Figure 1. Comparison of Codon-optimized (egfactor) and Native Genes for the Epidermal Growth Factor (EGF)

Sequence Range Egfactor: 4 to 165

```
                10          20          30          40          50
Egfactor    AAC TCC GAC TCG GAG TGC CCC CTC TCC CAC GAC GGT TAC TGC CTC CAC GAC GGG
             N   S   D   S   E   C   P   L   S   H   D   G   Y   C   L   H   D   G>

                        3360        3370        3380        3390        3400
Native Gene AAT GGT GAC TCT GAA TGT CCC CTG TCC CAC GAT GGG TAC TGC CTC CAT GAT GGT
            ||      ||| ||  ||  ||  ||| ||  ||| ||| ||  ||  ||| ||| ||| ||  ||  ||
Egfactor    AAC TCC GAC TCG GAG TGC CCC CTC TCC CAC GAC GGT TAC TGC CTC CAC GAC GGG

            60          70          80          90          100         110
Egfactor    GTC TGC ATG TAC ATC GAG GCC CTC GAC AAG TAC GCC TGC AAC TGC GTC GTG GGC
             V   C   M   Y   I   E   A   L   D   K   Y   A   C   N   C   V   V   G>

                    3410        3420        3430        3440        3450
Native Gene GTG TGC ATG TAT ATT GAA GCA TTG GAC AAG TAT GCA TGC AAC TGT GTT GTT GGC
            ||  ||| ||| ||  ||  ||  ||  |   ||| ||| ||  ||  ||| ||| ||  ||  ||  |||
Egfactor    GTC TGC ATG TAC ATC GAG GCC CTC GAC AAG TAC GCC TGC AAC TGC GTC GTG GGC

                120         130         140         150         160
Egfactor    TAC ATC GGC GAG CGG TGC CAG TAC CGC GAC CTC AAG TGG TGG GAG CTG CGC TGA
             Y   I   G   E   R   C   Q   Y   R   D   L   K   W   W   E   L   R   *>

              3460        3470        3480        3490        3500
Native Gene TAC ATC GGG GAG CGA TGT CAG TAC CGA GAC CTG AAG TGG TGG GAA CTG CGC
            ||| ||| ||  ||| ||  ||  ||| ||| ||  ||| ||  ||| ||| ||| ||  ||| |||
Egfactor    TAC ATC GGC GAG CGG TGC CAG TAC CGC GAC CTC AAG TGG TGG GAG CTG CGC TGA
```

Epidermal Growth Factor

Number of codons in mature peptide:	53
Number of codons changed:	27 (51%)
Number of nucleotides changed:	30 (19%)

Figure 2. Plasmid map of pAPI303 containing a chimeric gene for expressing human EGF under the control of the rice glutelin promoter in transgenic rice seeds.

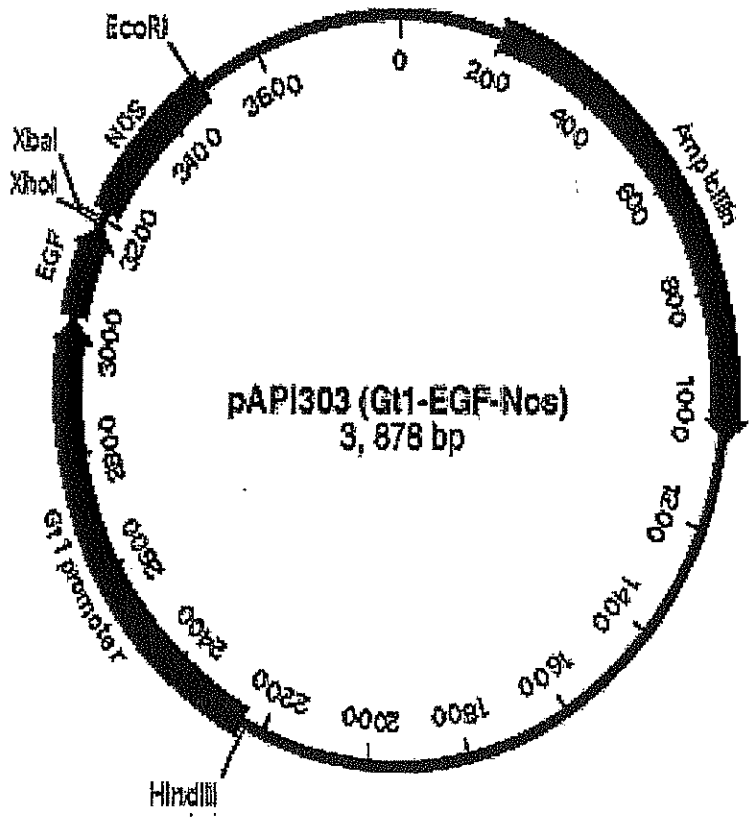


Figure 3. Plasmid map of pAPI270 containing a chimeric gene for expressing human EGF under the control of the rice globulin promoter in transgenic rice seeds.

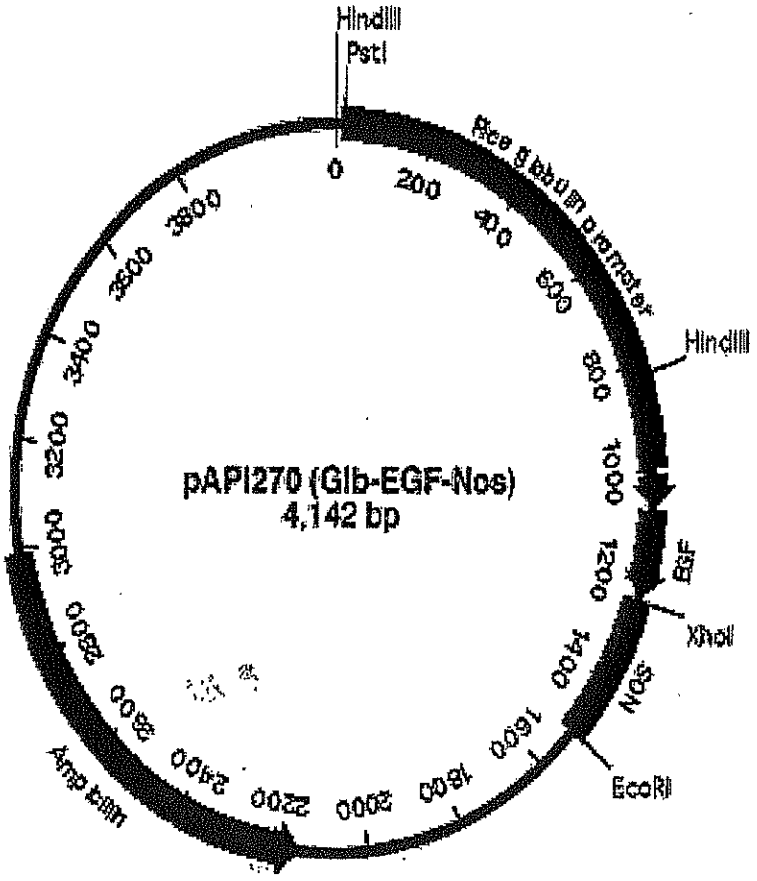


Figure 4. Western blot analysis of recombinant human epidermal growth factor (EGF) expressed in transgenic rice seeds.

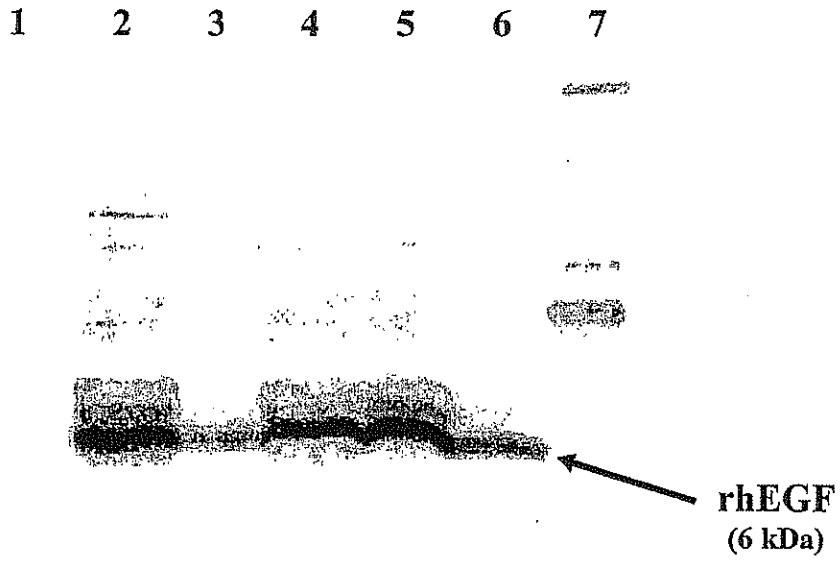


Figure 5. Comparison of Codon-optimized (Insgfact) and Native Genes for the Insulin-like Growth Factor (IGF)

