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Modulation of phenotypic and functional properties of human peripheral blood monocytes by interleukin-4 (IL-4)

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Introduction

IL-4, which was first described as B-cell stimulating factor-1 (BSF-1), has been shown to have important pleiotropic biologic effects in the mouse as well as in the human system [1]. In the present study we investigated the effect of rIL-4 on human peripheral blood monocytes. These cells were isolated by means of centrifugal elutriation, which prevented activation of the cells, and thus provided an excellent source of highly purified monocytes for functional and phenotypical studies upon culture with IL-4 [2].

Results and discussion

When human monocytes were cultured in the presence of rIL-4 for 5–7 days, the cells acquire a macrophage-like morphology with extensive processes and are considerably increased in size compared to control cultures. Culturing of monocytes in medium alone resulted in an enhanced class II MHC antigen expression. However, culturing of monocytes in the presence of IL-4 causes a further increase (2–6 fold) in the expression of HLA-DR and HLA-DQ antigens as compared with control cultures. Maximal increase in the expression of class II MHC antigens was found at concentrations of 50 U of purified IL-4 and this concentration was used for further phenotypic and functional characterization. The enhanced expression of class II MHC antigens was already observed after day 1 of culturing with and without IL-4, and maximal induction was found at day 6. Similarly, IL-4 increased the expression of the CR3 and p150,95 adhesion associated antigens, while the expression of LFA-1, the third member of the LFA-1 family of antigens, remained unchanged. Upon comparison of the data concerning enhanced expression of class II MHC antigens and LFA-1 family molecules with the literature [3, 4], it can be concluded that the phenotypic changes of monocytes cultured with IL-4 are similar to the changes observed when monocytes differentiate into macrophages. This might indicate that IL-4 induces differentiation of human monocytes. Upon activation, monocytes secrete a large number of immunoregulatory factors which mediate multiple activities on a variety of cells. When monocyts were cultured in the presence of IL-4 the secretion of such factors, especially those with auto-stimulatory chemotactic and anti-tumor cytostatic activity was diminished. Experiments have been started to identify these factors secreted in reduced amounts after incubation of monocytes with IL-4. A possible candidate is IL-1, which has chemotactic activity for human monocytes and has cytotoxic/cytostatic effects on certain tumor cell lines [5]. In order to investigate whether the reduced chemotactic and cytostatic actvities are attributed to a reduction in their capacity to pro-

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duce IL-1 activity, supernatants of monocytes cultured with and without IL-4 were tested for IL-1 activity. It was shown that IL-4 inhibits the production of IL-1 like activity identified by the reduced ability to co-stimulate (with Con A) the (^{3}H)-thymidine incorporation in murine thymocytes. Loss of IL-1 activity is associated with the *in vitro* maturation of monocytes to macrophages, which further supports the hypothesis that IL-4 induces *in vitro* monocyte differentiation into macrophages.

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