

**EXHIBIT B**  
**Part 1 of 3**



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Lin

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[54] **PRODUCTION OF ERYTHROPOIETIN**

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**ABSTRACT**

[57] Disclosed are novel polypeptides possessing part or all of the primary structural conformation and one or more of the biological properties of mammalian erythropoietin ("EPO") which are characterized in preferred forms by being the product of procaryotic or eucaryotic host expression of an exogenous DNA sequence. Illustratively, genomic DNA, cDNA and manufactured DNA sequences coding for part or all of the sequence of amino acid residues of EPO or for analogs thereof are incorporated into autonomously replicating plasmid or viral vectors employed to transform or transfect suitable procaryotic or eucaryotic host cells such as bacteria, yeast or vertebrate cells in culture. Upon isolation from culture media or cellular lysates or fragments, products of expression of the DNA sequences display, e.g., the immunological properties and in vitro and in vivo biological activities of EPO of human or monkey species origins. Disclosed also are chemically synthesized polypeptides sharing the biochemical and immunological properties of EPO. Also disclosed are improved methods for the detection of specific single stranded polynucleotides in a heterologous cellular or viral sample prepared from, e.g., DNA present in a plasmid or viral-borne cDNA or genomic DNA "library".

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Page 2

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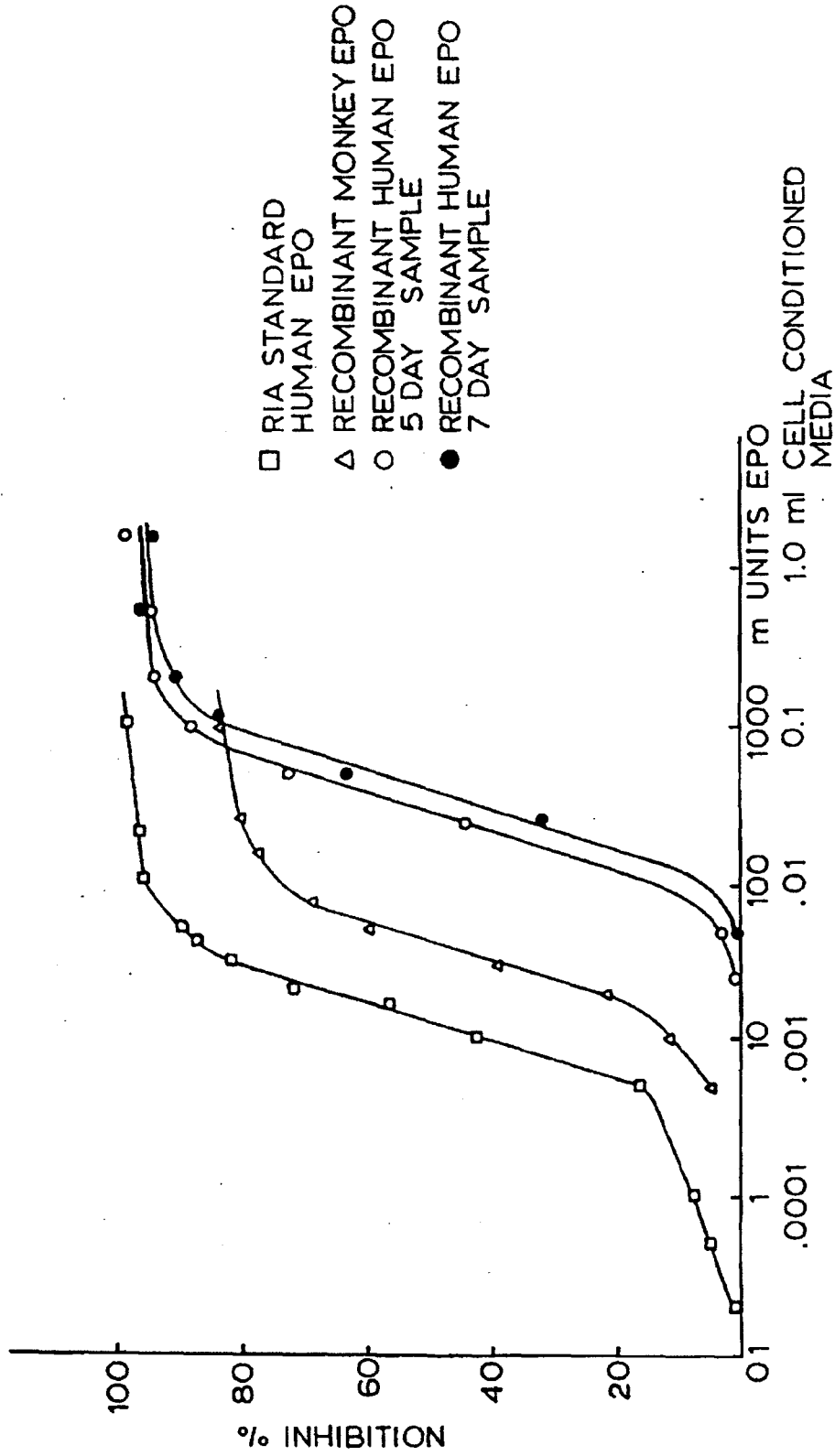
U.S. Patent