Sequence Range of Insgfact: 4 to 216

```
          10         20         30         40         50         60         70
Insgfact  GGC CCA GAG ACC CTG TGC GGT GCG GAG CTG GTG GAC GCC CTC CAG TTC GTC TGC GGG GAC CGG GGC TTC TAC TTC
           G   P   E   T   L   C   G   A   E   L   V   D   A   L   Q   F   V   C   G   D   R   G   F   Y   F>

                320        330        340        350        360        370        380
native gene GGA CCG GAG ACG CTC TGC GGG GCT GAG CTG GTG GAT GCT CTT CAG TTC GTG TGT GGA GAC AGG GGC TTT TAT TTC>
            ||  ||  |||  ||  ||  |||  ||  ||  |||  |||  |||  ||  ||  ||  |||  |||  ||  ||  ||  |||  ||  |||  ||  ||  |||
Insgfact    GGC CCA GAG ACC CTG TGC GGT GCG GAG CTG GTG GAC GCC CTC CAG TTC GTC TGC GGG GAC CGG GGC TTC TAC TTC

          80         90         100        110        120        130        140        150
Insgfact  AAC AAG CCA ACG GGC TAC GGG TCC TCC TCG CGC CGC GCC CCC CAG ACC GGC ATC GTG GAC GAG TGC TGC TTC CGC
           N   K   P   T   G   Y   G   S   S   S   R   R   A   P   Q   T   G   I   V   D   E   C   C   F   R>

            390        400        410        420        430        440        450        460
native gene AAC AAG CCC ACA GGG TAT GGC TCC AGC AGT CGG AGG GCG CCT CAG ACA GGC ATC GTG GAT GAG TGC TGC TTC CGG>
            |||  |||  ||  ||  ||  ||  ||  |||  |   |   ||  |   ||  ||  |||  ||  |||  |||  |||  ||  |||  |||  |||  |||  ||
Insgfact    AAC AAG CCA ACG GGC TAC GGG TCC TCC TCG CGC CGC GCC CCC CAG ACC GGC ATC GTG GAC GAG TGC TGC TTC CGC

          160        170        180        190        200        210
Insgfact  TCC TGC GAC CTC CGG CGG CTG GAG ATG TAC TGC GCC CCA CTC AAG CCC GCC AAG AGC GCC TGA
           S   C   D   L   R   R   L   E   M   Y   C   A   P   L   K   P   A   K   S   A   *>

                470        480        490        500        510        520
native gene AGC TGT GAT CTA AGG AGG CTG GAG ATG TAT TGC GCA CCC CTC AAG CCT GCC AAG TCA GCT>
             |  ||  ||  ||  ||  ||  |||  |||  |||  ||  |||  ||  ||  |||  |||  ||  |||  |||      ||
Insgfact     TCC TGC GAC CTC CGG CGG CTG GAG ATG TAC TGC GCC CCA CTC AAG CCC GCC AAG AGC GCC
```

Insulin-like Growth Factor

Number of codons in mature peptide: 70
Number of codons changed: 40 (57%)
Number of nucleotides changed: 47 (22%)

Figure 6. Plasmid map of pAPI271 containing a chimeric gene for expressing human IGF-1 under the control of the rice globulin promoter in transgenic rice seeds.

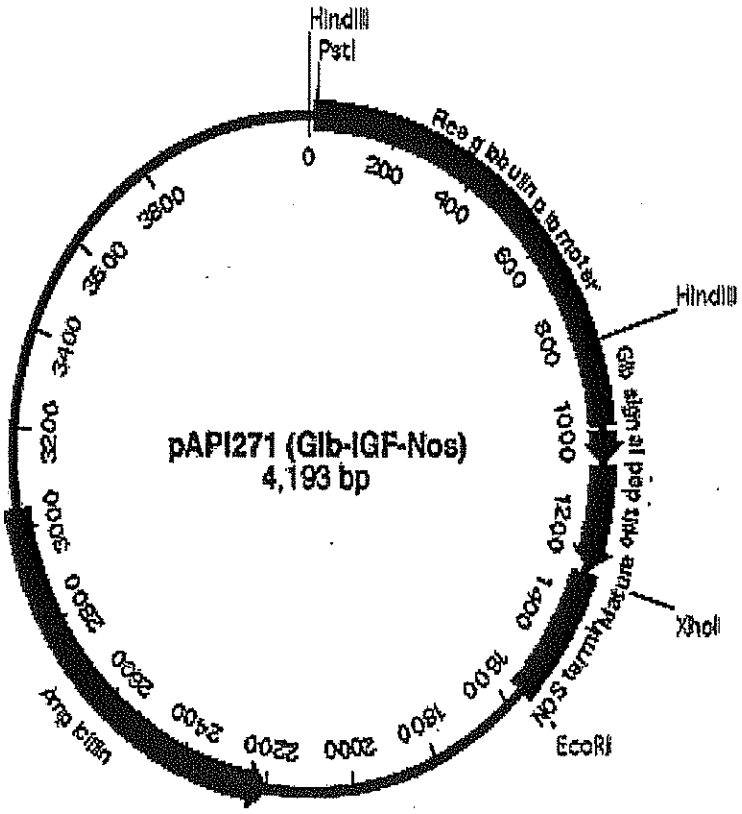


Figure 7. Plasmid map of pAPI304 containing a chimeric gene for expressing human IGF-1 under the control of the rice glutelin promoter in transgenic rice seeds.

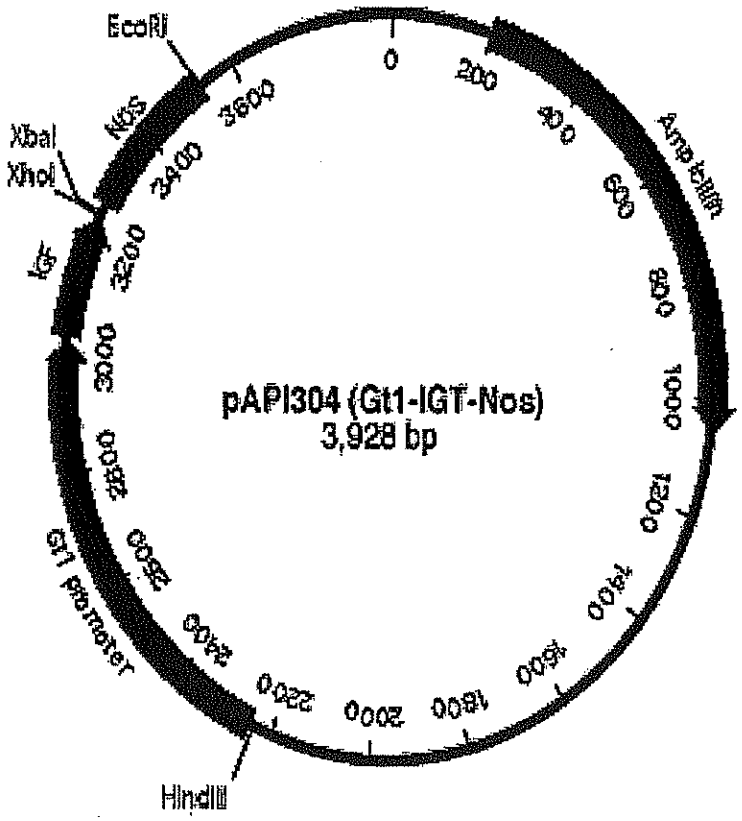


Figure 8. Western blot analysis of recombinant human insulin-like growth factor (IGF-1) expressed in transgenic rice seeds.

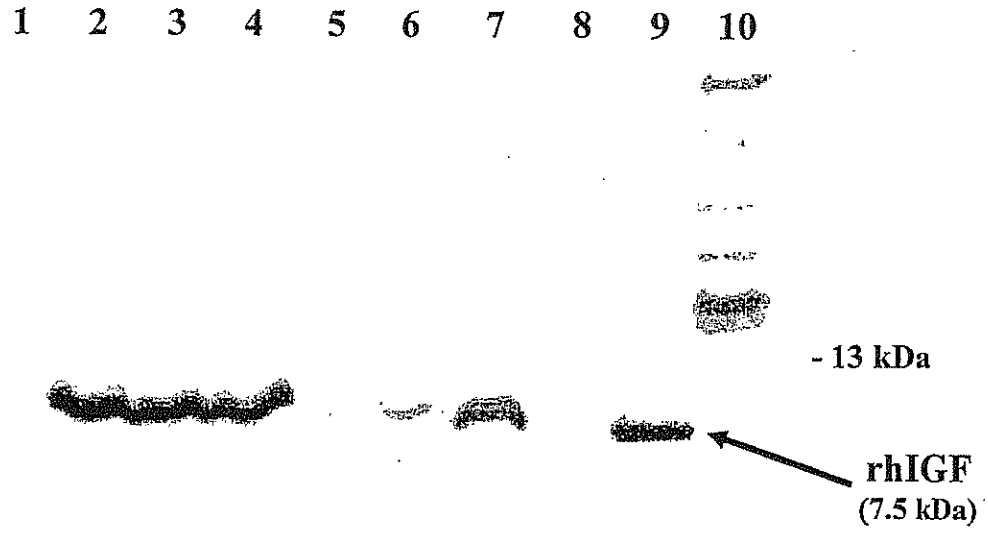


Figure 9. Comparison of Codon-optimized (Trefoil) and Native Genes for the Human Trefoil Peptide

Sequence Range of Trefoil: 6 to 188

```
                10          20          30          40          50          60          70          80
Trefoil     GAG GAG TAC GTC GGG CTC TCC GCT AAC CAA TGC GCG GTC CCG GCC AAG GAC CGG GTG GAC TGC GGC TAC CCC CAC
             E   E   Y   V   G   L   S   A   N   Q   C   A   V   P   A   K   D   R   V   D   C   G   Y   P   H>

                50          60          70          80          90          100         110
nativegene  GAG GAG TAC GTG GGC CTG TCT GCA AAC CAG TGT GCC GTG CCG GCC AAG GAC AGG GTG GAC TGC GGC TAC CCC CAT>
            ||| ||| ||| ||  ||  ||  ||  ||  ||| ||  ||  ||  ||  ||| ||| ||| |||  ||  ||| ||| ||| ||| ||| ||| ||
Trefoil     GAG GAG TAC GTC GGG CTC TCC GCT AAC CAA TGC GCG GTC CCG GCC AAG GAC CGG GTG GAC TGC GGC TAC CCC CAC

                90          100         110         120         130         140         150
Trefoil     GTG ACG CCG AAG GAG TGC AAC AAC CGG GGC TGC TGC TTC GAC TCC CGC ATC CCA GGC GTG CCG TGG TGC TTC AAG
             V   T   P   K   E   C   N   N   R   G   C   C   F   D   S   R   I   P   G   V   P   W   C   F   K>

            120         130         140         150         160         170         180         190
nativegene  GTC ACC CCC AAG GAG TGC AAC AAC CGG GGC TGC TGC TTT GAC TCC AGG ATC CCT GGA GTG CCT TGG TGT TTC AAG>
            ||  ||  ||  ||| ||| ||| ||| ||| ||| ||| ||| ||  ||| ||| |  ||| ||  ||  ||| ||  ||| ||  ||| |||
Trefoil     GTG ACG CCG AAG GAG TGC AAC AAC CGG GGC TGC TGC TTC GAC TCC CGC ATC CCA GGC GTG CCG TGG TGC TTC AAG

                160         170         180
Trefoil     CCC CTC ACC CGC AAG ACG GAG TGC ACG TTC TGA
             P   L   T   R   K   T   E   C   T   F   *>

                200         210         220
nativegene  CCC CTG ACT AGG AAG ACA GAA TGC ACC TTC TGA>
            ||| ||  ||  |  ||| ||  ||  ||| ||  ||| |||
Trefoil     CCC CTC ACC CGC AAG ACG GAG TGC ACG TTC TGA
```

Human Trefoil Peptide

Number of codons in mature peptide: 60
Number of codons changed: 26 (43%)
Number of nucleotides changed: 28 (15%)

Figure 10. Plasmid map of pAPI269 containing a chimeric gene for expressing human ITF under the control of the rice globulin promoter in transgenic rice seeds.

