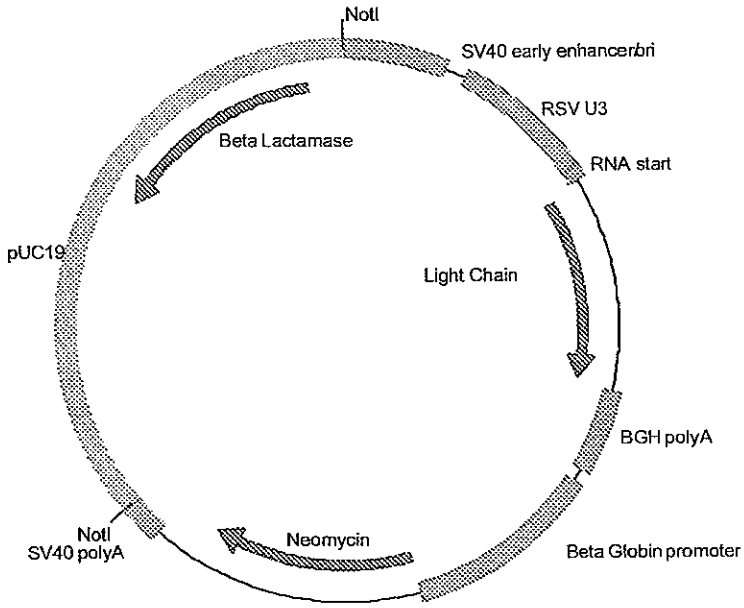
Figures

Figure 1.



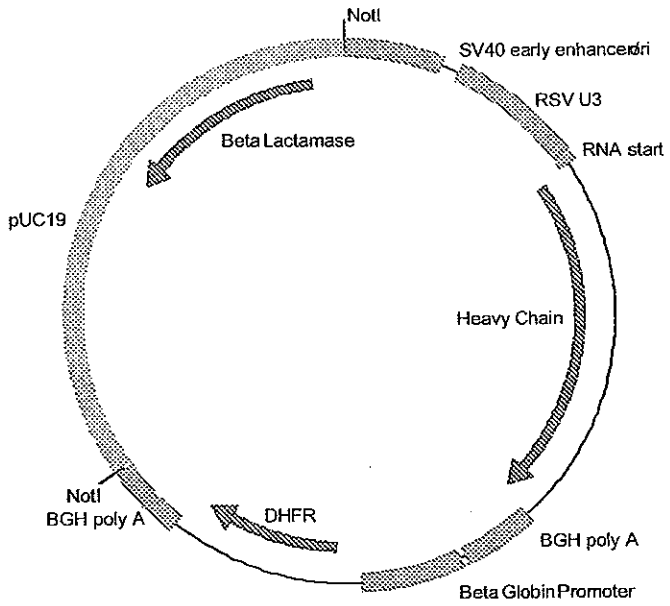


Figure 2.

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CGTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGT
AATTTGGCATATAGTATCGACTACGCAGACACTGTGACGGGCCGATTCACCATC
TCCAGAGACAATGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCC
GAGGACACGGCTGTGTATTACTGTGTCAGCGGGACCTGGTTTGCTTACTGGGG
CCAGGGCACACTAGTCACAGTCTCCTCAGCCTCCACCAAGGGCCCATCGGTCT
TCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGG
CTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAG
GCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGA
CTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCA
GACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGA
AAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCAC
CTGAACTCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGAC
ACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAG
CCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGC
ATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTG
GTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAA
GTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAA
AGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGG
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TCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAAC
TACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGC
AAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC
CGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGT
CTCCGGGTAAA

Figure 3.

ATGAGGCTCCCTGCTCAGCTCCTGGGGCTGCTAATGCTCTGGGTCTCTGGATC
CAGTGGGGATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGG
AGAGCCGGCCTCCATCTCCTGCAGAGTTAGTCAGAGCCTTTTACACAGTAATGG
ATACACCTATTTACATTGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT
GATCTATAAAGTTTCCAACCGATTTTCTGGGGTCCCTGACAGGTTCAGTGGCAG
TGGATCAGGCACAGATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGT
TGGGGTTTATTACTGCTCTCAAACTAGACATGTTCCGTACACGTTCGGCGGAGG
GACCAAGGTGGAAATCAAACGTACGGTGGCTGCACCATCTGTCTTCATCTTCCC
GCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAA
TAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGACAACGCCCTCC
AATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACC
TACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAA
AGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGA
GCTTCAACAGGGGAGAGTGT

Figure 4.