Aug. 20, 1996

Sheet 1 of 27

5,547,933

FIG. 1



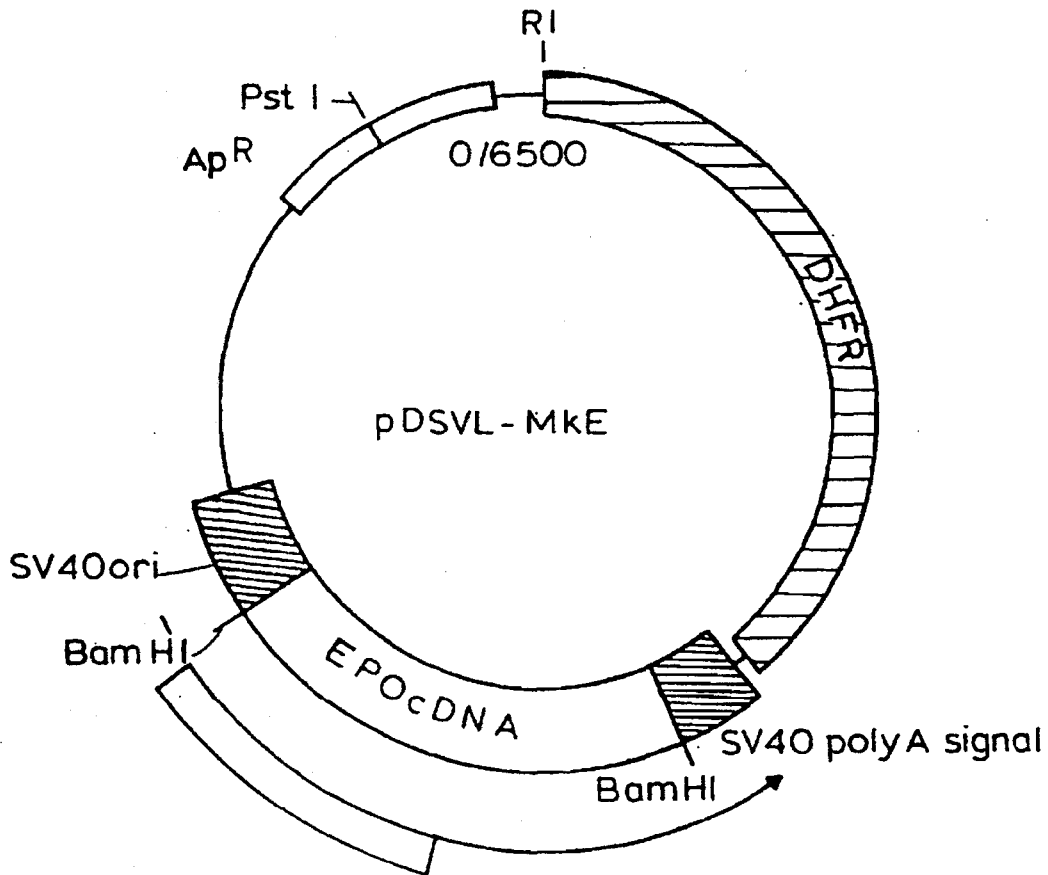
U.S. Patent

Aug. 20, 1996

Sheet 2 of 27

5,547,933

FIG. 2



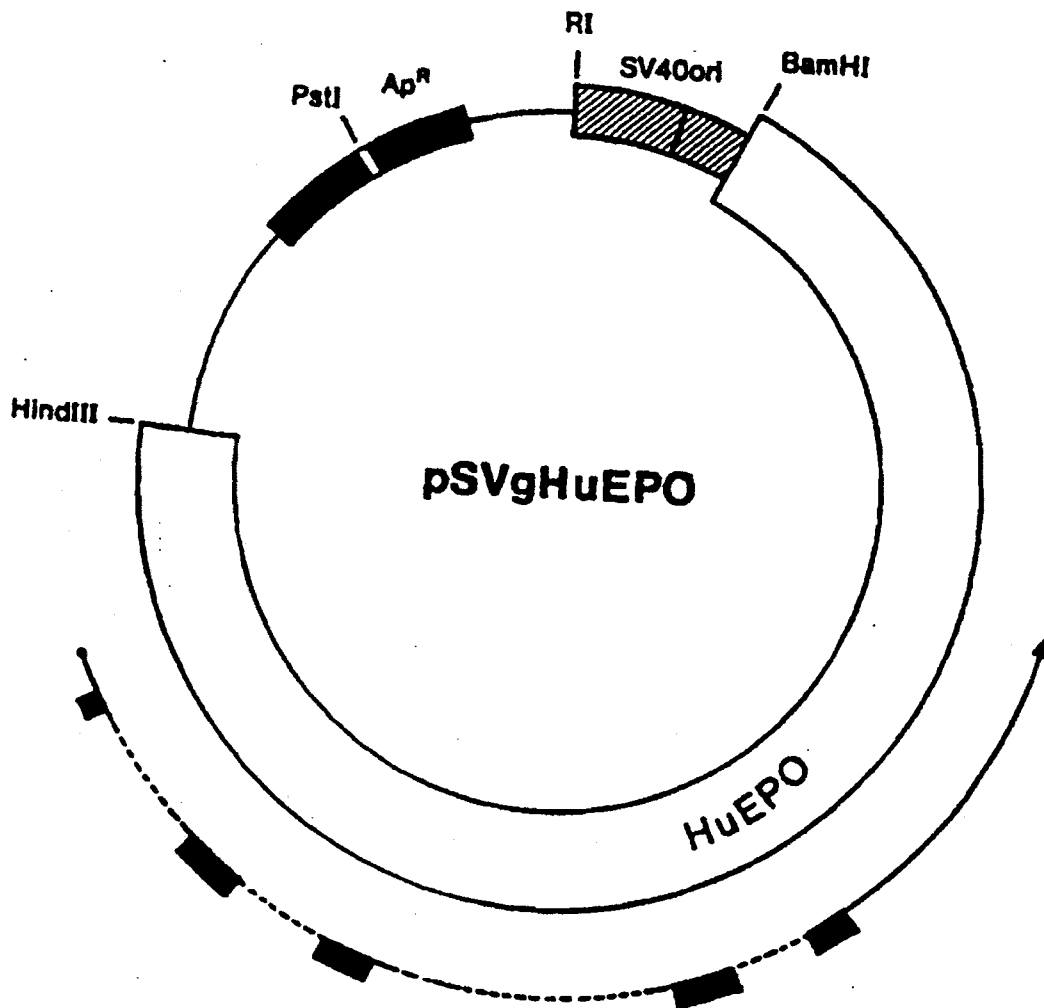
U.S. Patent

Aug. 20, 1996

Sheet 3 of 27

5,547,933

FIG. 3



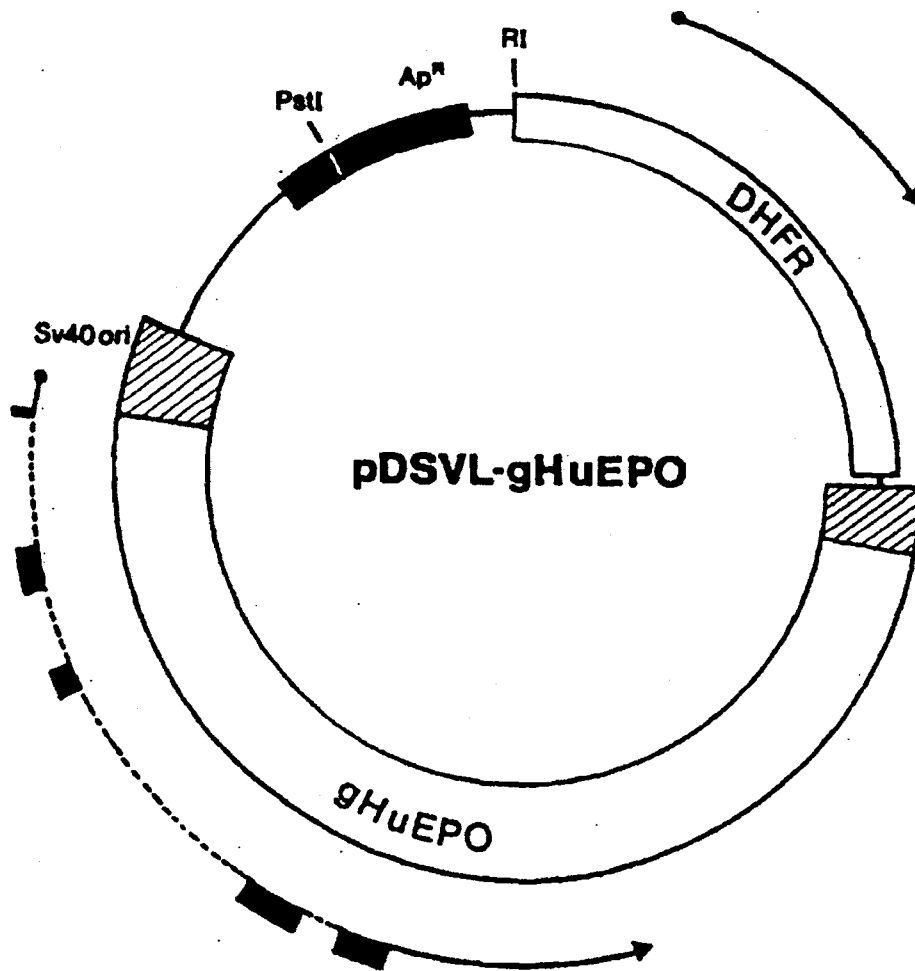
U.S. Patent

Aug. 20, 1996

Sheet 4 of 27

5,547,933

FIG. 4



U.S. Patent

Aug. 20, 1996

Sheet 5 of 27

5,547,933

FIG. 5A

GAUUA  
GATCCCCCCCCCTGGACAGCCCCCTCTCCAGCCCGCCCTGGGGCTGGCCCTGCC

CGCTGAACTTCCCCGGGATGAGGACTCCCGGTGTGTCTACCCCGCCCTAGGTCCTGAG

-27  
Met Gly Val His Glu Cys Pro Ala Trp  
GGACCCCGCCAGGCCGGGAGATG GGG GTG CAC GAA TGT CCT GCC TGG

