author Young investigator.

Introduction NLRP3 inflammasome-mediated pyroptosis is a highly inflammatory event. This cell death process is characterized by cell explosion and IL-1 β release.¹ Our previous data have revealed that NLRP3 inflammasome-mediated pyroptosis plays an essential role in the pathogenesis of collagen-induced arthritis mice and lupus-like mice. While blockade of NLRP3 inflammasome-mediated pyroptosis alleviates the inflammation and organ damage in these autoimmune mice models.

Objectives Interesting, Toluene diisocyanate(TDI), the most common organic compound causing occupational asthma, has been proven to drive bronchial epithelium damage and IL-1 β production in patients with TDI-induced asthma. Therefore, in this study, we investigated whether NLRP3 inflammasome-mediated pyroptosis was involved in bronchial epithelial injury and airway inflammation in TDI-induced asthma.

Methods *In vitro*, 16HBEs (a human bronchial epithelial cell line) were stimulated with TDI. Then the cell death form was identified. *In vivo*, TDI-induced asthmatic mice were established after sensitization and challenge with TDI. After treatment with the NLRP3 inflammasome specific inhibitor, the airway hyperresponsiveness (AHR) and airway inflammation in asthmatic mice were assessed.

Results Here we found that TDI induced 16HBEs pyroptosis in a time and dose-dependent manner, as evidenced by the increased ratio of caspase-1⁺PI⁺ cells and the enhanced levels of LDH and IL-1 β . Importantly, the NLRP3 inflammasome specific inhibitor significantly blocked TDI-induced pyroptosis. In TDI-induced asthmatic mice, NLRP3 inflammasome inhibitor attenuated AHR and airway inflammatory infiltration by inhibiting the activation of caspase-1 and the cleavage of pyroptotic executioner GSDMD in the lungs. Moreover, NLRP3 inflammasome inhibitor decreased the levels of IL-1 β in the plasma and bronchoalveolar lavage fluid (BALF), accompanied by lower level of IgE in the plasma and Th2-related cytokines in the BALF.

Conclusions Our data demonstrated for the first time that bronchial epithelial pyroptosis was critical for TDI-induced asthma pathogenesis via the activation of NLRP3 inflammasome and the cleavage of GSDMD. Inhibition of NLRP3 inflammasome-mediated pyroptosis may be a valuable therapeutic strategy for TDI-induced asthma.

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