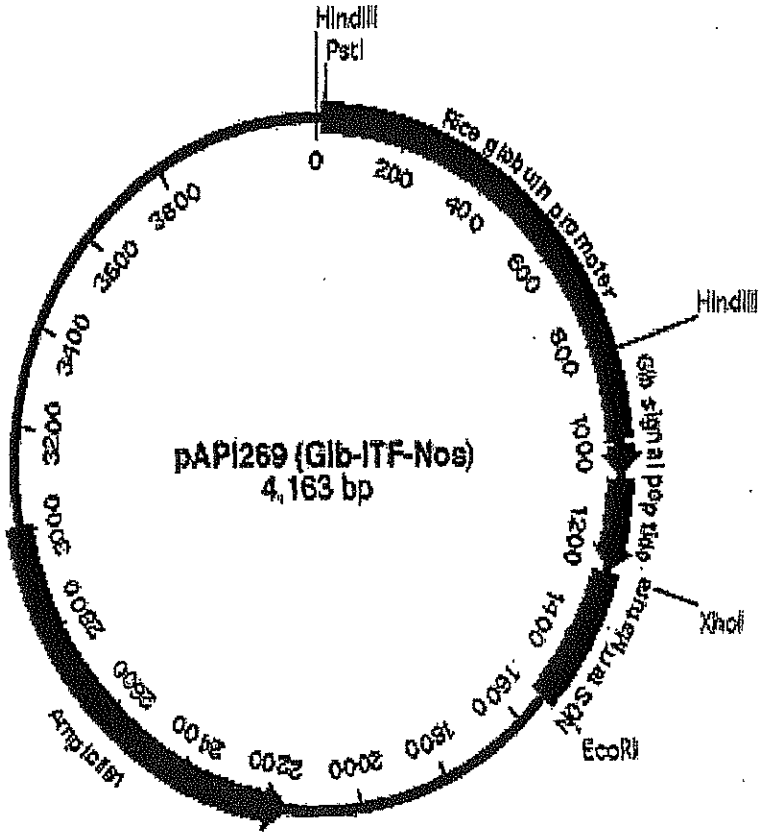


Figure 11. Plasmid map of pAPI307 containing a chimeric gene for expressing human ITF under the control of the rice glutelin promoter in transgenic rice seeds.

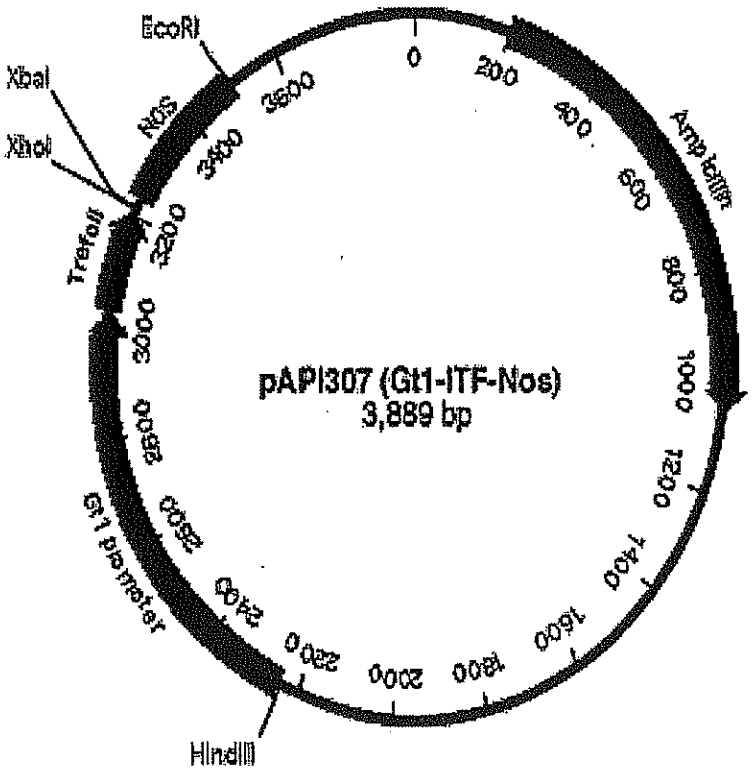


Figure 12. Western blot analysis of recombinant human intestinal trefoil factor (ITF) expressed in transgenic rice seeds.