-10  
Leu Trp Leu Leu Leu Ser Leu Val Ser Leu Pro Leu Gly Leu Pro  
CTG TGG CTT CTC CTG TCT CTC CTC GTG TCG CTC CCT CTG GGC CTC CCA

-1 +1  
Val Pro Gly Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu  
GTC CCG GGC GCC CCA CCA CCG CTC ATC TGT GAC AGC CCA GTC CTG

20  
Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Val Thr Met  
GAG AGG TAC CTC TTG GAG GCC AAG GAG GCC GAG AAT GTC ACC ATG

30  
Gly Cys Ser Glu Ser Cys Ser Leu Asn Glu Asn Ile Thr Val Pro  
GGC TGT TCC GAA AGC TGC AGC TTG AAT GAG AAT ATC ACC GTC CCA

40



U.S. Patent

Aug. 20, 1996

Sheet 6 of 27

5,547,933

FIG. 5B

50  
ASP THR LYS VAL ASN PHE TYR ALA TIP LYS ARG MET GLU VAL GLY  
GAC ACC AAA GTT AAC TTC TAT GCC TGG AAG AGG ATG GAG CTC GGG

60  
GLN GLN ALA VAL GLU VAL TIP GLN GLY LEU ALA LEU LEU SER GLU  
CAG CAG GCT GTA GAA GTC TGG CAG GGC CTG GCC CTG CTC TCA GAA

70  
ALA VAL LEU ARG GLY GLN ALA VAL LEU ALA ASN SER SER GLN PRO  
GCT GTC CTG CCG GGC CAG GCC GTG TTG GCC AAC TCT TCC CAG CCT

80  
PHE GLU PRO LEU GLN LEU HIS MET ASP LYS ALA ILE SER GLY LEU  
TTC GAG CCC CTG CAG CTG CAC ATG GAT AAA GCC ATC AGT GGC CTT

90  
ARG SER ILE THR THR LEU LEU ARG ALA LEU GLY ALA GLN GLU ALA  
CGC AGC ATC ACC ACT CTG CTT CCG GCG GCG CTG GGA GCC CAG GAA GCC

100  
ILE SER LEU PRO ASP ALA ALA SER ALA ALA PRO LEU ARG THR ILE  
ATC TCC CTC CCA GAT GGC GCC TCG GCT GCT CCA CTC CGA ACC ATC

110  
THR ALA ASP THR PHE CYS LYS LEU PHE ARG VAL TYR SER ASN PHE  
ACT GCT GAC ACT TTC TGC AAA CTC TTC CCA GTC TAC TCC AAT TTC

120  
130  
140

FIG. 5C

150           Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Arg  
 Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Arg  
 CTC CGG GGA AAG CTG AAG CTG TAC ACC GGG GAG GCC TGC AGG AGA  
 160  
 Gly Asp Arg OP  
 GGG GAC AGA TGA CCAGGTGCTCCAGCTGGGCACATCCACCACCTCCCTGCACCAACA  
 CTGCCCTGTGCCACACCCCTCCCTCACCCACTCCCGAACCCCTCCGAGGGGCTCTCAGCTAAG  
 CGCCAGCCCTGTCCCATGGACACTCCAGTCCAGCCATGACATCTCAGGGGCCAGGGGAAC  
 TGTCGAGGACCAACTCTGAGATCTAAGGATGTCCGAGGGCCCAACTTGAAGGGCCCAAGC  
 AGGAGCATTTCAGGAGCCAGCTTTAAACTCAGGAGCAGAGACAAATGCAGGGGAAACACCT  
 GAGCTACTGGCCACCTGCAAAATTTGATGCCAGGACACGCTTTGGAGGCCAATTTACCTG  
 TTTTTCACCTACCATCAGGGACAGGATGACTGGAGAACTTAGGTGGCCAACTGTGACTT  
 CTCAGGCCCTCACGGCCACTCCCTTGGTGGCAAGAGCCCTTGCACACTGAGAGATATT  
 TTGCCAATCTGCAGCCAGGAAAATTTACGGACAGGTTTTGGAGGTTGGAGGGTACTTGCAG  
 GTGTGGGGAAAGCAGGGCCGGJAGGGGTTGGAGCTGGGATGCCAGGTCAGAACCGGTGAGAC  
 AGGATGGGGGCTGGCCCTGTGGTTCTCGTGGGGGCTCCAAAGCTT  
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U.S. Patent

