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LETTER TO THE EDITOR

Potentialized 15d-PGJ_2 activity: a promising therapeutic strategy for inflammatory diseases

Atividade da 15d-PGJ_2 potencializada: uma estratégia terapêutica promissora para doenças inflamatórias

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Although the inflammatory response is essential for protecting tissues from injury and infection, unrestrained inflammation can cause chronic inflammatory diseases, such as periodontitis and arthritis. Leukocyte migration from the vascular system into an injured tissue is the major process towards inflammation. It is well known that the inflammatory process might be controlled by pro-inflammatory molecules such as prostaglandins and cytokines. Thus, most therapeutic efforts to reduce inflammation are based on these mediators. However, recent studies have reported complex resolutions for inflammation. Quick resolution for an acute inflammation is essential to protect tissues and nurture homeostasis, avoiding a chronic inflammatory process.

Cyclooxygenase (COX)-2 produces pro-inflammatory prostaglandins, leading to acute inflammation. However, multiple evidences suggest that COX-2 can also produce anti-inflammatory molecules contributing to the resolution phase of an inflammation. At the initial phase of an acute inflammation, pro-inflammatory lipid mediators, such as PGE_2 and leukotrienes, are generated from arachidonic acid via the COX-2 pathways. These mediators are inducers of the redirecting arachidonic acid which produces anti-inflammatory lipid mediators, such as resolvins, protectins, lipoxins and 15-deoxy$^{\Delta 12,14}$-prostaglandin J_2.

The 15d-PGJ_2, one of pro-resolving prostaglandins, induces inflammation resolution through several putative mechanisms: reduction in infiltration of polymorphonuclear cells (PMN); apoptosis of residual PMNs; facilitation of non-phlogistic monocyte infiltration; uptake of apoptotic PMNs; and activation of exit of macrophages engulfing apoptotic PMNs via lymphatics, promoting the clearance of epithelial-bound leukocytes and inhibition of intercellular

adhesion molecule-1 (ICAM-1) expression (1, 2, 3). According to these mechanisms, in the last years it has been demonstrated that peripheral and systemic administration of the 15d-PGJ_2 induce an anti-inflammatory effect in different models of inflammatory diseases such as inflammatory pain conditions, peritonitis, arthritis and periodontal disease (1, 4, 5, 2, 6, 7). These studies demonstrated that exogenous administration of 15d-PGJ_2 was able to inhibit inflammatory cells activity, several pro-inflammatory cytokines and chemokines release, phosphorilation of protein kinases and periodontal bone loss.

The use of nanomaterials as targeted delivery agents for drugs holds therapeutic promise for various diseases. Since solubility, pharmacokinetics and biodistribution of nanoparticle-based drugs have improved, the interest of the pharmaceutical industry in nanoenabled drug delivery systems has been increasing exponentially. Besides, nanoparticle-based drugs, many of which are commercially available (8), have biodegradable, biocompatible, and low toxic properties, which could potentialize the effect of conventional pharmaceutical agents. Nanoencapsulation (NC) of 15d-PGJ_2 improves its efficacy and bioavailabitily by providing sustained drug release to the inflamed site. The systemic or peripheral administration of 15d-PGJ_2-NC, at a much smaller dose when compared to unloaded 15d-PGJ_2, was found to improve its latency and anti-inflammatory effect (9, 10, 7). Thus, the future studies may focus on new molecules to facilitate the resolution of inflammation and the 15d-PGJ_2, encapsulated or not, could be considered a new promising strategy for targeting debilitating disorders associated with inflammation.

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