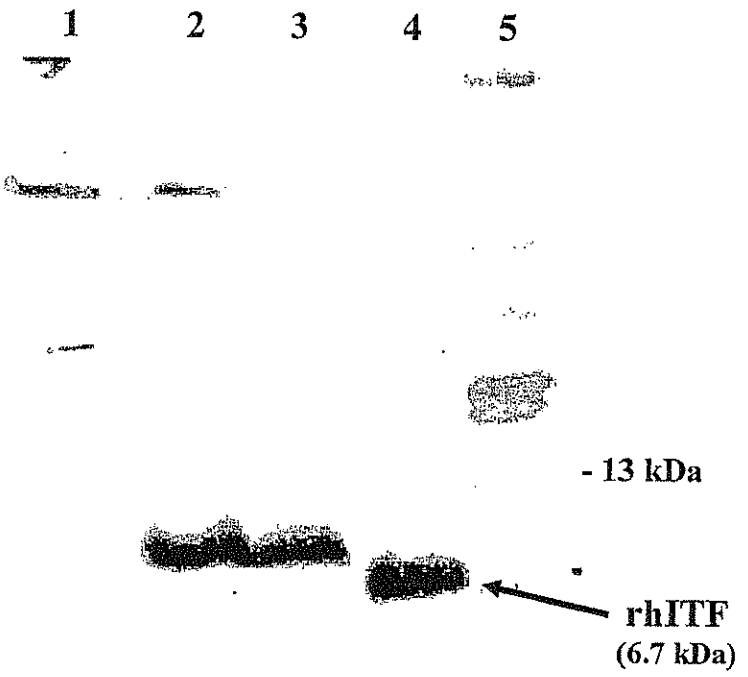
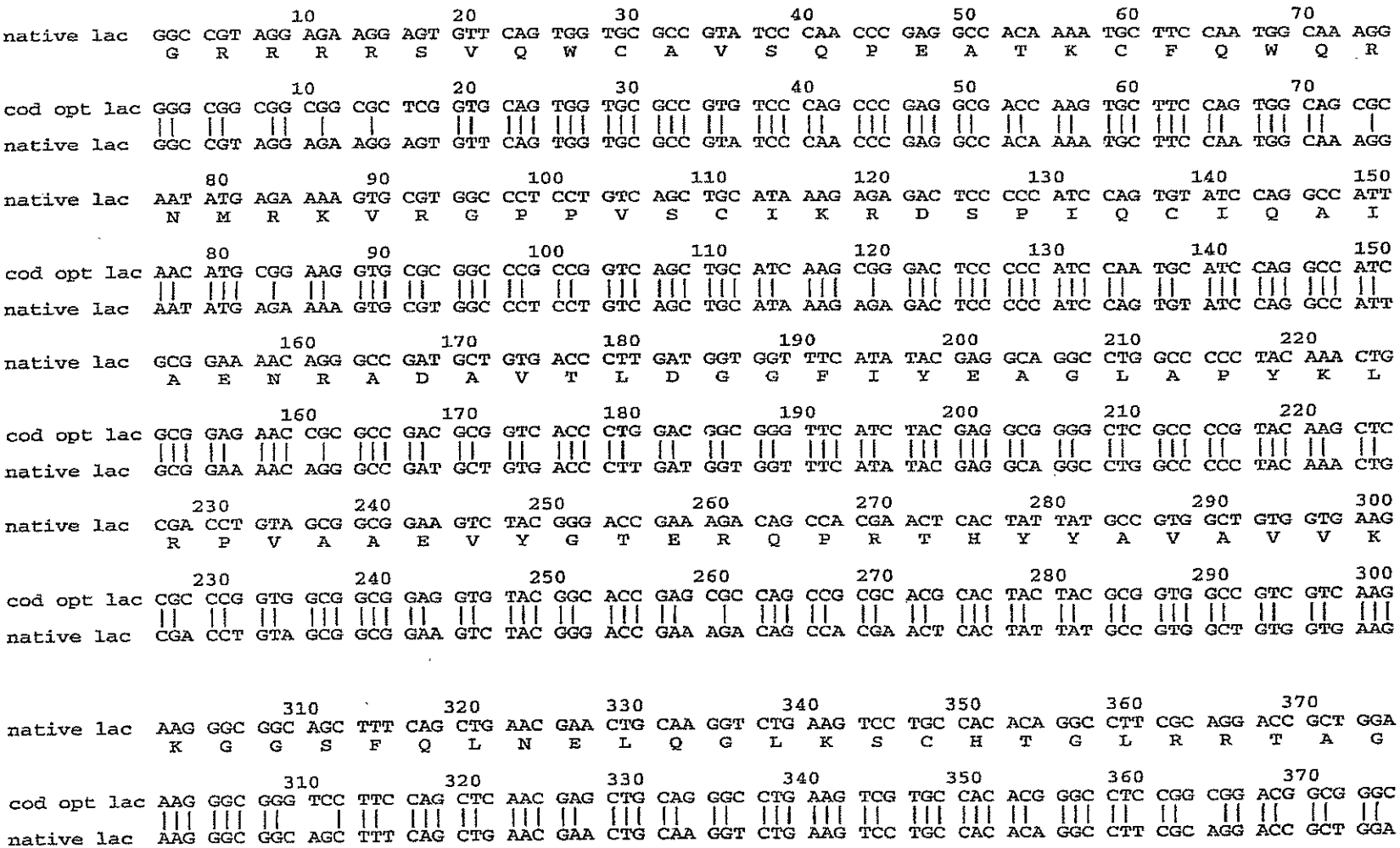
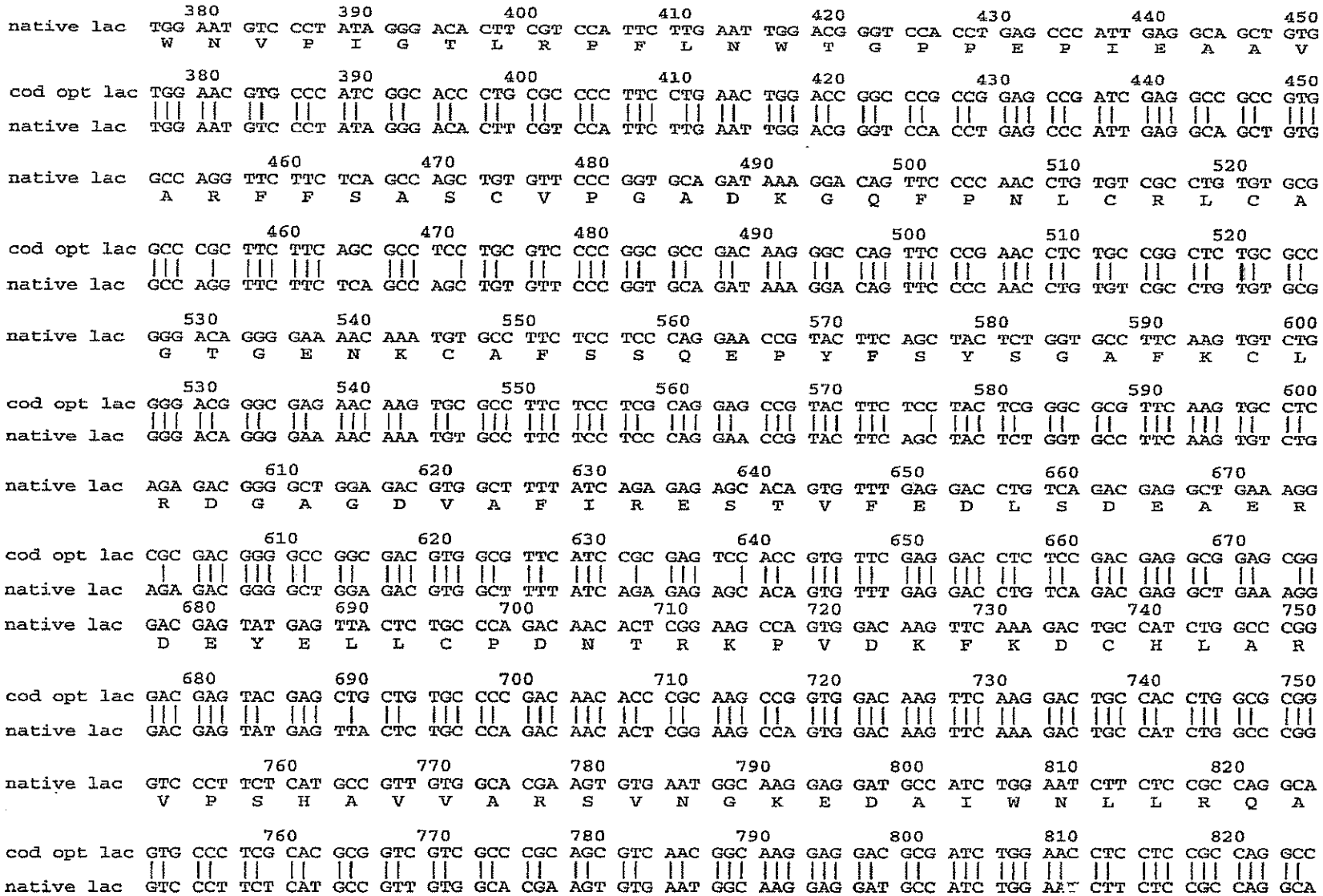
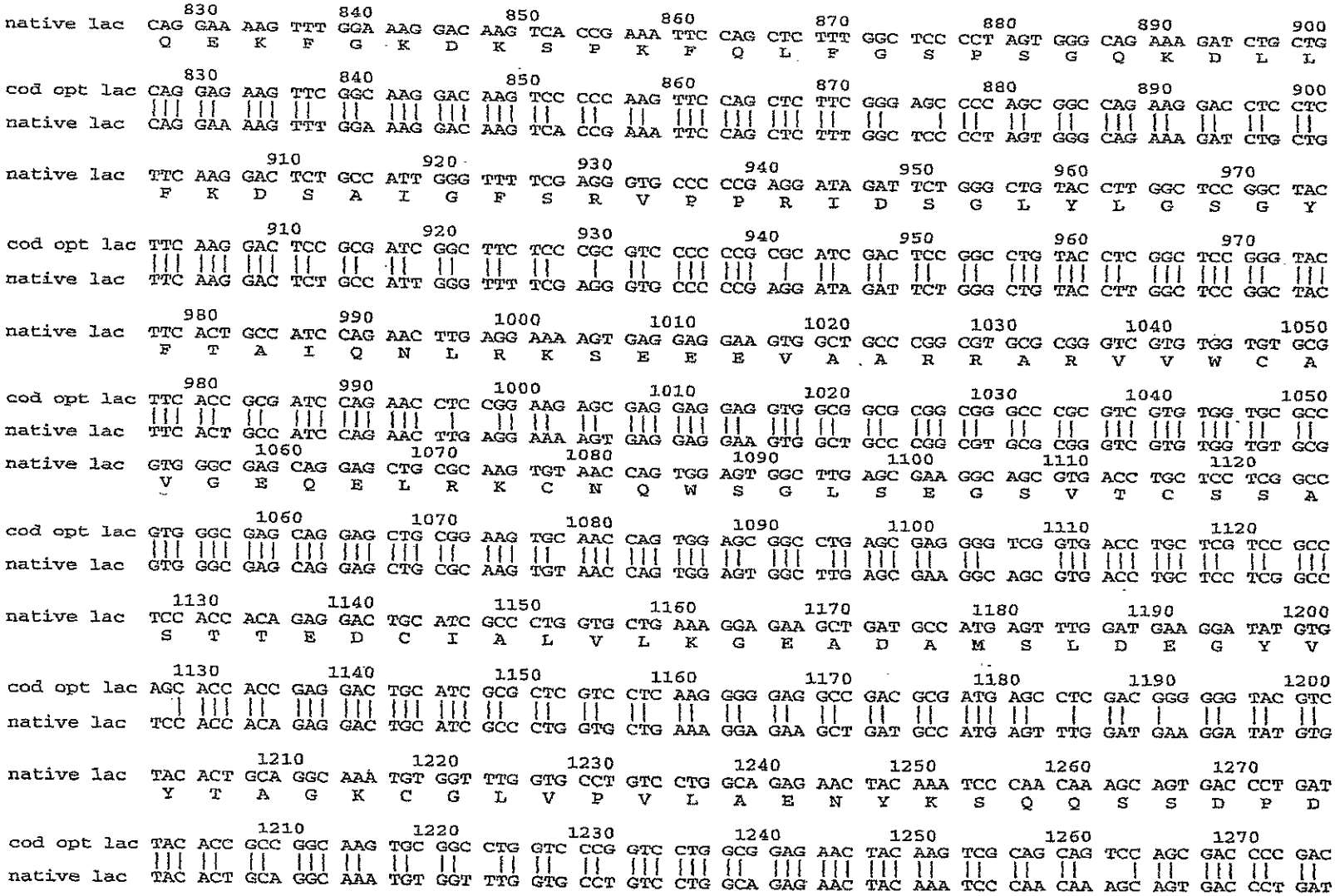
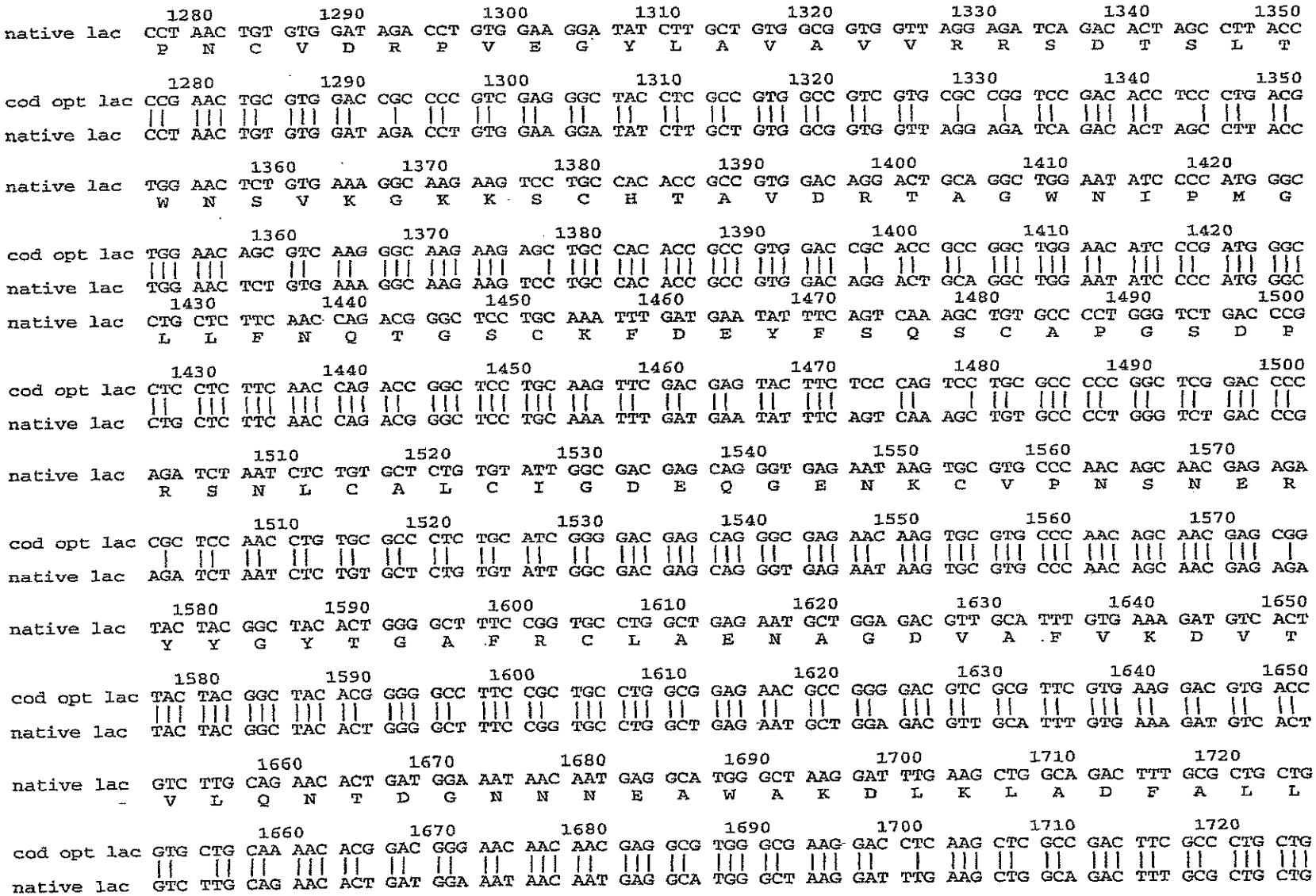