Aug. 20, 1996

Sheet 8 of 27

5,547,933

FIG. 6A

AAGCTTCTGGGCTTCCAGACCCAGCTACTTTCGGAACTCAGCCAACCCAGGCATCTCTGATCTCCGCCCA  
 AGACCGGATGCCCCCAAGGGAGGTGTCCGGGAGCCCAAGCCTTTCCTCCAGATAGCAGCCTCCGCCCAAGTCCC  
 AAGGTTCCGCAACCGGCTGACTCCCTCCCGGACCCAGGGCCCGGAGCAGCCCCCATGACCCACACCGC  
 ACGTCTGAGCAGCCCGCTCAGCCCGGCGAGCCCTCAACCCAGGCGTCCCTGCCCTGCTGACCCCGG  
 GTGCCCTTACCCTGGCGACCCCTCAGCGCACAGCCTCTCCCGCCACCCCGCCACCGCCACACATG  
 CAGATAACAGCCCGAACCCCGGCGAGGCCGTAAGTCCCTGGGCCACCCCGCCCTGCCCTGCCGCTG  
 CGCCGACCCGCGTGTCTCCCGGAGCCCGGACCCGGGCGCACCGCCCTGCTGCTCCGACACCGCGCC  
 CTGGACAGCCCGCTCTCTCTAGGCCCGTGGGCTGCGCCCTGACCCCGGAGCTTCCCGGATGAGGIX  
 CCGGTTACCGGCGCCCGCAAGTCCCTGAGGGGACCCCGCCCAAGCCCGGAG ATG GGG GTG CAC G  
 GTGAGTACTCGGGGCTGGCGCTCCCGCGCGGTTCTCTGTTGAGCGGGGATTTAGCGCCCGGCT

-27                      -24  
                          Met Gly Val His

FIG. 6B

ATGGCCAAAGGTTGGCTGGGTTCAAAGGACCCGGGACTTGTCAAGGACCCCGGAAAGGGGGGAGGGGGGTGGG  
 GCAGCCCTCCACGTTGCCCGGGGAACTTGGGGGAGTTCTTGGGGGATGGCAAAAACCTGGCCCTGTTGAGGGGGCA  
 CAGTTTGGGTTGGGGAGGAGGTTTGGGTTCTGCTGTGCAAGTTGTGTGCTGCTGCTCG[I · B · ]  
 TTGCACCCACAGATCAATAAGCCAGAGGCGACCCCTGAGTCTTGCATGGTTGGGACAGGAAAGGACCGAG  
 CTGGGCGAGAGCGTGGGGATGAAAGGAAAGCTGTCTTCCACAGCCACCCCTTCTCCCCCGCCCTGACTCT  
 CAGCCTGGCTATCTGTTCTAG  
 -23                   -20  
 Glu Cys Pro Ala Tip Leu Tip Leu Leu Leu Ser Leu  
 AA TGT CCT GCC TGG CTG TGG CTT CTC CTG TCC CTG  
 -10                   -1   +1  
 Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Leu Gly Ala Pro Pro Arg Leu Ile Cys  
 CTG TCG CTC CCT CCT CTG GGC CTC CCA GTC CTC GGC GGC CCA CCA CCG CTC ATC TGT  
 Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile  
 GAC AGC CGA GTC CTC GAG AGG TAC CTC TTG GAG GCC AAG GAG GAG GCC GAG AAT ATC  
 10                   20  
 26  
 Thr  
 ACC GTGAGACCCCTTCCCCAGCACATTCACAGAACTCACGGCTTCAGGGGAACTCCTCCCAGAT  
 CCAGGAACTGGCACCTTGGTTTGGGGTGGAGTTGGGAAAGCTAGACACTGCCCGCCCTACATAAGAAATAAGTC

FIG. 6C

TGGTGGCCCAACCATACCTGAAACTAGCCAAAGGAGCAAGCCAGCAGATCCTACGCCCTGTGGGCCCAAGGG

CCAGAGCCTTCAGGGACCCTTGACTCCCGGGCTGTGTGCATTTTCAG      27      Thr Gly Cys Ala Glu  
ACG GGC TGT GCT GAA      30

His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr  
CAC TGC AGC TTG AAT GAG AAT ATC ACT GTC CCA ACC AAC GTT AAT TTC TAT

50      55  
Ala Trp Lys Arg Met Glu  
GCC TGG AAG AGG ATG GAG GTGAGTTCCTTTTTTTTTTTTTCCTTCTTTTGGGAAATCTCATTT

TCCGAGCCTGATTTGGATGAAAGGGAGAAATGATCGGGGAAAAGGTAATAATGGAGCAGAGATGAGGCT  
GCCTGGGGCAGAGGCTCAGTCTATATATCCAGGCTGATGATGGCCGAGATGGGAGAAATTGCTTGAAGCCCT

GGAGTTTCAGACCACCTAGGCAGCATAGTGAATCCCCCATCTCTACAAACATTTTAAATAAATAATAGTCA  
GTGAAAGTGGTCATGGTGGTAGTCCAGATATTTGGAAAGGCTGAGCCGGGAGGATCCGCTTGAAGCCCAAGAA