ATGGAGCTCGGGCTGTGCTGGGTGTTCCTCGTGGCCATCCTGGAGGGAGTGCA
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CAGCCTGCGGCTGTCGTGCGCCGTGAGCGGCTTCACCTTCAGTGACAACGGCA
TGGCTTGGGTCAGGCAGGCCCCCGGAAAGGGGCTCGAGTGGGTGAGCTTCAT
CAGTAACCTGGCCTACAGTATCGACTATGCTGACACCGTGACCGGCCGCTTCA
CTATCTCTCGGGATAATGCTAAGAACAGCCTGTACCTCCAGATGAACAGCCTGC
GCGCTGAGGACACCGCCGTGTACTACTGCGTGTCTGGAACCTGGTTCGCCTAC
TGGGGCCAGGGTACACTAGTCACAGTCTCCTCAGCCTCCACCAAGGGCCCATC
GGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCC
CTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAA
CTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCT
CAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGC
ACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGA
CAAGAAAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCC
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AGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGAC
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GGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC
GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG
TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATC
TCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATC
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CAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCAT
GCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCC
CTGTCTCCGGGTAAA

Figure 5.

ATGCGCCTGCCTGCCCAGCTGCTCGGCCTGCTGATGCTGTGGGTGTCGGGCA
GCTCCGGCGACATCGTCATGACCCAGAGCCCCCTGAGTCTCCCCGTCACCCCC
GGCGAACCTGCCAGCATCAGCTGCAGGGTGTCCCAGTCGCTGCTCCATTCCAA
CGGGTACACGTACCTGCATTGGTACCTGCAGAAGCCCGGGCAATCCCCTCAGC
TGCTGATCTACAAGGTGAGCAACCGCTTCTCCGGCGTCCCGGACCGGTTCAGT
GGCAGCGGCTCTGGAACCGACTTCACCCTGAAAATCAGCCGCGTGGAAGCTGA
GGACGTGGGCGTCTACTACTGCAGCCAGACCCGGCATGTGCCCTACACCTTCG
GCGGCGGCACAAAGGTGGAGATCAAGCGTACGGTGGCTGCACCATCTGTCTTC
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CTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGACAAC
GCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGA
CAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGA
AACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTC
ACAAAGAGCTTCAACAGGGGAGAGTGT

Figure 6.

ATGGAGCTGGGCCTGTGCTGGGTGTTCCTGGTGGCCATCCTGGAGGGCGTGC
AGTGCGAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCG
GCAGCCTGCGCCTGAGCTGCGCCGTGAGCGGCTTCACCTTCAGCGACAACGG
CATGGCCTGGGTGCGCCAGGCCCCCGGCAAGGGCCTGGAGTGGGTGAGCTTC
ATCAGCAACCTGGCCTACAGCATCGACTACGCCGACACCGTGACCGGCCGCTT
CACCATCAGCCGCGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCC
TGCGCGCCGAGGACACCGCCGTGTACTACTGCGTGAGCGGCACCTGGTTCGC
CTACTGGGGCCAGGGCACACTAGTCACAGTCTCCTCAGCCTCCACCAAGGGCC
CATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCG
GCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTG
GAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGT
CCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTG
GGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGT
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CCCAGCACCTGAACTCGCGGGGGCACCGTCAGTCTTCCTCTTCCCCCCAAAAC
CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG
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GGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGT
ACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAG
GAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAAC
CATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCC
CATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAA
GGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGG
AGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTC
CTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTT
CTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCC
TCTCCCTGTCTCCGGGTAAA

Figure 7.