Figure 13. Codon-optimized Human Lactoferrin Gene and its Alignment to its Native Form




native lac
cod opt lac


native lac
cod opt lac
native lac
cod opt lac
native lac
native lac
cod opt lac
native lac
native lac
cod opt lac
native lac
native lac
cod opt lac
native lac


1280 1290 1300 1310 1320 1330 1340 1350
native lac CCT AAC TGT GTG GAT AGA CCT GTG GAA GGA TAT CTT GCT GTG GCG GTG GTT AGG AGA TCA GAC ACT AGC CTT ACC
P N C V D R P V E G Y L A V A V V R R S D T S L T
1280 1290 1300 1310 1320 1330 1340 1350
cod opt lac CCG AAC TGC GTG GAC CGC CCC GTC GAG GGC TAC CTC GCC GTG GCC GTC GTG CGC CGG TCC GAC ACC TCC CTG ACG
native lac CCT AAC TGT GTG GAT AGA CCT GTG GAA GGA TAT CTT GCT GTG GCG GTG GTT AGG AGA TCA GAC ACT AGC CTT ACC
1360 1370 1380 1390 1400 1410 1420
native lac TGG AAC TCT GTG AAA GGC AAG AAG TCC TGC CAC ACC GCC GTG GAC AGG ACT GCA GGC TGG AAT ATC CCC ATG GGC
W N S V K G K K S C H T A V D R T A G W N I P M G
1360 1370 1380 1390 1400 1410 1420
cod opt lac TGG AAC AGC GTC AAG GGC AAG AAG AGC TGC CAC ACC GCC GTG GAC CGC ACC GCC GGC TGG AAC ATC CCG ATG GGC
native lac TGG AAC TCT GTG AAA GGC AAG AAG TCC TGC CAC ACC GCC GTG GAC AGG ACT GCA GGC TGG AAT ATC CCC ATG GGC
1430 1440 1450 1460 1470 1480 1490 1500
native lac CTG CTC TTC AAC CAG ACG GGC TCC TGC AAA TTT GAT GAA TAT TTC AGT CAA AGC TGT GCC CCT GGG TCT GAC CCG
L L F N Q T G S C K F D E Y F S Q S C A P G S D P
1430 1440 1450 1460 1470 1480 1490 1500
cod opt lac CTC CTC TTC AAC CAG ACC GGC TCC TGC AAG TTC GAC GAG TAC TTC TCC CAG TCC TGC GCC CCC GGC TCG GAC CCC
native lac CTG CTC TTC AAC CAG ACG GGC TCC TGC AAA TTT GAT GAA TAT TTC AGT CAA AGC TGT GCC CCT GGG TCT GAC CCG
1510 1520 1530 1540 1550 1560 1570
native lac AGA TCT AAT CTC TGT GCT CTG TGT ATT GGC GAC GAG CAG GGT GAG AAT AAG TGC GTG CCC AAC AGC AAC GAG AGA
R S N L C A L C I G D E Q G E N K C V P N S N E R
1510 1520 1530 1540 1550 1560 1570
cod opt lac CGC TCC AAC CTG TGC GCC CTC TGC ATC GGG GAC GAG CAG GGC GAG AAC AAG TGC GTG CCC AAC AGC AAC GAG CGG
native lac AGA TCT AAT CTC TGT GCT CTG TGT ATT GGC GAC GAG CAG GGT GAG AAT AAG TGC GTG CCC AAC AGC AAC GAG AGA
1580 1590 1600 1610 1620 1630 1640 1650
native lac TAC TAC GGC TAC ACT GGG GCT TTC CGG TGC CTG GCT GAG AAT GCT GGA GAC GTT GCA TTT GTG AAA GAT GTC ACT
Y Y G Y T G A F R C L A E N A G D V A F V K D V T
1580 1590 1600 1610 1620 1630 1640 1650
cod opt lac TAC TAC GGC TAC ACG GGG GCC TTC CGC TGC CTG GCG GAG AAC GCC GGG GAC GTC GCG TTC GTG AAG GAC GTG ACC
native lac TAC TAC GGC TAC ACT GGG GCT TTC CGG TGC CTG GCT GAG AAT GCT GGA GAC GTT GCA TTT GTG AAA GAT GTC ACT
1660 1670 1680 1690 1700 1710 1720
native lac GTC TTG CAG AAC ACT GAT GGA AAT AAC AAT GAG GCA TGG GCT AAG GAT TTG AAG CTG GCA GAC TTT GCG CTG CTG
V L Q N T D G N N N E A W A K D L K L A D F A L L
1660 1670 1680 1690 1700 1710 1720
cod opt lac GTG CTG CAA AAC ACG GAC GGG AAC AAC AAC GAG GCG TGG GCG AAG GAC CTC AAG CTC GCC GAC TTC GCC CTG CTG
native lac GTC TTG CAG AAC ACT GAT GGA AAT AAC AAT GAG GCA TGG GCT AAG GAT TTG AAG CTG GCA GAC TTT GCG CTG CTG

```
                1730        1740        1750        1760        1770        1780        1790        1800
native lac      TGC CTC GAT GGC AAA CGG AAG CCT GTG ACT GAG GCT AGA AGC TGC CAT CTT GCC ATG GCC CCG AAT CAT GCC GTG
                 C   L   D   G   K   R   K   P   V   T   E   A   R   S   C   H   L   A   M   A   P   N   H   A   V

                1730        1740        1750        1760        1770        1780        1790        1800
cod opt lac     TGC CTC GAC GGC AAG CGC AAG CCC GTC ACC GAG GCG CGG TCC TGC CAC CTG GCG ATG GCC CCC AAC CAC GCC GTC
                ||| ||| ||  ||| ||  ||  ||| ||  ||  ||  ||| ||  |   |   ||| ||| ||| ||  ||  ||  ||| ||  ||| ||
native lac      TGC CTC GAT GGC AAA CGG AAG CCT GTG ACT GAG GCT AGA AGC TGC CAT CTT GCC ATG GCC CCG AAT CAT GCC GTG
                                1810        1820        1830        1840        1850        1860        1870
native lac      GTG TCT CGG ATG GAT AAG GTG GAA CGC CTG AAA CAG GTG TTG CTC CAC CAA CAG GCT AAA TTT GGG AGA AAT GGA
                 V   S   R   M   D   K   V   E   R   L   K   Q   V   L   L   H   Q   Q   A   K   F   G   R   N   G

                        1810        1820        1830        1840        1850        1860        1870
cod opt lac     GTC TCC CGC ATG GAC AAG GTC GAG CGC CTC AAG CAG GTG CTC CTG CAC CAG CAG GCC AAG TTC GGC CGG AAC GGC
                ||  ||  ||  ||| ||  ||| ||  ||  ||| ||  ||  ||| ||| |   ||  ||| ||  ||| ||  ||  ||  ||  |   ||  ||
native lac      GTG TCT CGG ATG GAT AAG GTG GAA CGC CTG AAA CAG GTG TTG CTC CAC CAA CAG GCT AAA TTT GGG AGA AAT GGA

                1880        1890        1900        1910        1920        1930        1940        1950
native lac      TCT GAC TGC CCG GAC AAG TTT TGC TTA TTC CAG TCT GAA ACC AAA AAC CTT CTG TTC AAT GAC AAC ACT GAG TGT
                 S   D   C   P   D   K   F   C   L   F   Q   S   E   T   K   N   L   L   F   N   D   N   T   E   C

                1880        1890        1900        1910        1920        1930        1940        1950
cod opt lac     AGC GAC TGC CCG GAC AAG TTC TGC CTG TTC CAG TCG GAG ACC AAG AAC CTC CTC TTC AAC GAC AAC ACC GAG TGC
                    ||| ||| ||| ||| ||| ||  ||| |   ||| ||| ||  ||  ||| ||  ||| ||  ||| ||  ||| ||| ||  ||| ||
native lac      TCT GAC TGC CCG GAC AAG TTT TGC TTA TTC CAG TCT GAA ACC AAA AAC CTT CTG TTC AAT GAC AAC ACT GAG TGT

                        1960        1970        1980        1990        2000        2010        2020
native lac      CTG GCC AGA CTC CAT GGC AAA ACA ACA TAT GAA AAA TAT TTG GGA CCA CAG TAT GTC GCA GGC ATT ACT AAT CTG
                 L   A   R   L   H   G   K   T   T   Y   E   K   Y   L   G   P   Q   Y   V   A   G   I   T   N   L

                        1960        1970        1980        1990        2000        2010        2020
cod opt lac     CTG GCG CGC CTC CAC GGC AAG ACC ACC TAC GAG AAG TAC CTC GGC CCG CAG TAC GTC GCC GGC ATC ACC AAC CTC
                ||| ||  |   ||| ||  ||| ||  ||  ||  ||  ||  ||  |   ||  ||  ||| ||  ||| ||  ||| ||  ||  ||  ||
native lac      CTG GCC AGA CTC CAT GGC AAA ACA ACA TAT GAA AAA TAT TTG GGA CCA CAG TAT GTC GCA GGC ATT ACT AAT CTG

                        2030        2040        2050        2060        2070
native lac      AAA AAG TGC TCA ACC TCC CCC CTC CTG GAA GCC TGT GAA TTC CTC AGG AAG TAA
                 K   K   C   S   T   S   P   L   L   E   A   C   E   F   L   R   K

                        2030        2040        2050        2060        2070
cod opt lac     AAG AAG TGC TCC ACC TCC CCC CTC CTG GAG GCG TGC GAG TTC CTC CGC AAG TGA
                ||  ||| ||| ||  ||| ||| ||| ||| ||| ||  ||  ||  ||  ||| ||| |   ||| | |
native lac      AAA AAG TGC TCA ACC TCC CCC CTC CTG GAA GCC TGT GAA TTC CTC AGG AAG TAA
```

