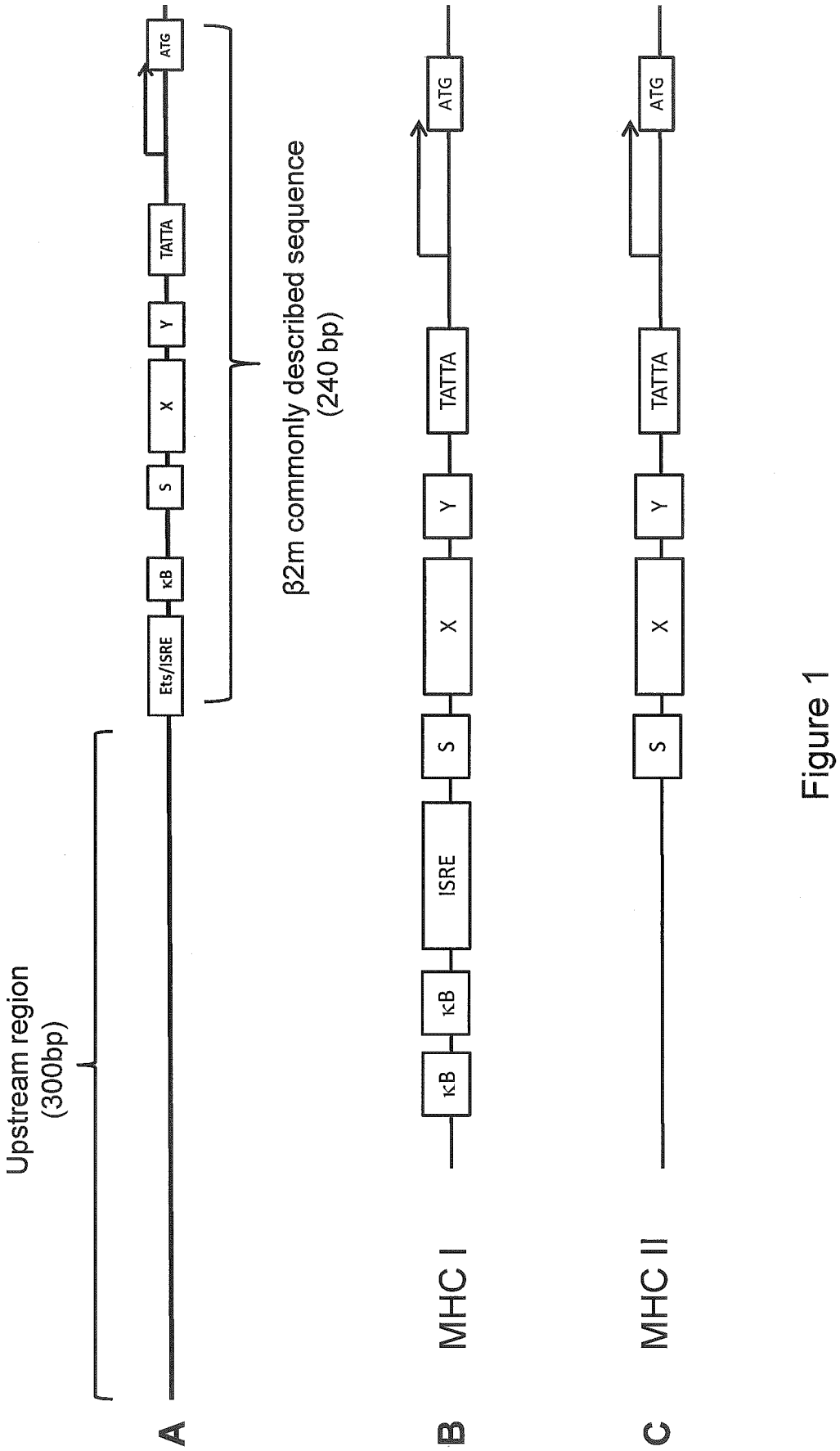

A
Upstream region
(300bp)
Ets/ISRE
κB
S
X
Y
TATTA
ATG
β2m commonly described sequence
(240 bp)
B
MHC I
κB
κB
ISRE
S
X
Y
TATTA
ATG
C
MHC II
S
X
Y
TATTA
ATG