ATGCGCCTGCCCGCCCAGCTGCTGGGCCTGCTGATGCTGTGGGTGAGCGGCA
GCAGCGGCGACATCGTGATGACCCAGAGCCCCCTGAGCCTGCCCGTGACCCC
CGGCGAGCCCGCCAGCATCAGCTGCCGCGTGAGCCAGAGCCTGCTGCACAGC
AACGGCTACACCTACCTGCACTGGTACCTGCAGAAGCCCGGCCAGAGCCCCCA
GCTGCTGATCTACAAGGTGAGCAACCGCTTCAGCGGCGTGCCCGACCGCTTCA
GCGGCAGCGGCAGCGGCACCGACTTCACCCTGAAGATCAGCCGCGTGGAGGC
CGAGGACGTGGGCGTGTACTACTGCAGCCAGACCCGCCACGTGCCCTACACCT
TCGGCGGCGGCACCAAGGTGGAGATCAAGCGTACGGTGGCTGCACCATCTGT
CTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGT
GTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGG
ACAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGC
AAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTA
CGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGC
CCGTCACAAAGAGCTTCAACAGGGGAGAGTGT

Figure 8.

ATGGAGCTGGGCCTGTGCTGGGTGTTCCTGGTGGCCATCCTGGAGGGCGTGC
AGTGCGAGGTGCAGCTGGTGGAGTCTGGCGGCGGACTGGTGCAGCCTGGCGG
CAGCCTGAGACTGAGCTGTGCCGTGTCCGGCTTCACCTTCAGCGACAACGGCA
TGGCCTGGGTGAGGCAGGCCCCTGGCAAGGGCCTGGAGTGGGTGTCCTTCAT
CAGCAACCTGGCCTACAGCATCGACTACGCCGACACCGTGACCGGCAGATTCA
CCATCAGCCGGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTG
AGAGCCGAGGACACCGCCGTGTACTACTGTGTGAGCGGCACCTGGTTCGCCTA
CTGGGGCCAGGGCACCCTGGTGACCGTGTCCAGCGCCAGCACCAAGGGCCCC
AGCGTGTTCCCCCTGGCCCCCAGCAGCAAGAGCACCAGCGGCGGCACAGCCG
CCCTGGGCTGCCTGGTGAAGGACTACTTCCCCGAACCGGTGACCGTGTCCTGG
AACAGCGGAGCCCTGACCAGCGGCGTGCACACCTTCCCCGCCGTGCTGCAGA
GCAGCGGCCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCCAGCAGCAGCCT
GGGCACCCAGACCTACATCTGTAACGTGAACCACAAGCCCAGCAACACCAAGG
TGGACAAGAAGGTGGAGCCCAAGAGCTGTGACAAGACCCACACCTGCCCCCCC
TGCCCTGCCCCCGAGCTGGCCGGAGCCCCCAGCGTGTTCCTGTTCCCCCCCAA
GCCTAAGGACACCCTGATGATCAGCAGAACCCCCGAGGTGACCTGTGTGGTGG
TGGATGTGAGCCACGAGGACCCTGAGGTGAAGTTCAACTGGTACGTGGACGGC
GTGGAGGTGCACAATGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACAGCA
CCTACCGGGTGGTGTCCGTGCTGACCGTGCTGCACCAGGATTGGCTGAACGGC
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AACCATCAGCAAGGCCAAGGGCCAGCCCAGAGAGCCCCAGGTGTACACCCTG
CCCCCTAGCAGAGATGAGCTGACCAAGAACCAGGTGTCCCTGACCTGCCTGGT
GAAGGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAG
CCCGAGAACAACTACAAGACCACCCCCCCTGTGCTGGACAGCGATGGCAGCTT
CTTCCTGTACAGCAAGCTGACCGTGGACAAGAGCAGATGGCAGCAGGGCAACG
TGTTCAGCTGCTCCGTGATGCACGAGGCCCTGCACAATCACTACACCCAGAAG
AGCCTGAGCCTGTCCCCTGGCAAG

Figure 9.

ATGAGACTGCCCGCCCAGCTGCTGGGCCTGCTGATGCTGTGGGTGTCCGGCA
GCAGCGGCGACATCGTGATGACCCAGAGCCCCCTGAGCCTGCCCGTGACCCC
TGGCGAGCCCGCCAGCATCAGCTGTAGAGTGAGCCAGAGCCTGCTGCACAGC
AACGGCTACACCTACCTGCACTGGTATCTGCAGAAGCCTGGCCAGAGCCCTCA
GCTGCTGATCTACAAGGTGTCCAACCGGTTCAGCGGCGTGCCTGATAGATTCA
GCGGCAGCGGCTCCGGCACCGACTTCACCCTGAAGATCAGCAGAGTGGAGGC
CGAGGATGTGGGCGTGTACTACTGCTCCCAGACCAGACACGTGCCTTACACCT
TTGGCGGCGGAACAAAGGTGGAGATCAAGCGTACGGTGGCCGCCCCCAGCGT
GTTCATCTTCCCCCCCAGCGATGAGCAGCTGAAGAGCGGCACCGCCAGCGTGG
TGTGTCTGCTGAACAACTTCTACCCCCGGGAGGCCAAGGTGCAGTGGAAGGTG
GACAATGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACCGAGCAGGACA
GCAAGGACTCCACCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGAC
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CCCCGTGACCAAGAGCTTCAACCGGGGCGAGTGC