2079 = Total number of nucleotides

467 = Number of nucleotides changed

693 = Total Number of codons

413 = Number of codons changed

Figure 14: Plasmid map of pAPI164

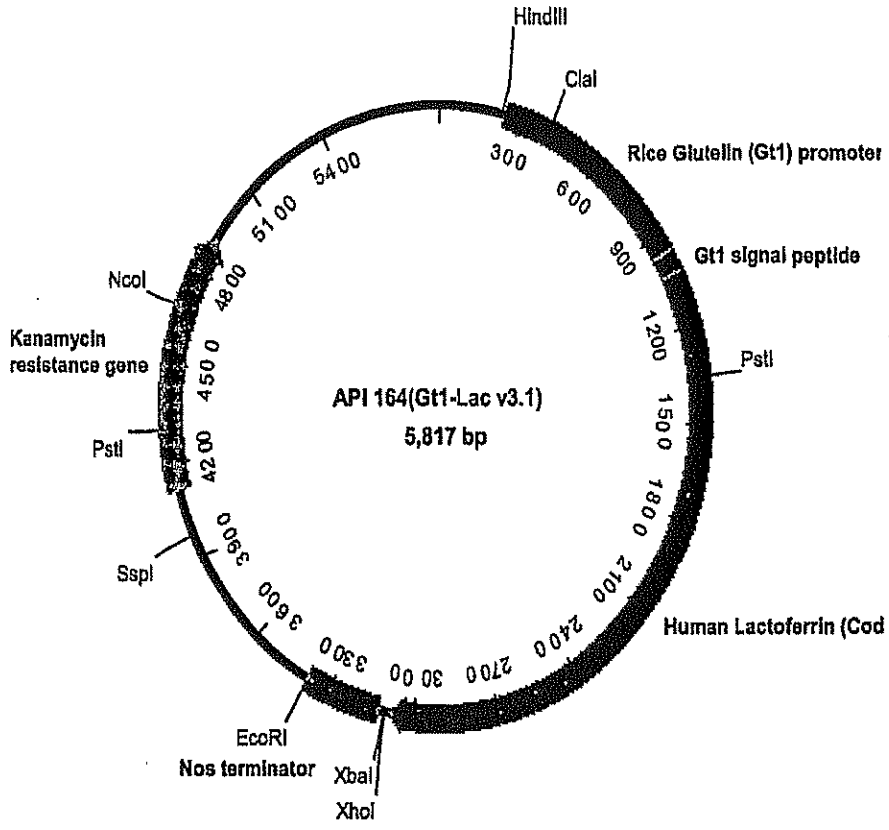


Figure 15: Recombinant human lactoferrin expressed in transgenic rice grains

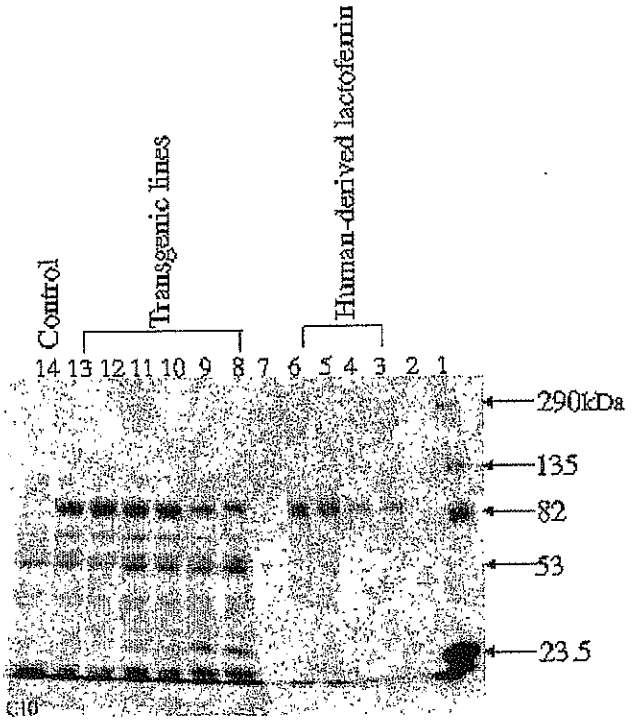


Figure 16. Stable expression of rhLF in transgenic rice grains from R_2 through R_{10} generations.

