

Immunostimulatory activity of low-molecular-weight hyaluronan on dendritic cells stimulated with *Aggregatibacter actinomycetemcomitans* or *Porphyromonas gingivalis*

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Objectives: Periodontitis is a chronic inflammatory disease characterized by tooth-supporting tissue destruction, which is elicited by the host's immune response triggered against periodonto-pathogen bacteria. During periodontal tissue destruction, extracellular matrix components are metabolized and fragmented. Some extracellular matrix component-derived fragments, such as low-molecular-weight hyaluronan (LMW-HA), have potent immunogenic potential, playing a role as damage-associated molecular patterns (DAMPs) during activation of immune cells. Dendritic cells (DCs) play a central role in the host's immune response displayed during periodontitis; thus, this study aimed to analyze whether LMW-HA has an immunostimulatory activity on DCs when stimulated with periodonto-pathogen bacteria. **Materials and methods:** LMW-HA-treated and non-treated DCs were stimulated with *Aggregatibacter actinomycetemcomitans* or *Porphyromonas gingivalis* and the mRNA expression for cytokines tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and interleukin-23 (IL-23A) was quantified by RT-qPCR. In addition, transcription factors interferon regulatory factor 4 (IRF4), interferon regulatory factor 8 (IRF8), neurogenic locus notch homolog protein 2 (NOTCH2), and basic leucine zipper ATF-like transcription factor 3 (BATF3), involved in DC activation, were analyzed. **Results:** Higher expression levels of TNF- α ,

IL-1B, IL-6, and IL-23A were detected in LMW-HA-treated DCs after bacterial infection, as compared with non-treated DCs. When LMW-HA-treated DCs were infected with *A. actinomycetemcomitans*, higher levels of IRF4, NOTCH2, and BATF3 were detected compared with non-treated cells; whereas against *P. gingivalis* infection, increased levels of IRF4 and NOTCH2 were detected.

Conclusion: LMW-HA plays an immunostimulatory role on the immune response triggered by DCs during infection with *A. actinomycetemcomitans* or *P. gingivalis*. Clinical relevance: Detection of extracellular matrix component-derived fragments produced during periodontal tissue destruction, such as LMW-HA, could explain at least partly unsuccessful periodontal treatment and the chronicity of the disease. © 2018, Springer-Verlag GmbH Germany, part of Springer Nature.

Aggregatibacter actinomycetemcomitans

Cytokines

Dendritic cells

Hyaluronan

LMW-HA

Porphyromonas gingivalis

Transcription factors

cytokine

hyaluronic acid

immunological adjuvant

Aggregatibacter actinomycetemcomitans

cell culture

dendritic cell

drug effect

extracellular matrix

human

immunology

microbiology

molecular weight

periodontitis

Porphyromonas gingivalis

Adjuvants, Immunologic

Aggregatibacter actinomycetemcomitans

Cells, Cultured

Cytokines

Dendritic Cells

Extracellular Matrix

Humans

Hyaluronic Acid

Molecular Weight

Periodontitis

Porphyromonas gingivalis