TTTGAAGCCTGCAATGAGCTGTGATCAGACCACCTGCACTCCAGCCTCAGTGAACAGTGAAGGCCCTGTCTCA

U.S. Patent

Aug. 20, 1996

Sheet 11 of 27

5,547,933

FIG. 6D

AAAAAGAAAAGAAAATAATGAGGGGCTGTATGGAAATACATTTCATTTCACCTCAGCTCAGCT

CAGCTCATTTCATTTCATTTCATTCACAAAGTCTTATTGTCATACCTTCTGTTGCTCAGCTTGGTCTTGG

GGCTGCTGAGGGGCGAGGGGAGGGGTGCATGGGTGAGCTCCAGCTCCAGAGTCCAGCTCCCTGTAG

56 60

70

Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala  
GTC GGG CAG CAG GCC GTA GAA GTC TGG CAG GGC CTG GCC CTG TCG GAA GCT

80

\*

90

Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu  
GTC CTG CGG GGC CAG GCC CAG CTG TTG GTC AAC TCT TCC CAG CCG TGG GAG CCC CTG

100

Gln Leu His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu  
CAG CTG CAT GTG GAT AAA GCC GTC AGT GGC CTT CGC AGC CTC ACC ACT CTG CTT

110

115

Arg Ala Leu Gly Ala Gln

CGG GCT CTG GGA GCC CAG GTGAGTAGGAGCGGACACTTCTGCTTCCCTTCTGTAAAGAGGGGA

GAAGGGTCTTGTAGGAGTACAGGAACTGTCGGTATTCCTTCCCTTCTGTGTGGCAGCTCCAGGACCTCCT

116

120

Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala  
GTTTTCCTTGGCAG AAG GAA GCC ATC TCC CCT CCA GAT GCG GCC TCA GCT GCT

FIG. 6E

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130      Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser
CCA CTC CGA ACA ATC ACT GCT GAC ACT TTC CGC AAA CTC TTC CGA GTC TAC TCC

140      Asp Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly
AAT TTC CTC CGG GGA AAG CTG AAG CTG TAC ACA GGG GAG GCC TGC AGG ACA GGG

150      Asp Arg OP
GAC AGA TGA CCAGGTGTGTCCACCTGGGCATATCCACCCTCCCTCACCACCATTTGCTGTGCCACA

166      CCTCCCCGCCACTCCTGAAACCCCGTCCAGGGGCTCTCAGCTCAGCCCAAGCCCTGTCCATGGACACTCC
AGTGCCAGCAATGACATCTCAGGGGCCAGAGGACTGTCCAGAGAGCACTCTGAGATCTAAGGATGTCCAC
AGGGCCAACTTGAAAGGGCCCAAGCAGGAAACATTCAGAGAGCAGCTTAAACTCAGGGACAGGCCATGC
TGGGAAAGACCCCTGAGCTCAGTCCGGCACCCCTGCCAAAATTTGATGCCAGGACACCGCTTTGGAGGCCGATTTAC
CTGTTTTCGCACCTACCATCAGGGACAGGATGACCTGGAAGAACTTAGGTGGCAAGCTGTGACTTCTCCAGG
TCTCACGGGCATGGGCACCTCCCTTGGTGGCAAGAGCCCCCTTGACACCGGGGGTGGTGGAAACCNTGAAAGAC
AAGATGGGGCTGGCCCTCTGGCTCTCATGGGGTCCAAAGTTTTGTGTATTTCTCAACCTATTGACAGACTGAA
ACACAAATATGAC