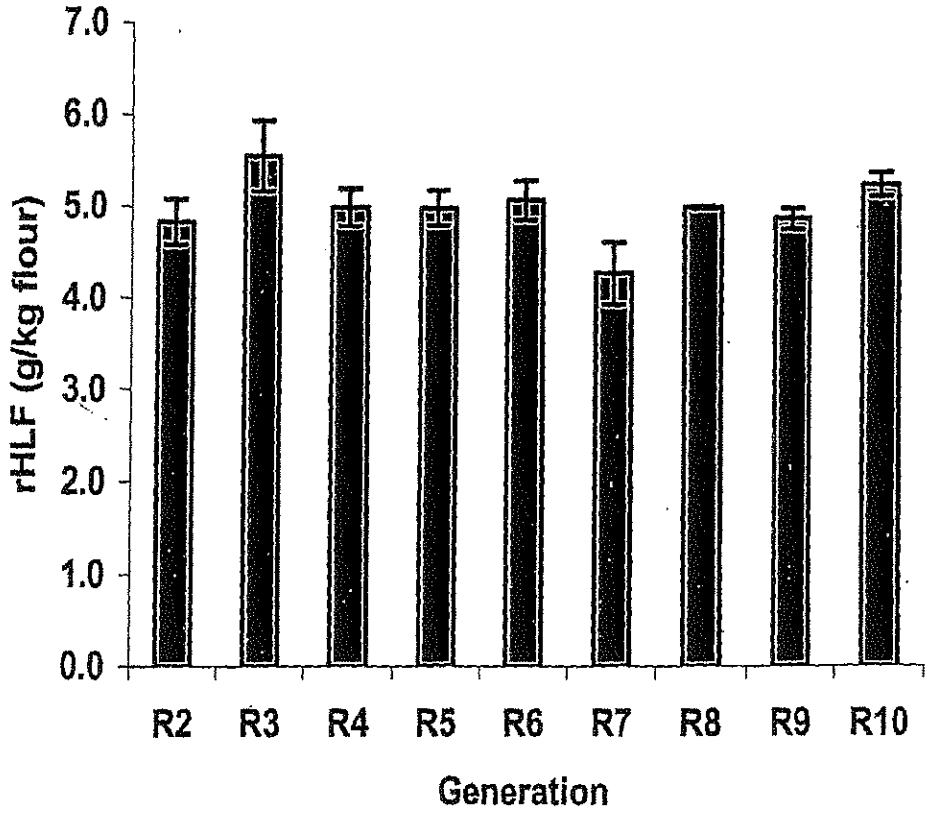


Figure 17 DNA and protein sequence of fusion between Gt1 signal peptide (Gt1 SP) and codon-optimized human serum albumin (OPTIMIZED HSA)

```
          10          20          30          40
ATG GCA TCC ATA AAT CGC CCC ATA GTT TTC TTC ACA GTT TGC TTG
 M   A   S   I   N   R   P   I   V   F   F   T   V   C   L>
___a___a___a___a___a___a__GT1 SP___a___a___a___a___a___a___>

    50          60          70          80          90
TTC CTC TTG TGC GAT GGC TCC CTA GCC GAC GCC CAC AAG AGC GAG
 F   L   L   C   D   G   S   L   A>
___a___a___a__GT1 SP___a___a___a___>
                                      D   A   H   K   S   E>
                                     ____OPTIMIZED HSA _b___>

         100         110         120         130
GTG GCC CAC CGC TTC AAG GAC CTC GGC GAG GAG AAC TTC AAG GCC
 V   A   H   R   F   K   D   L   G   E   E   N   F   K   A>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

   140         150         160         170         180
CTC GTG CTC ATC GCC TTC GCC CAG TAC CTC CAG CAG TGC CCG TTC
 L   V   L   I   A   F   A   Q   Y   L   Q   Q   C   P   F>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

         190         200         210         220
GAG GAC CAC GTG AAG CTC GTG AAC GAG GTG ACC GAG TTC GCC AAG
 E   D   H   V   K   L   V   N   E   V   T   E   F   A   K>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

   230         240         250         260         270
ACC TGC GTG GCC GAC GAG AGC GCC GAG AAC TGC GAC AAG AGC CTC
 T   C   V   A   D   E   S   A   E   N   C   D   K   S   L>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

         280         290         300         310
CAC ACC CTC TTC GGC GAC AAG CTC TGC ACC GTG GCC ACC CTC CGC
 H   T   L   F   G   D   K   L   C   T   V   A   T   L   R>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

   320         330         340         350         360
GAG ACC TAC GGC GAG ATG GCC GAC TGC TGC GCC AAG CAG GAG CCG
 E   T   Y   G   E   M   A   D   C   C   A   K   Q   E   P>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

         370         380         390         400
GAG CGC AAC GAG TGC TTC CTC CAG CAC AAG GAC GAC AAC CCG AAC
 E   R   N   E   C   F   L   Q   H   K   D   D   N   P   N>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

   410         420         430         440         450
CTC CCG CGC CTC GTG CGC CCG GAG GTG GAC GTG ATG TGC ACC GCC
 L   P   R   L   V   R   P   E   V   D   V   M   C   T   A>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>
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          460           470           480           490
TTC CAC GAC AAC GAG GAG ACC TTC CTC AAG AAG TAC CTC TAC GAG
 F   H   D   N   E   E   T   F   L   K   K   Y   L   Y   E>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

   500           510           520           530           540
ATC GCC CGC CGC CAC CCG TAC TTC TAC GCC CCG GAG CTC CTC TTC
 I   A   R   R   H   P   Y   F   Y   A   P   E   L   L   F>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

          550           560           570           580
TTC GCC AAG CGC TAC AAG GCC GCC TTC ACC GAG TGC TGC CAG GCC
 F   A   K   R   Y   K   A   A   F   T   E   C   C   Q   A>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

   590           600           610           620           630
GCC GAC AAG GCC GCC TGC CTC CTC CCG AAG CTC GAC GAG CTC CGC
 A   D   K   A   A   C   L   L   P   K   L   D   E   L   R>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

          640           650           660           670
GAC GAG GGC AAG GCC TCC AGC GCC AAG CAG CGC CTC AAG TGC GCC
 D   E   G   K   A   S   S   A   K   Q   R   L   K   C   A>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

   680           690           700           710           720
AGC CTC CAG AAG TTC GGC GAG CGC GCC TTC AAG GCC TGG GCC GTG
 S   L   Q   K   F   G   E   R   A   F   K   A   W   A   V>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

          730           740           750           760
GCC CGC CTC AGC CAG CGC TTC CCG AAG GCC GAG TTC GCC GAG GTG
 A   R   L   S   Q   R   F   P   K   A   E   F   A   E   V>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

   770           780           790           800           810
TCC AAG CTC GTG ACC GAC CTC ACC AAG GTG CAC ACC GAG TGC TGC
 S   K   L   V   T   D   L   T   K   V   H   T   E   C   C>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

          820           830           840           850
CAC GGC GAC CTC CTG GAG TGC GCC GAC GAC CGC GCC GAC CTC GCC
 H   G   D   L   L   E   C   A   D   D   R   A   D   L   A>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

   860           870           880           890           900
AAG TAC ATC TGC GAG AAC CAG GAC AGC ATC TCC AGC AAG CTC AAG
 K   Y   I   C   E   N   Q   D   S   I   S   S   K   L   K>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

          910           920           930           940
GAG TGC TGC GAG AAG CCG CTC CTG GAG AAG TCC CAC TGC ATC GCC
 E   C   C   E   K   P   L   L   E   K   S   H   C   I   A>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>
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   950          960          970          980          990
GAG GTG GAG AAC GAC GAG ATG CCG GCC GAC CTC CCG TCC CTC GCC
 E   V   E   N   D   E   M   P   A   D   L   P   S   L   A>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

         1000         1010         1020         1030
GCC GAC TTC GTG GAG AGC AAG GAC GTG TGC AAG AAC TAC GCC GAG
 A   D   F   V   E   S   K   D   V   C   K   N   Y   A   E>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

  1040         1050         1060         1070         1080
GCC AAG GAC GTC TTC CTC GGC ATG TTC CTC TAC GAG TAC GCC CGC
 A   K   D   V   F   L   G   M   F   L   Y   E   Y   A   R>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

         1090         1100         1110         1120
CGC CAC CCG GAC TAC TCC GTG GTG CTC CTC CTC CGC CTC GCC AAG
 R   H   P   D   Y   S   V   V   L   L   L   R   L   A   K>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

  1130         1140         1150         1160         1170
ACC TAC GAG ACC ACC CTG GAG AAG TGC TGC GCC GCC GCC GAC CCG
 T   Y   E   T   T   L   E   K   C   C   A   A   A   D   P>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

         1180         1190         1200         1210
CAC GAG TGC TAC GCC AAG GTG TTC GAC GAG TTC AAG CCG CTC GTG
 H   E   C   Y   A   K   V   F   D   E   F   K   P   L   V>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

  1220         1230         1240         1250         1260
GAG GAG CCG CAG AAC CTC ATC AAG CAG AAC TGC GAG CTC TTC GAG
 E   E   P   Q   N   L   I   K   Q   N   C   E   L   F   E>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

         1270         1280         1290         1300
CAG CTC GGC GAG TAC AAG TTC CAG AAC GCC CTC CTC GTG CGC TAC
 Q   L   G   E   Y   K   F   Q   N   A   L   L   V   R   Y>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

  1310         1320         1330         1340         1350
ACC AAG AAG GTG CCG CAG GTG TCC ACC CCG ACC CTC GTG GAG GTG
 T   K   K   V   P   Q   V   S   T   P   T   L   V   E   V>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

         1360         1370         1380         1390
TCC CGC AAC CTC GGC AAG GTG GGC AGC AAG TGC TGC AAG CAC CCG
 S   R   N   L   G   K   V   G   S   K   C   C   K   H   P>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

  1400         1410         1420         1430         1440
GAG GCC AAG CGC ATG CCG TGC GCC GAG GAC TAC CTC TCC GTG GTG
 E   A   K   R   M   P   C   A   E   D   Y   L   S   V   V>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>
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          1450         1460         1470         1480
CTC AAC CAG CTC TGC GTG CTC CAC GAG AAG ACC CCG GTG AGC GAC
 L   N   Q   L   C   V   L   H   E.  K   T   P   V   S   D>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

  1490         1500         1510         1520         1530
CGC GTG ACC AAG TGC TGC ACC GAG AGC CTC GTG AAC CGC CGC CCG
 R   V   T   K   C   C   T   E   S   L   V   N   R   R   P>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

          1540         1550         1560         1570
TGC TTC TCC GCC CTG GAG GTC GAC GAG ACC TAC GTC CCG AAG GAG
 C   F   S   A   L   E   V   D   E   T   Y   V   P   K   E>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

  1580         1590         1600         1610         1620
TTC AAC GCC GAG ACC TTC ACC TTC CAC GCC GAC ATC TGC ACC CTC
 F   N   A   E   T   F   T   F   H   A   D   I   C   T   L>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

          1630         1640         1650         1660
TCC GAG AAG GAG CGC CAG ATC AAG AAG CAG ACC GCC CTC GTC GAG
 S   E   K   E   R   Q   I   K   K   Q   T   A   L   V   E>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

  1670         1680         1690         1700         1710
CTC GTG AAG CAC AAG CCG AAG GCC ACC AAG GAG CAG CTC AAG GCC
 L   V   K   H   K   P   K   A   T   K   E   Q   L   K   A>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

          1720         1730         1740         1750
GTG ATG GAC GAC TTC GCC GCC TTC GTG GAG AAG TGC TGC AAG GCC
 V   M   D   D   F   A   A   F   V   E   K   C   C   K   A>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

  1760         1770         1780         1790         1800
GAC GAC AAG GAG ACC TGC TTC GCC GAG GAG GGC AAG AAG CTC GTG
 D   D   K   E   T   C   F   A   E   E   G   K   K   L   V>
___b___b___b___b___b__OPTIMIZED HSA ___b___b___b___b___b___>

          1810         1820         1830
GCC GCC AGC CAG GCC GCC CTC GGC CTC TGA
 A   A   S   Q   A   A   L   G   L   *>
___b___b____OPTIMIZED HSA _b___b___b___>
```

