Production of Interleukin-1 Inhibitors by the Murine Macrophage Cell Line P388D₁ Which Produces Interleukin-1

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Key Words

Interleukin-1
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The macrophage has a critical role in the immune response, both as an accessory cell and as a regulatory cell, which can either enhance or suppress immune reactions. The immunoenhancing function of the macrophages involves secretion of a soluble product, interleukin-1 (IL-1), which is a 15-kD protein that is defined by its ability to induce the differentiation of thymocytes and peripheral T lymphocytes. IL-1 is also well known as a product of many other cells such as neutrophils, NK cells, dendritic cells, endothelial cells, epithelial cells or fibroblasts. As for the biological effects of IL-1, it is also known to regulate a variety of cells such as the granulocytes, fibroblasts, epithelial cells, central nerve cells, synovial cells, osteo-clasts, liver cells, vascular endothelial cells, muscle cells or chondrocytes, and activates many biological functions of these cells.

The question that arises is how the production and effect of IL-1 are regulated. With such a broad range of biological activities, it would be extremely informative to characterize factors that may play a role in regulating activity of this potent cytokine. At present, very little is known about the negative regulation of IL-1, but increasing evidence indicates that the inhibitors of IL-1, as well as IL-1, are produced as a result of inflammation or immune responses. Characterization of such a factor may provide a lot of information on the regulation of both immune responses and inflammation.

In the present study, we report that a murine macrophage cell line, P388DJ in vitro culture, without any specific stimulation produced both IL-1 and IL-1 inhibitor which inhibits mitogenic response of murine thymocytes to IL-1 in the culture fluids. The factor(s) responsible for inhibiting IL-1-induced thymocyte proliferation consisted of at least two molecules: factor I (FI) with an isoelectric point of 6.0 and factor II (FII) with an isoelectric point of 5.3. both of which had a similar molecular weight (40–60 kD). FI activity was sensitive to heat (56 °C) treatment and acid pH (3.0) treatment while FII was resistant to both treatments. Both FI and FII inhibited mitogenic responses of thymocytes to IL-1

but not proliferation of murine lymphoid cells induced by other interleukins
namely

IL-2

IL-3 or IL-4. Neither showed any inhibition of spontaneous proliferation of murine tumor cell
lines

suggesting that inhibition was specific for IL-1

but not nonspecifically inhibiting for cellular DNA. These IL-1 inhibitors were also suggested to
be acting in the early phase of interaction between IL-1 and lymphoid cells.