Expression of Interleukin-6 Receptor Subunits in Human Macrophage Subsets

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Key Words

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Interleukin-6 (IL-6) is a pleiotropic cytokine that exerts multiple functions during the immune response, hemato-poiesis and acute-phase reaction [1]. It acts via a cell surface receptor complex composed of an IL-6-binding subunit (gp80) and a signal-transducing subunit (gp130) which is also shared by some other cytokines, e.g. IL-11 [2]. The IL-6 receptor is expressed by a variety of cells including monocytes and macrophages [3, 4]. Since these cells display functional and phenotypic heterogeneity, we asked whether they might also differ with respect to the IL-6 receptor. Therefore, we studied the expression of the IL-6 receptor subunits gp80 and gp130 during in vitro maturation of monocytes to macrophages and in the macrophage subsets RM3/1 and 27E10. The glucocorticoid-inducible macrophage subtype RM3/1 is associated with anti-inflammatory properties since it appears during the downregulatory phase of the inflammatory process and secretes anti-inflammatory proteins [5, 6]. The 27E10 subtype is found only in acute inflammatory reactions and produces large quantities of inflammatory mediators such as PGE₂, TNF or IL-1, therefore exerting inflammatory effects [7, 8].

To investigate the expression of the IL-6 receptor in different macrophage maturation stages, cultures of human blood monocytes were obtained from buffy coats of healthy donors by two-step density gradient centrifugation [7]. They were cultured in hydrophobic Teflon bags in the absence (controls) or presence of lipopolysaccharide (1 µg/ml), phorbol ester (TPA; 10⁻⁸ M) or glucocorticoid (prednylidene; 10⁻⁷ M). The macrophage subpopulations RM3/1 and 27E10 were isolated from 48-hour cultures treated with prednylidene or TPA, respectively, employing an indirect immunomagnetic sorting procedure using Paesel beads (Paesel-Lorei, Frankfurt, Germany) that resulted in a purity > 95% of either subset. For Northern blot analysis, total RNA was isolated from the macrophage cultures or from purified subtypes with Microspin columns. 10 µg RNA/lane were separated on a 1% denaturing

agarose gel and transferred to a nitrocellulose membrane. Hybridization was performed with cDNA fragments for gp80, gp130 and IL-6 labeled by random priming.

An increase in IL-6 mRNA after 18 or 48 h was caused only by lipopolysaccharide treatment, but not by TPA or prednylidene. Both IL-6 receptor subunits were weakly expressed by monocytes cultured for 18 h but were similarly upregulated in monocytes cultured for 2 days with glucocorticoid or TPA, or in untreated control cells. Thereafter, they declined. TPA treatment decreased the mRNA for gp130 compared to controls, while prednylidene had no significant effect. The gp80 expression was not essentially affected by TPA or glucocorticoid. No essential difference in the expression of the IL-6 receptor subunits by RM3/1 and 27E10 subsets was found, even though the mRNA for the gp130 might be slightly diminished in the inflammatory subtype 27E10, probably due to TPA treatment.

The macrophage subpopulations RM3/1 and 27E10 differ markedly in their functions including mediator secretion [4-8], but vary only marginally in their IL-6 receptor expression. The transient upregulation of gp80 and gp130 during in vitro maturation seems to be associated with a distinct stage of macrophage differentiation.

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IL-6 Receptor Expression in Macrophage Subsets

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301
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