Figure 10:

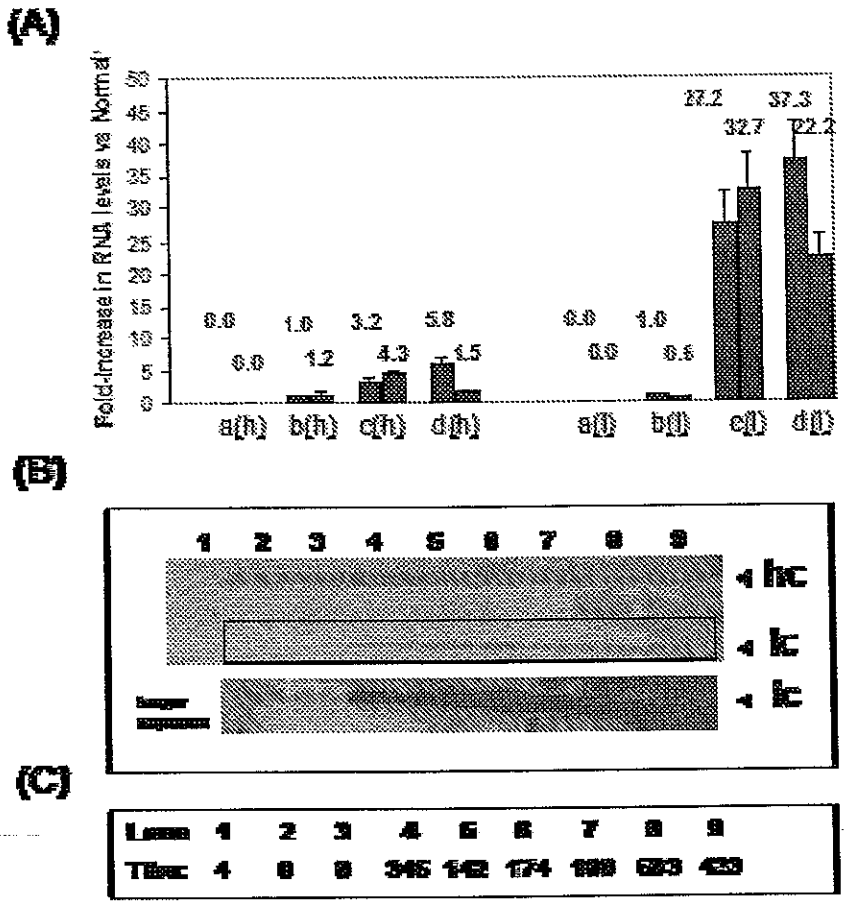
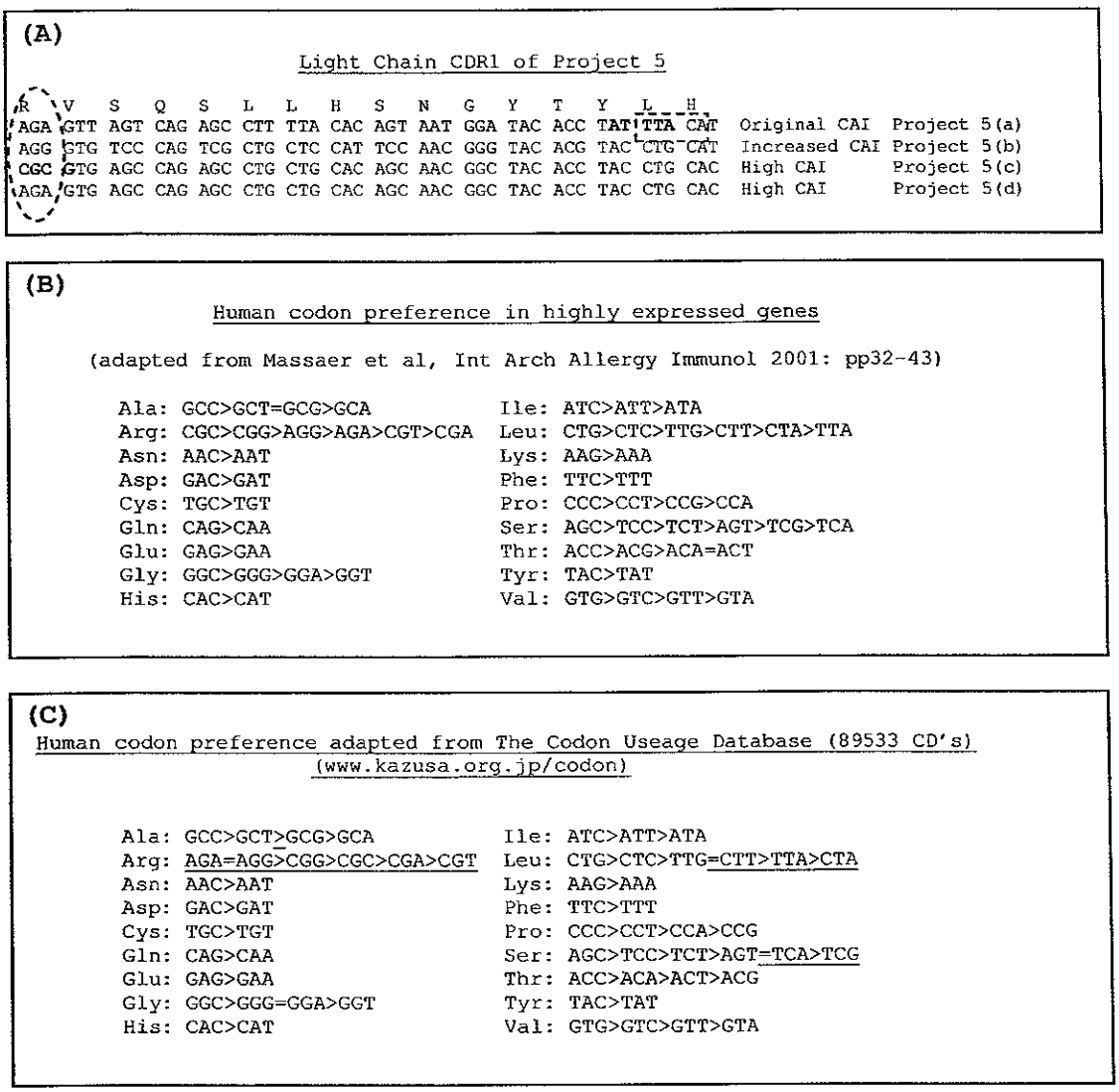