Figure 18. Plasmid map of pAPI504

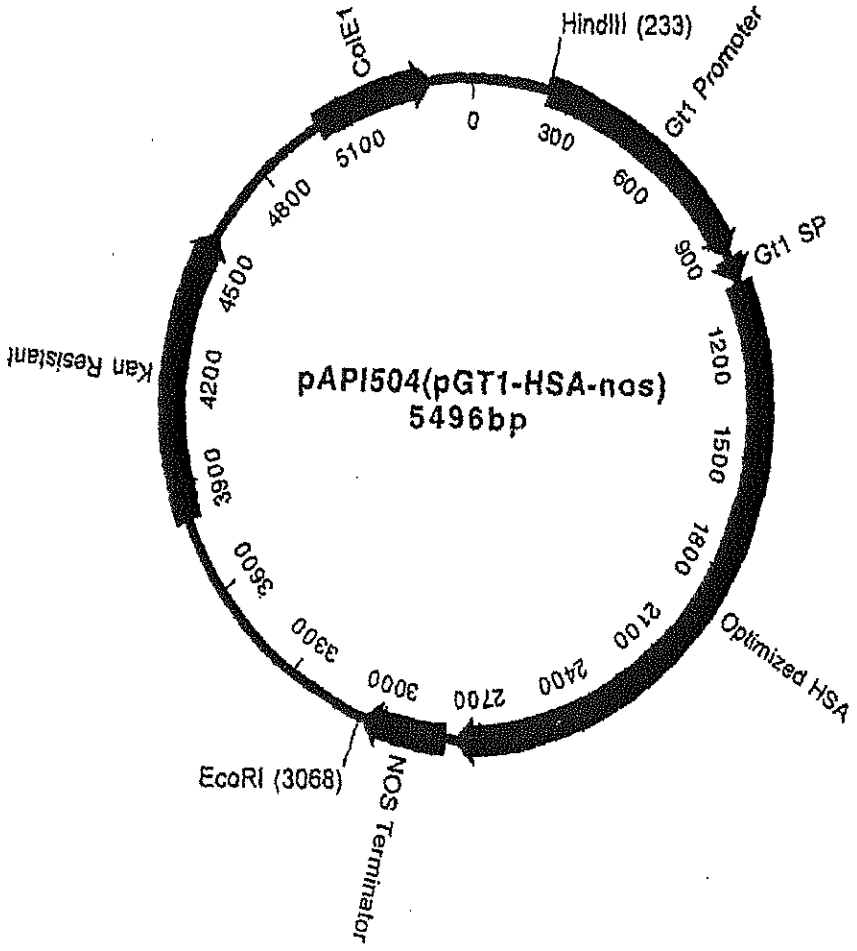


Figure 19. Plasmid map of pAPI508

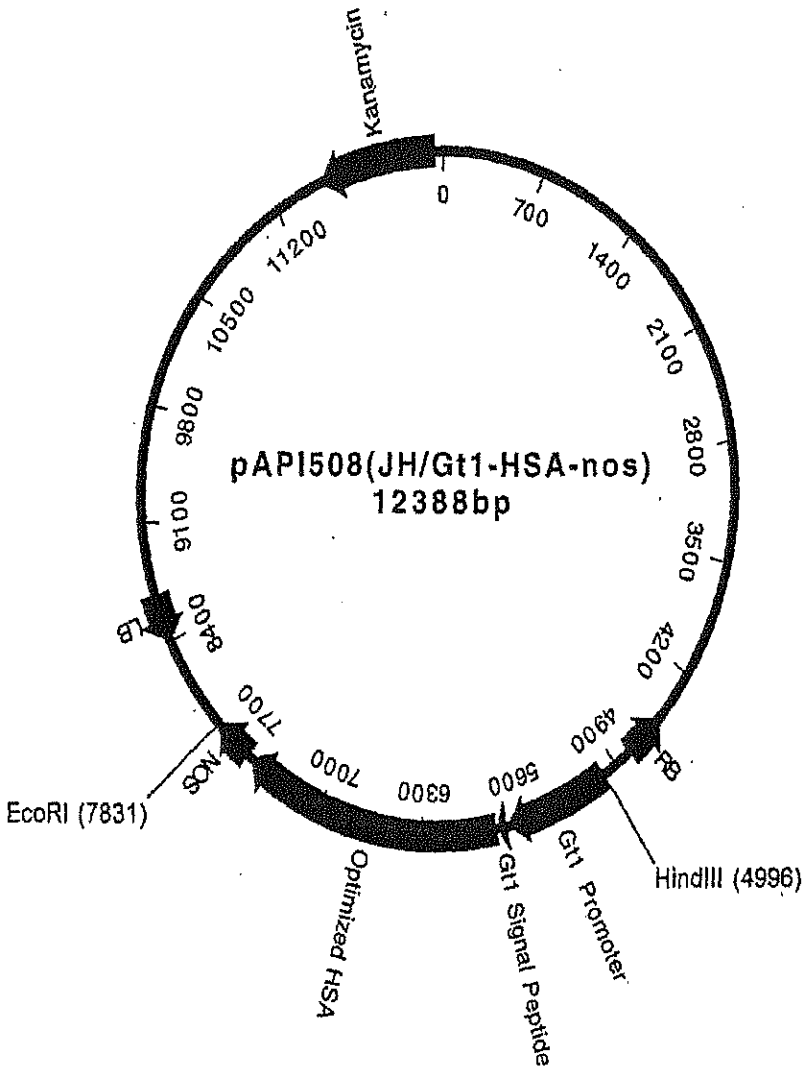


Figure 20 Impact of recombinant human lactoferrin on DNA replication of HT29 cells

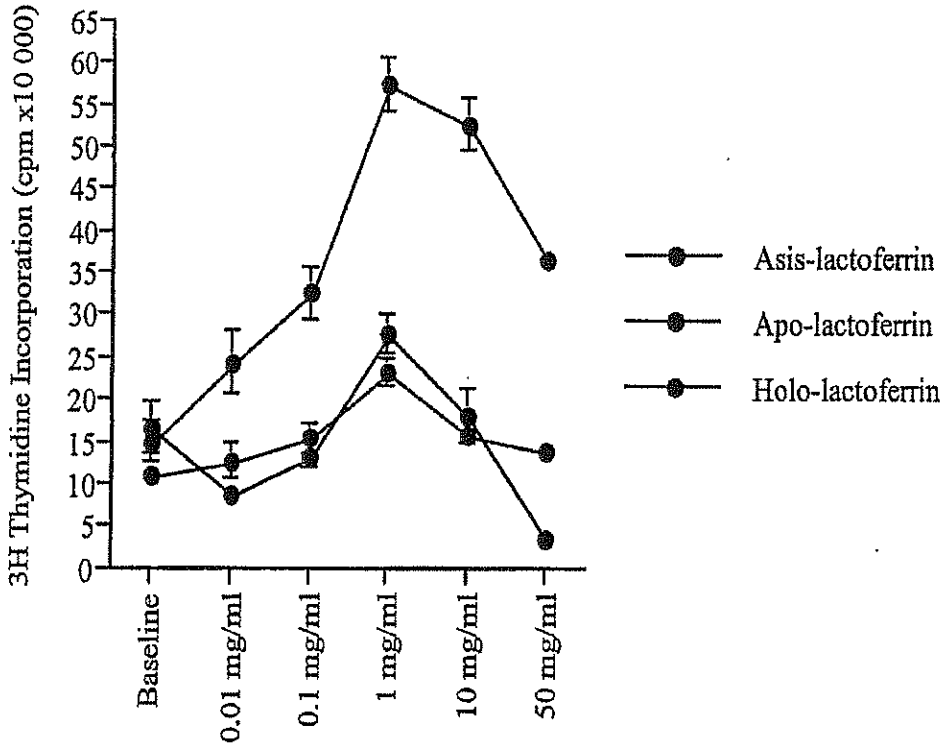


Figure 21. Cell culture media supplemented with recombinant human lactoferrin expressed in rice grain promotes cell growth and increases the cell number.

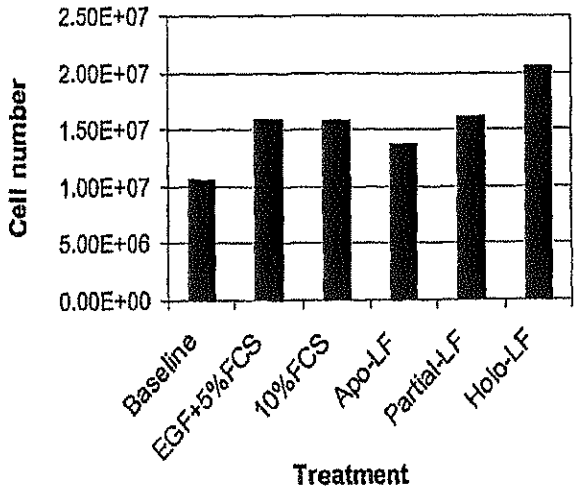


Figure 22. Cell culture media supplemented with recombinant human lactoferrin (Lacromin™) expressed in rice grain promotes hybridoma cell growth and increases hybridoma cell number.

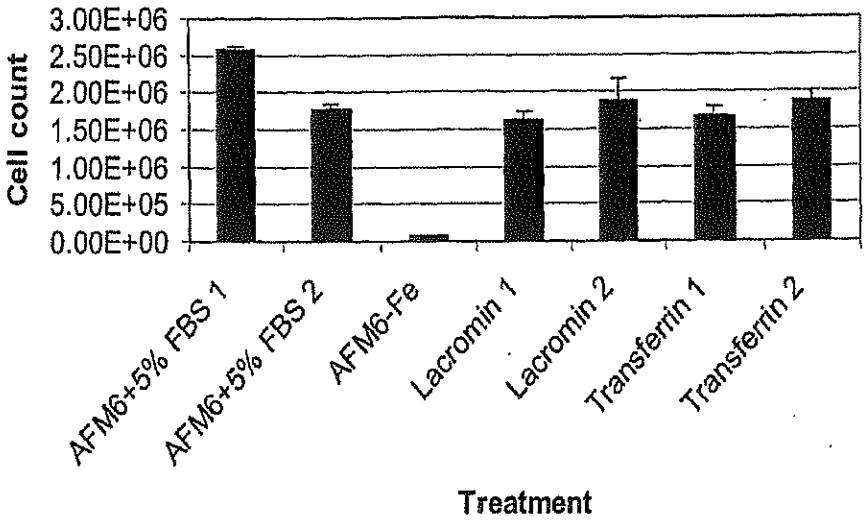


Figure 23 Effect of recombinant human serum albumin (rHSA) and plasma-derived human serum albumin (pHSA) on the growth of hybridoma AE1 cells in common medium (DMEM containing reduced 1% FBS) (CM). Cells were gradually adapted to CM with either 1)pHSA 2)nHSA or 3) no HSA and maintained for 10 passages to obtain a stable phenotype. On the 10^{th} passage cells were seeded at $1x10^5$ cell/ml on day 0 and cell numbers were counted daily for four days.

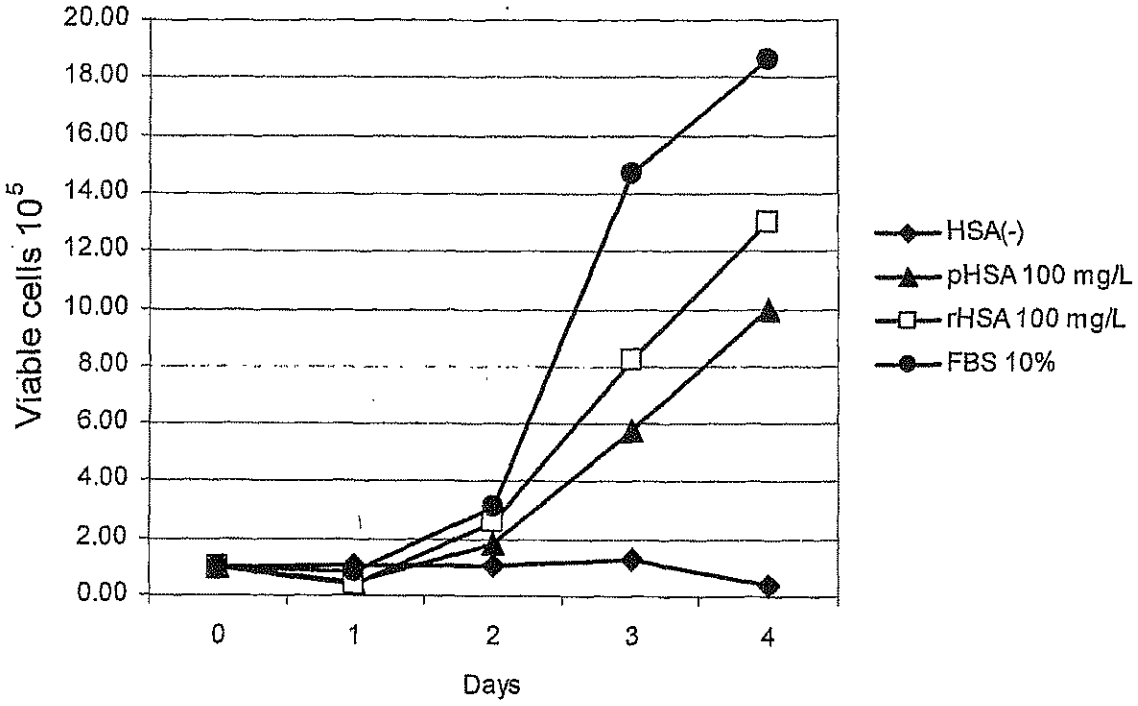


Figure 24. Effect of recombinant human serum albumin (rHSA) and plasma-derived human serum albumin (pHSA) on the growth of hybridoma AE1 cells in DMEM/F12 serum-free medium (SFM). Cells were gradually adapted to SFM with either 1) pHSA 2)rHSA or 3) no HSA and maintained for 6 passages to obtain a stable phenotype. On the 7th passage cells were seeded at 1x10^{5} cell/ml on day 0 and viable cell numbers were counted daily for 5 days.