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U.S. Patent

Aug. 20, 1996

Sheet 13 of 27

5,547,933

FIG. 7

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Kp1 MetA1

CTAG AAACCATGAG GGTAAATAAA TAATGGCTCC GCCGCGTCTG  
TTTGGTACTC CCATTATTTT ATTACCGAGG CCGCGCAGAC

ATCTGCGACT CGAGAGTTCT GGAACGTTAC CTGCTGGAGG CTAAGAAGCC  
TAGACGCTGA GCTCTCAGA CTTGCAATG GACGACCTTC GATTTCTTCG

TGAAAACATC ACCACTGGTT GTGCTGAACA CTGTTCTTTG AACGAAAACA  
ACTTTTGTAG TGGTGACCAA CACGACTTGT GACAAGAAC TTGCTTTTGT

TTACGGTACC AGACACCAAG GTTAACTTCT ACGCTTGGAA ACGTATGGAA  
AATGCCATGG TCTGTGGTTC CAATTGAAGA TCGAACCCTT TGCATACCTT

GTGGTCAAC AAGCAGTTGA AGTTGGCAG GGTCTGGCAC TGCTGAGCGA  
CAACCACTTG TTCGTCAACT TCAAACCGTC CCAGACCGTG ACGACTCGCT

GGCTGTACTG CGTGGCCAGG CACTGCTGGT AACTCCTCT CAGCCGTGGG  
CCGACATGAC GCACCGGTCC GTGACGACCA TTTGAGGAGA GTCCGCACCC

AACCGCTGCA GCTGCATGTT GACAAAGCAG TATCTGGCCT GAGATCTCTG  
TTGGCGACGT CGACGTACAA CTGTTTCGTC ATAGACCGGA CTCTAGAGAC

ACTACTCTGC TGGTGCTCT GGGTGACAG AAAGAGGCTA TCTCTCCGCC  
TGATGAGACG ACGCACGAGA CCCACGTGTC TTTCTCCGAT AGAGAGGCCG

GGATGCTGCA TCTGCTGCAC CGCTGCGTAC CATCACTGCT GATACCTTCC  
CCTACGACGT AGACGACGTG GCGACCGATG GTAGTGACGA CTATGGAGG

GCAAACTGTT TCGTGTATAC TCTAACTTCC TCGGTGGTAA ACTGAAACTG  
CGTTTGACAA AGCACATATG AGATTGAAGG ACGCACCATT TGACTTTGAC

B11

TATACTGGCG AAGCATGCCG TACTGGTGAC CGCTAATAG  
ATATGACCGC TTCGTACGGC ATGACCACTG GCGATTATCA GCT



U.S. Patent

Aug. 20, 1996

Sheet 14 of 27

5,547,933

FIG. 8

	-1	+1		
<b>HindIII</b>	<b>Arg</b>	<b>Ala</b>		
<b>AGCTTGGATA</b>	<b>AAAGAGCTCC</b>	<b>ACCAAGATTG</b>	<b>ATCTGTGACT</b>	<b>CGAGAGTTT</b>
<b>ACCTAT</b>	<b>TTTCTCGAGG</b>	<b>TGGTTCCTAC</b>	<b>TAGACTGTA</b>	<b>GCTCTCAAA</b>
<b>GGAAAGATAC</b>	<b>TTGTTGGGAG</b>	<b>CTAAGAAGC</b>	<b>TGAAAACATC</b>	<b>ACCACTGGT</b>
<b>CCTTCTATG</b>	<b>AACAACCTC</b>	<b>GATTCTTTC</b>	<b>ACTTTGTAG</b>	<b>TGGTGACCA</b>
<b>GTGCTGAACA</b>	<b>CTGTTCTTTG</b>	<b>AACGAAAACA</b>	<b>TTACGGTACC</b>	<b>AGACACCAAG</b>
<b>CAGCACTTGT</b>	<b>GACAAGAAAC</b>	<b>TTGCTTTTGT</b>	<b>AATGCCATGG</b>	<b>TCTGTGGTTC</b>
<b>GTTAACTTCT</b>	<b>ACGCTTGGAA</b>	<b>ACGTATGGAA</b>	<b>GTTGGTCAAC</b>	<b>AAGCTGTTGA</b>
<b>CAATTGAAGA</b>	<b>TCCGAACCTT</b>	<b>TGCATACCTT</b>	<b>CAACCACTTG</b>	<b>TTCGACAACT</b>
<b>AGTTTGGCAA</b>	<b>GTTTTGGCCT</b>	<b>TGTTATCTGA</b>	<b>AGCTGTTTTG</b>	<b>AGAGGTCAAG</b>
<b>TCAAACCGTT</b>	<b>CCAAACCGGA</b>	<b>ACAATAGACT</b>	<b>TGGACAAAAC</b>	<b>TCTCCAGTTC</b>
<b>CCTTGTGGT</b>	<b>TAACTCTTCT</b>	<b>CAACCATGGG</b>	<b>AACCATTGCA</b>	<b>ATTGCACGTC</b>
<b>GGAAACAACCA</b>	<b>ATTGAGAAGA</b>	<b>GTTGGTACCC</b>	<b>TTGGTAACGT</b>	<b>TAACGTCCAG</b>
<b>GATAAAGCCG</b>	<b>TCTCTGGTTT</b>	<b>GAGATCTTTG</b>	<b>ACTACTTTGT</b>	<b>TGAGAGCTTT</b>
<b>CTATTTGGGC</b>	<b>AGAGACCAA</b>	<b>CTCTAGA AAC</b>	<b>TGATGAAACA</b>	<b>ACTCTCGAAA</b>
<b>GGGTGCTCAA</b>	<b>AAGGAAGCCA</b>	<b>TTCCCCACC</b>	<b>AGACGCTGCT</b>	<b>TCTGCCGCTC</b>
<b>CCCACGAGTT</b>	<b>TTCCTTCGGT</b>	<b>AAAGGGGTGG</b>	<b>TCTGCGACGA</b>	<b>AGACGGCGAG</b>
<b>CATTGAGAAC</b>	<b>CATCACTGCT</b>	<b>GATACCTTCA</b>	<b>GAAAGTTATT</b>	<b>CAGAGTTTAC</b>
<b>GTA ACTCTTG</b>	<b>GTAGTGACGA</b>	<b>CTATGGAACT</b>	<b>CTTCAATAA</b>	<b>GTCTCAAATG</b>
<b>TCCAACTTCT</b>	<b>TGAGAGGTAA</b>	<b>ATTGAAGTTG</b>	<b>TACACCGGTC</b>	<b>AAGCCTGTAG</b>
<b>AGTTTGAAGA</b>	<b>ACTCTCCATT</b>	<b>TAACTTCAAC</b>	<b>ATGTGGCCAC</b>	<b>TTCGGACATC</b>
<b>AAGTGGTGAC</b>	<b>AGATAAGCCC</b>	<b>GACTGATAAC</b>	<b>AACAGTGTAG</b>	
<b>TGACCACTG</b>	<b>TCTATTCGGG</b>	<b>CTGACTATTG</b>	<b>TTGTCAATC</b>	
	<b>SalI</b>			
<b>ATGTAACAAA</b>	<b>G</b>			
<b>TACATTGTTT</b>	<b>CAGCT</b>			

