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Research Article

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Anti-inflammatory effect of polymer oxide nanocrystals in aqueous solution

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Abstract Molecular mechanisms of inflammsome activation remains an interesting area of research. Recently, polymer oxides provided new insight into therapeutic approach. Therefore, this work aims to investigate the chemical preparation of novel nanomaterials in aqueous solution and their biological activities were studied *in vitro*. Polymer oxides nanocrystals (PONK) were prepared using sol gel method. Size and morphology of the crystals were examined using Atomic force microscopy (AFM). The spectroscopic results showed absorption in a blue region. based on the experimental results, polymer oxides show highly anti-inflammatory effects evidenced by specific inhibition of interleukin one beta production and release in vitro using Elisa, western blotting, and RT PCR.

Keywords Nanotechnology, Polymer oxide, Inflammatory Disease, Diabetes

Introduction

Obesity and chronic inflammation are important to insulin resistance and type 2 diabetes (T2D) [1]. A body of evidence indicates that interleukin-1b (IL-1b) and IL-18, are involved in obesity-associated inflammation and insulin resistance [2]. Indeed, IL-1b treatment reduces the insulin-induced glucose uptake in 3T3 adipocytes [3] and reduces the expression of insulin sensitivity gene PPARg, adiponectin, and GLUT4 during adipocyte differentiation [4]. In addition, lack of IL-1 receptor 1 (IL-1 R1) protects mice from high-fat diet (HFD)-induced adipose tissue inflammation [5]. Of note, mice fed a HFD have increased IL-1b protein levels in adipose tissue in comparison to mice fed a low fat diet [6] suggesting that adipose tissue-derived IL-1b is associated with obesity and insulin resistance. Moreover, although plasma IL-18 has been also positively associated with increased risk of insulin resistance and T2D [7-8]. Its role in the homeostasis of energy intake and insulin sensitivity is however more complex since IL-18 and IL-18 receptor deficient mice exhibit hyperphagia and insulin resistance [9].

Cells of the innate immune system, namely macrophages and dendritic cells, express sensors for "danger" signals. These include the family of transmembrane Toll-like receptors (TLRs), RIG-1-like helicases (RLRs), and the nucleotide-binding domain and leucine-rich repeat-containing receptors (NLRs) [10]. They are involved in innate immune recognition of pathogen associated molecular patterns (PAMPs) as well as intracellular and extracellular damage associated molecular patterns (DAMPs). Several members of the NLR family such as NLRP1, NLRP3, and NLRC4 have been shown to assemble into large multiprotein complexes named inflammasomes to control caspase-1 activity [11-12].

The inflammasome is a multiprotein platform that activates procaspase-1 to caspase-1 and the latter one, in turn, can convert pro-IL-1β and pro-IL-18 into their bioactive secreted forms [13-14]. Both IL-1b and IL-18 are major mediators of inflammation and a number of laboratories have shown that both cytokines induce severe inflammatory diseases, such gout, atherosclerosis and T2D [15-17]. Among inflammasomes, NLRP3 inflammasome is the most extensively studied. It regulates host defense response to microbes and also it regulates sterile inflammation induced

by host-derived stimulatory factors. NLRP3 inflammasome has been found to be activated in response to a variety of signals among which monosodium urate crystals [15], fibrillar amyloid-b [18], amyloid-containing amylin-islet amyloid polypeptide (IAPP) [17] or cholesterol crystals [16].

Experimental Design

Cell culture

Rat insulinoma INS-1 cells were cultured in RPMI 1640 medium buffered with 10 mM HEPES containing 10% (vol/vol) FBS, 2 mM L-glutamine, 1 mM sodium pyruvate and 50 mM b-mercaptoethanol, and 100 units/ml penicillin/streptomycin. Cells were cultured in 6-well plates until reaching 80% confluence. The cells were washed and, serum-free RPMI-1640 medium containing glutamine and antibiotics, was added. Next, the cells were first treated with LPS (10 ng/ml) for 4 hrs, then incubated with vehicle (DMSO) or with PONC at different doses. One hour later, the cells were activated with cholesterol crystals (CC) (1mg/ml) and the level of biologically active IL-1b was evaluated 24 h later in the supernatants using the ELISA procedure.

