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Interleukin-12 (IL-12) plays a prominent role in the development of Th1 cell-mediated immune responses. Th1 cell-mediated immune responses have been implicated in the pathogenesis of chronic inflammatory autoimmune diseases. Thus, pharmacological control of IL-12 production may be a key therapeutic strategy for modulating immunological diseases dominated by Th1-derived cytokine responses. In this study we investigated the effects of costunolide, a prominent sesquiterpene lactone of *Saussureae radix*, on IL-12 production in mouse macrophages stimulated with lipopolysaccharide. Costunolide potently inhibited the production of IL-12 in a dose-dependent manner. The effect of costunolide on IL-12 p40 promoter activation was analyzed by transfecting RAW264.7 monocytic cells with p40 promoter/reporter constructs. The repressive effect mapped to a region in the p40 promoter containing a binding site for nuclear factor kappaB (p40-kappaB). Furthermore, activation of macrophages by lipopolysaccharide resulted in markedly enhanced binding activity to the kappaB site, which significantly decreased upon addition of costunolide. These results suggest that costunolide inhibited-inhibition of IL-12 production in macrophages may explain some of the biological effects of costunolide including its anti-inflammatory activity.

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Possible receptors for bovine lactoferrin on human monocytic THP-1 cells

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A variety of biological functions of human LF (H-LF) and bovine LF (B-LF) have been demonstrated in host defense, especially in immune responses, antibacterial activity and transcriptional activation of cells. Here, we discuss the characteristics of the binding of B-LF to THP-1 cells and partly compare the binding patterns of B-LF and H-LF. When we examined the binding of B-LF to THP-1 cells by Western blot analysis using B-LF labeled with biotin and a lysate of THP-1 cells, we found that B-LF binds to at least three types of molecules with molecular weights of about 25, 35 and 65 kDa in THP-1 cells. Also, the binding of B-LF to THP-1 cells was strictly dose-dependent. Further analysis revealed that the molecules with a M.W. of about 35 kDa among those that bound to B-LF are associated with the surface membrane of THP-1 cells, whereas the other molecules were derived from the cytosolic fraction. Inhibition tests using various saccharides showed that the binding was not inhibited by addition of a high concentration (100 mM) of GlcNAc, GalNAc, mannose or lactose, suggesting that oligosaccharides attached to B-LF are not involved in the binding of this glycoprotein to THP-1 cells. Comparison of the binding capacity of B-LF and H-LF showed that B-LF more strongly binds to THP-1 cells, although both B-LF and H-LF bind to the same molecules in THP-1 cells. Further analysis to characterize the specific binding of B-LF to THP-1 cells is now in progress.

Poster Presentations - Field C1. Biochemistry

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SELECTIVE INHIBITION OF HUMAN CYTOCHROME P450 1A1 BY 3, 3',4, 5, 5'-PENTAMETHOXYSTILBENE