FIG. 9

-20            -10            +1            10            20            30            40  
 Human        MGVHECPAWLWLLSLLSPLGLPVLGAPPRLLICDSRVLERYLEAKEAENITTGCAEHCSLNENITVPDTK  
 \*\*\*\*\*  
 Monkey        MGVHECPAWLWLLSLLSPLGLPVPGAPPRLLICDSRVLERYLEAKEAENVTMGCSBSCSLNENITVPDTK

50            60            70            80            90            100            110  
 Human        VNFYANKRMEVGGQAVEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLRSLTLLRALGAQKE  
 \*\*\*\*\*  
 Monkey        VNFYANKRMEVGGQAVEVWQGLALLSEAVLRGQAVLANSSQPFPEPLQLHMDKAI SGLRSITLLRALGAQ-E

120            130            140            150            160  
 Human        AISLPPDAASAAPLRTITADTFKLFRRVYSNFLRGLKLYTGEACRTGDR  
 \*\*\*\*\*  
 Monkey        AISLPPDAASAAPLRTITADTFKLFRRVYSNFLRGLKLYTGEACRRGDR

U.S. Patent

Aug. 20, 1996

Sheet 16 of 27

5,547,933

**FIG. 10**

1.           **AATTCTAGAAACCATGAGGGTAATAAAATA**  
2.           **CCATTATTTTATTACCCTCATGGTTTCTAG**  
3.           **ATGGCTCCGCCCGCTCTGATCTCCGAC**  
4.           **CTCGAGTCGCAGATCAGACGCCGCCGAG**  
5.           **TCGAGAGTTCTGGAACGTTACCTGCTG**  
6.           **CTTCCAGCAGGTAACGTTCCAGAACT**  
7.           **GAAGCTAAAGAAGCTGAAAACATC**  
8.           **GTGGTGATGTTTTTCAGCTTCTTTAG**  
9.           **ACCACTGGTTGTGCTGAACACTGTTT**  
10.          **CAAAGAACAGTGTTTCAGCACAACCA**  
11.          **TTTGAACGAAAACATTACGGTACCG**  
12.          **GATCCGGTACCGTAATGTTTTTCGTT**

U.S. Patent

Aug. 20, 1996

Sheet 17 of 27

5,547,933

FIG. 11

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EcoRI 1 3  
**AATTCTAG AAACCATGAG GGTAAATAAAA TAATGGCTCC GCCCGCTCTG**  
**GATC TTTGGTACTC CCATTATTTT ATTACCGAGG CCGCGCAGAC**  
2 4

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**ATCTGGGACT CGAGAGTTCT GGAACGTTAC CTGCTGGAA GCTAAAGAAGC**  
**TAGACCGCTGA GCTCTCAAGA CCTTGCAATG GACGACCTTC GATTTCTTCG**  
6

7 9 11  
**TGAAAACATC ACCACTGGTT GTGCTGAACA CTGTTCTTTC AACGAAAACA**  
**ACTTTTGTAG TGGTGACCAA CACGACTTGT GACAAGAAAC TTGCTTTTGT**  
8 10

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KpnI BamHI  
**TTACGGTACC G**  
**AATGCCATGG CCTAG**  
12

U.S. Patent

Aug. 20, 1996

Sheet 18 of 27

5,547,933

**FIG. 12**

1. **AATTCGGTACCAGACACCAAGGT**
2. **GTTAACCTTGGTGTCTGGTACCG**
3. **TAACTTCTACGCTTGGAAACGTAT**
4. **TTCCATACGTTTCCAAGCGTAGAA**
5. **GGAAGTTGGTCAACAAGCAGTTGAAGT**
6. **CCAAACTTCAACTGCTTGTGACCAAC**
7. **TTGGCAGGGTCTGGCACTGCTGAGCG**
8. **GCCTCGCTCAGCAGTGCCAGACCCTG**
9. **AGGCTGTACTGCGTGGCCAGGCA**
10. **GCAGTGCCTGGCCACGCAGTACA**
11. **CTGCTGGTAAACTCCTCTCAGCCGT**
12. **TTCCCACGGCTGAGAGGAGTTACCA**
13. **GGGAACCGCTGCAGCTGCATGTTGAC**
14. **GCTTTGTCAACATGCAGCTGCAGCGG**
15. **AAAGCAGTATCTGGCCTGAGATCTG**
16. **GATCCAGATCTCAGGCCAGATACT**

U.S. Patent

Aug. 20, 1996

Sheet 19 of 27

5,547,933

FIG. 13

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