Effect of Metallothionein on Granulocyte Chemotaxis and Superoxide Generation

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Much of the recent interest in metallothionein (MT) has focused on the induction mechanism or regulation of the gene. Less attention has been directed toward understanding the physiology of the protein. Since the localization of MT in rat and human skin tissues was demonstrated [1], the physiological roles of MT in the skin have attracted our interest. In the present paper, the influences of MT on chemotactic activity and superoxide anion obtained from granulocytes in healthy volunteers are discussed.

In chemotaxis assay using modified Boyden chamber [2], various amounts of MT (1.2. 6.0 μ M) and heated MT (6.0 μ M) to 8×10^5 granulocytes were obtained from 4 healthy adults. The essential steps for the isolation of rat hepatic MT-1 have been detailed previously [3]. Formyl-methionyl-leucyl-phenylalanine with a final concentration of 10^{-7} M was used as a chemoattractant. The chemotactic responsiveness was significantly depressed in the samples containing MT with dose-dependent tendency.

To estimate the ability of granulocytes to generate superoxide, a chemiluminescence (CL) probe with the Cypridina luciferin analog was used. CL in granulocytes obtained from 4 volunteers was measured under the stimulation of phorbol myristate acetate and opsonized zymosan. The activated oxygen derived from granulocytes incubated with MT was reduced with an increase of the MT dose. Heated MT incompletely depressed the superoxide generation.

Recent reports demonstrated that the induction of MT was made not only by heavy metals but also by glucocorti-

coid, IL-1, interferon and 1-alpha, 25(OH)2D3 in certain cultured cells. However, the physiological roles of MT are still not well known. Present studies revealed that chemotactic activity of granulocytes can be depressed by MT. In addition, MT action as an exceedingly efficient scavenger of activated oxygen was recognized. It was demonstrated that ultraviolet light could cause the expression of MT in the epidermis. Therefore, the present data suggest that MT may play an important role in phototherapy localized and generalized pustular psoriasis.

References

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