(A)
Fold-Increase in RNA levels vs Normal
0.0
1.0
3.2
5.8
0.0
1.2
4.3
4.5
0.0
1.0
27.2
37.3
0.0
0.5
32.7
22.2
a(h)
b(h)
c(h)
d(h)
a(l)
b(l)
c(l)
d(l)
(B)
1 2 3 4 5 6 7 8 9
hc
lc
lc
(C)
Lane 1 2 3 4 5 6 7 8 9
Titer 4 8 8 345 142 174 189 283 429

Figure 11.



(A)

Light Chain CDR1 of Project 5

R	V	S	Q	S	L	L	H	S	N	G	Y	T	Y	L	H		
AGA	GTT	AGT	CAG	AGC	CTT	TTA	CAC	AGT	AAT	GGA	TAC	ACC	TAT	TTA	CAT	Original CAI	Project 5(a)
AGG	GTG	TCC	CAG	TCG	CTG	CTC	CAT	TCC	AAC	GGG	TAC	ACG	TAC	CTG	CAT	Increased CAI	Project 5(b)
CGC	GTG	AGC	CAG	AGC	CTG	CTG	CAC	AGC	AAC	GGC	TAC	ACC	TAC	CTG	CAC	High CAI	Project 5(c)
AGA	GTG	AGC	CAG	AGC	CTG	CTG	CAC	AGC	AAC	GGC	TAC	ACC	TAC	CTG	CAC	High CAI	Project 5(d)

