RECOMBINANT HUMAN EPO-FC FUSION PROTEINS WITH PROLONGED HALF-LIFE AND ENHANCED ERYTHROPOIETIC ACTIVITY IN VIVO

ABSTRACT

A recombinant fusion protein comprising a human erythropoietin peptide portion linked to an immunoglobulin peptide portion is described. The fusion protein has a prolonged half-life in vivo in comparison to naturally occurring or recombinant native human erythropoietin. In one embodiment of the invention, the protein has a half-life in vivo at least three fold higher than native human erythropoietin. The fusion protein also exhibits enhanced erythropoietic bioactivity in comparison to native human erythropoietin. In one embodiment, the fusion protein comprises the complete peptide sequence of a human erythropoietin (EPO) molecule and the peptide sequence of an Fc fragment of human immunoglobulin IgG1. The Fc fragment in the fusion protein includes the hinge region, CH2 and CH3 domains of human immunoglobulin IgG1. The EPO molecule may be linked directly to the Fc fragment to avoid extraneous peptide linkers and lessen the risk of an immunogenic response when administered in vivo. In one embodiment the hinge region is a human Fc fragment variant having a non-cysteine residue at amino acid 6. The invention also relates to nucleic acid and amino acid sequences encoding the fusion protein and transfected cell lines and methods for producing the fusion protein. The invention further includes pharmaceutical compositions comprising the fusion protein and methods of using the fusion protein and/or the pharmaceutical compositions, for example to stimulate erythropoiesis in subjects in need of therapy.

Figure 1

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Figure 1