Pediatric Rheumatology

Poster presentation

The Damage Associated Molecular Pattern (DAMP) molecule S100A12 induces pro-inflammatory responses in monocytes via innate immunity signalling pathways

H Wittkowski*[1], D Viemann[1], A Lueken[2], K Barczyk[2], T Vogl[2], J Roth[2] and D Foell[1]

Address: [1]University Hospital Muenster, Department of Pediatrics, Muenster, Germany and [2]University Hospital Muenster, Institute of Immunology, Muenster, Germany

* Corresponding author

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Background

In a previous study, we demonstrated excessive activation of neutrophils leading to high concentrations of S100A12, a member of the damage-associated molecular pattern molecules (DAMP), in systemic-onset juvenile idiopathic arthritis (SOJIA) which is not found in other inflammatory diseases. Binding to the Receptor for Advanced Glycation Endproducts (RAGE) has been shown but exact molecular mechanisms of S100A12 leading to pro-inflammatory responses in immune cells are still lacking.

Methods

We analyzed the S100A12-induced expression pattern in human monocytes by microarray technology. Results were independently confirmed by real-time polymerase chain reaction (PCR) and flow cytometry. Additionally we used different knock down approaches of signalling pathways to identify common inflammatory and ligand-specific effects on gene expression changes.

Results

Functional clustering indicated induction of monocytic properties such as pro-inflammatory activation, chemotaxis, and repression of apoptosis. 43% of 745 S100A12-induced genes are also up-regulated by LPS already indicating a strong overlap. Inhibition revealed TLR-4 and NFκB as key signalling pathways.

Conclusion

In terms of gene expression changes S100A12 shows strong overlaps with LPS. Similar to LPS a significant portion of gene expression changes induced by S100A12 are dependent on TLR4 and NF-kB. Additionally, S100A12 activates an at least second strong signalling pathway which might be a RAGE-dependent cascade.