(B)

Human codon preference in highly expressed genes

(adapted from Massaer et al, Int Arch Allergy Immunol 2001: pp32-43)

Ala:	GCC>GCT=GCG>GCA	Ile:	ATC>ATT>ATA
Arg:	CGC>CGG>AGG>AGA>CGT>CGA	Leu:	CTG>CTC>TTG>CTT>CTA>TTA
Asn:	AAC>AAT	Lys:	AAG>AAA
Asp:	GAC>GAT	Phe:	TTC>TTT
Cys:	TGC>TGT	Pro:	CCC>CCT>CCG>CCA
Gln:	CAG>CAA	Ser:	AGC>TCC>TCT>AGT>TCG>TCA
Glu:	GAG>GAA	Thr:	ACC>ACG>ACA=ACT
Gly:	GGC>GGG>GGA>GGT	Tyr:	TAC>TAT
His:	CAC>CAT	Val:	GTG>GTC>GTT>GTA

(C)

Human codon preference adapted from The Codon Useage Database (89533 CD's)
(www.kazusa.org.jp/codon)

Ala:	GCC>GCT>GCG>GCA	Ile:	ATC>ATT>ATA
Arg:	AGA=AGG>CGG>CGC>CGA>CGT	Leu:	CTG>CTC>TTG=CTT>TTA>CTA
Asn:	AAC>AAT	Lys:	AAG>AAA
Asp:	GAC>GAT	Phe:	TTC>TTT
Cys:	TGC>TGT	Pro:	CCC>CCT>CCA>CCG
Gln:	CAG>CAA	Ser:	AGC>TCC>TCT>AGT=TCA>TCG
Glu:	GAG>GAA	Thr:	ACC>ACA>ACT>ACG
Gly:	GGC>GGG=GGA>GGT	Tyr:	TAC>TAT
His:	CAC>CAT	Val:	GTG>GTC>GTT>GTA

Figure 12.

(A)

	Production Model	%NGHC	Average*
Non-adapted Open Reading frames (Seq ID 10 and 11; CAI: HC 0.809, LC 0.761) Host: CHO-K1 Vectors: pEE14.4/6.4 Vectors Selection/Maintenance/Amplification: Glutamine withdrawal plus MSX Media: CD-CHO (Invitrogen) Feed: Non-animal hydrolysate (Day 4) One clone (chosen on titre) is the only clone for which NGHC data was generated:	Clone 1 Shake Flask Clone 1 5-Litre Clone 1 80-Litre (1) Clone 1 80-Litre (2) Clone 1 80-Litre (3) Clone 1 80-Litre (4) Clone 1 1000-Litre (1) Clone 1 1000-Litre (2)	1 2.3 14.5 5.5 6.1 4.6 12.4 8.3	6.8
Project 5(a): Non-adapted open reading frames (CAI: HC 0.809, LC 0.761) Host: CHO-DG44 Vectors: RLN/RLD Selection/Maintenance/Amplification: G418, nucleoside withdrawal plus MTX Media: G70 (GSK) Feed: None Clone 1,2,3 and 4 (chosen on titre) are the clones for which NGHC data was generated	Clone 1 Shake Flask Clone 2 Shake Flask Clone 3 Shake Flask Clone 4 Shake Flask	4.7 10.9 2.3 7.7	6.4
Project 5(c): Adapted open reading frames (CAI : HC 0.872, LC 0.894) Same vector backbones, cell line development protocols and media as project 5A Clones 1,2 and 3 (chosen on titre) are the clones for which NGHC data was generated	Clone 1 Shake Flask Clone 2 Shake Flask Clone 3 Shake Flask Clone 3 Shake Flask (Repeat) Clone 3 2-Litre Reactor	1.5 0.8 2.3 1.7 1.6	1.6
Project 5(d): Adapted open reading frames (CAI: HC 0.982, LC 0.976) Same vector backbones, cell line development protocols and media as project 5A Clones 1,2,3 & 4 (chosen on titre) are the clones for which NGHC data was generated Best Clone (clone 1 (O97-7) scaled to 1000-Litre to supply clinical trial material	Clone 1 Shake Flask Clone 1 Shake Flask (Repeat) Clone 2 Shake Flask Clone 3 Shake Flask Clone 4 Shake Flask Clone 1 2-Litre Clone 1 80-Litre Clone 1 1000-Litre	1.4 1.3 1.1 1.1 1 1.8 1.9 1.3	1.4
*Average for each process. Note different processes have differing levels of clone and/or scale data.			