Results and Discussion

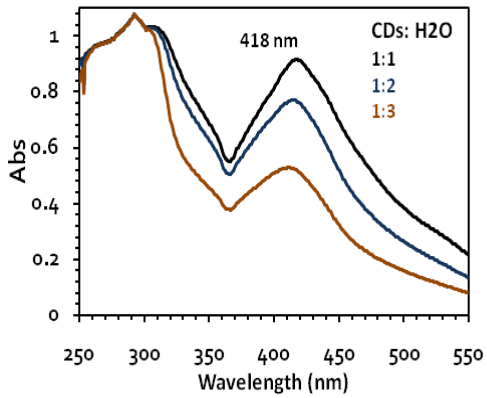

Figure 1: Absorption spectra of different concentrations of polymer oxides in water.

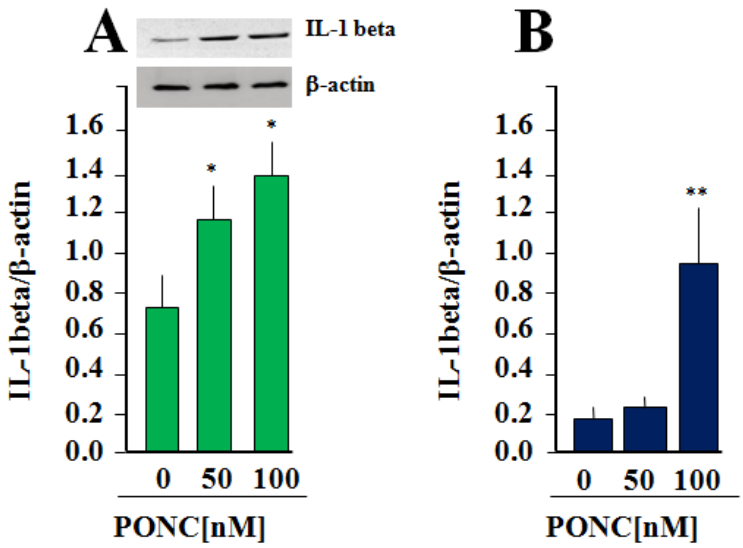

Figure 2: The effect of PONC at different concentration on the expression and translation of IL-1 beta.

Discussion

Chronic inflammation has long been associated with metabolic disorders, such as type 2 diabetes (T2D). Inflammatory cytokines such as IL-1 and TNF-α have been implicated in the development of several metabolic disorders. Because of the central role of the inflammasome in the generation of active IL-1, several laboratories have studied the role of inflammasomes in metabolic disorders. In mice lacking components of the inflammasome such as NLRP3, ASC or caspase-1, glucose tolerance and insulin sensitivity were improved following feeding on a HFD (41). In addition, a direct association between NLRP3 activation and the development of insulin resistance was reported (1; 42). Moreover, activation of inflammasomes in macrophages was reported to induce insulin resistance in other cell type such as hepatocytes or T cells (1; 42). Therefore, identification of specific inhibitors of inflammasomes might be of great importance for the treatment of metabolic disorders such as T2D. Significant progress in power conversion efficiencies and stabilities of polymer solar cells has been achieved using semiconducting metal oxides as charge extraction interlayers. Both n- and p-type transition metal oxides with good transparency in the visible as well as infrared region make good Ohmic contacts to both donors and acceptors in polymer bulk heterojunction solar cells. Their compatibility with roll-to-roll processing makes them very attractive for low cost manufacturing of polymer solar cells. Thus, our results suggest a potential anti-inflammatory effect evidenced by the downregulation of IL-1beta expression.

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