Cloning of a potentially soluble receptor for human GM-CSF

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Granulocyte–macrophage colony-stimulating factor (GM-CSF) is a growth and differentiation factor which acts on cells of the eosinophil, neutrophil and monocyte/macrophage lineages (1). GM-CSF is a glycoprotein that is thought to mediate its effects via interaction with a cell surface receptor. Recently cDNA clones for a human GM-CSF receptor (GM-CSFR) have been isolated (2). Sequence analysis suggests that the receptor is a transmembrane protein that is part of the hematopoietin receptor superfamily (2, 3). We have utilized oligonucleotides directed towards the N- and C-terminus of this protein and PCR to isolate full-length cDNA clones for GM-CSFR from human placental cDNA. During the analysis of these clones we noticed that 3 out of 16 encoded shorter forms of the receptor. Sequence analysis showed that these molecules lacked the 97 bp encoding the putative transmembrane domain of the receptor (see Figure 1) but were otherwise identical to the published sequence. The deletion of this domain, presumably as a result of alternative splicing, causes a shift in reading frame resulting in termination of the open reading frame after 18 amino acids. The effect of these changes should be to prevent retention of the receptor in the plasma membrane resulting in the production of a secreted receptor for GM-CSF. The number of clones isolated for this form of the receptor suggests that it may be a reasonable proportion of the mRNA for GM-CSFR in human placenta and not simply an artifact of PCR. The existence of soluble forms of the Interleukin 4 and Interleukin 7 receptors (4, 5) suggests that this phenomenon may be a general feature of receptors of this class and of biological significance in the regulation of these growth factors.

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Figure 1. Structure of the two forms of the GM-CSF receptor. Only the 3′ end of the coding region is shown. GM-CSFR A is identical to the sequence previously reported for the membrane-bound form of the receptor (2). GM-CSFR B is identical to GMCSFR A apart from the absence of 97bp encoding the putative membrane spanning domain. The sequence is numbered according to Gearing *et al.* (2).