(B)

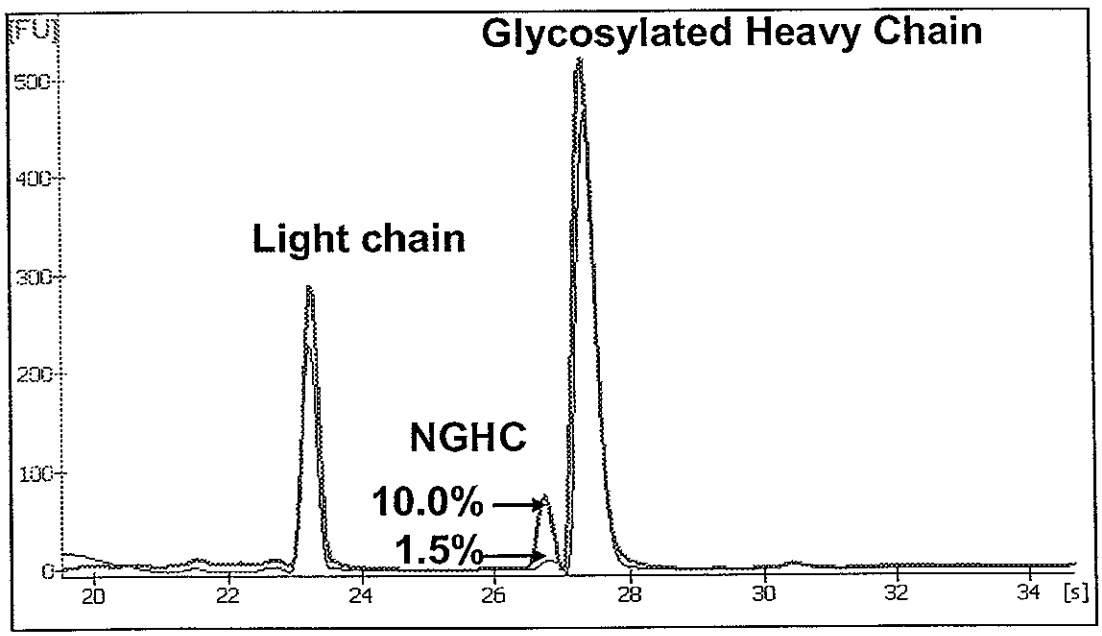


Figure 13.

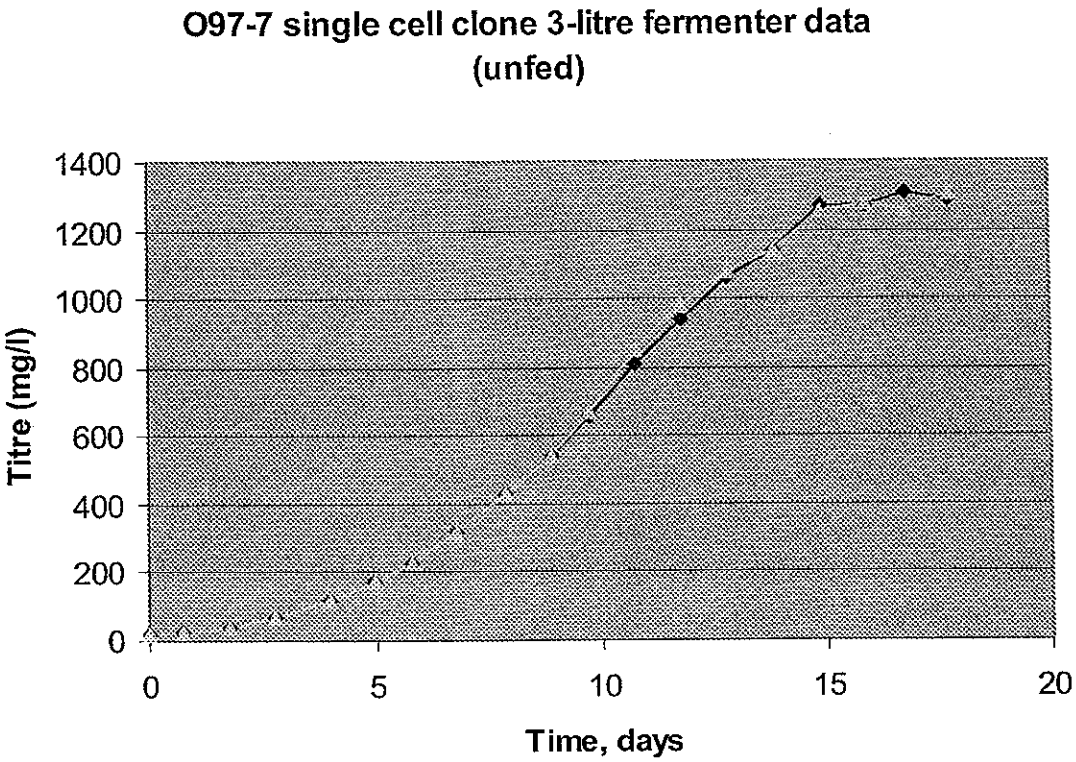
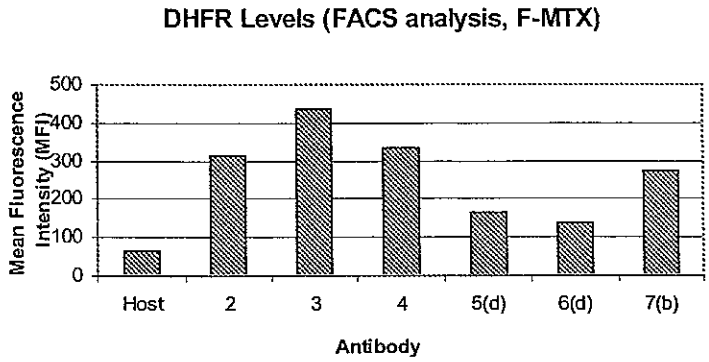
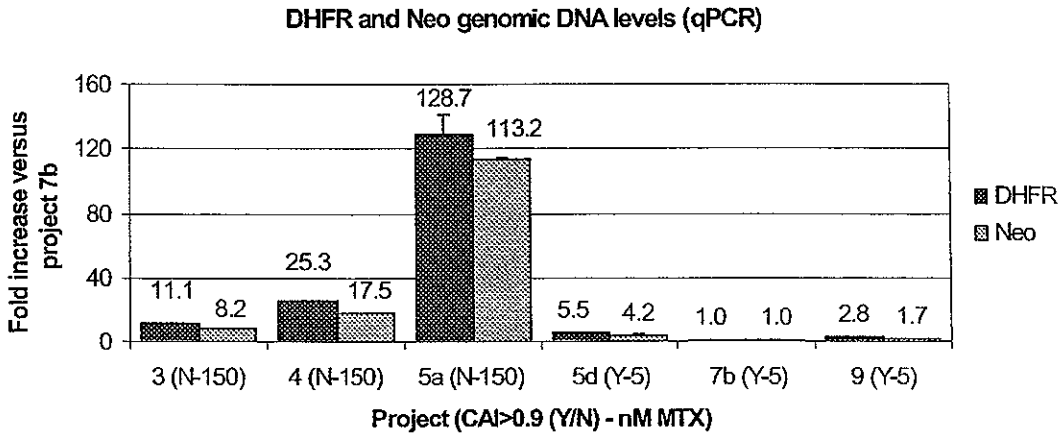

O97-7 single cell clone 3-litre fermenter data
(unfed)
Titre (mg/l)
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
Time, days

Figure 14.

(A)


DHFR Levels (FACS analysis, F-MTX)
Mean Fluorescence Intensity (MFI)
500
400
300
200
100
0
Host
2
3
4
5(d)
6(d)
7(b)
Antibody

(B)


DHFR and Neo genomic DNA levels (qPCR)
Fold increase versus project 7b
160
120
80
40
0
11.1
8.2
25.3
17.5
128.7
113.2
5.5
4.2
1.0
1.0
2.8
1.7
3 (N-150)
4 (N-150)
5a (N-150)
5d (Y-5)
7b (Y-5)
9 (Y-5)
Project (CAI>0.9 (Y/N) - nM MTX)
DHFR
Neo