Figure 1

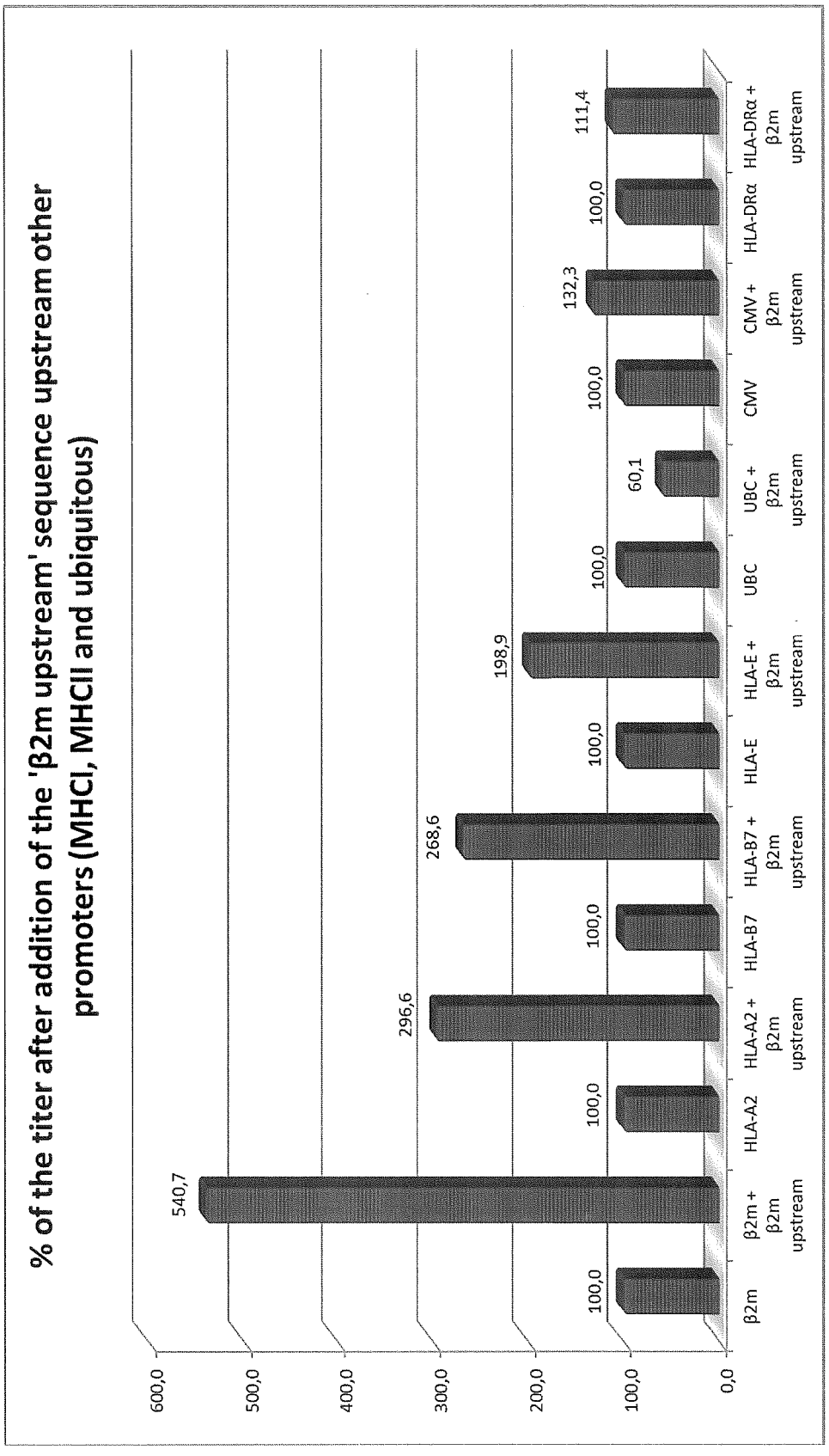

% of the titer after addition of the 'β2m upstream' sequence upstream other promoters (MHCI, MHCII and ubiquitous)
600,0
500,0
400,0
300,0
200,0
100,0
0,0
β2m
β2m + β2m upstream
HLA-A2
HLA-A2 + β2m upstream
HLA-B7
HLA-B7 + β2m upstream
HLA-E
HLA-E + β2m upstream
UBC
UBC + β2m upstream
CMV
CMV + β2m upstream
HLA-DRα
HLA-DRα + β2m upstream
100,0
540,7
100,0
296,6
100,0
268,6
100,0
198,9
100,0
60,1
100,0
132,3
100,0
111,4

Figure 2

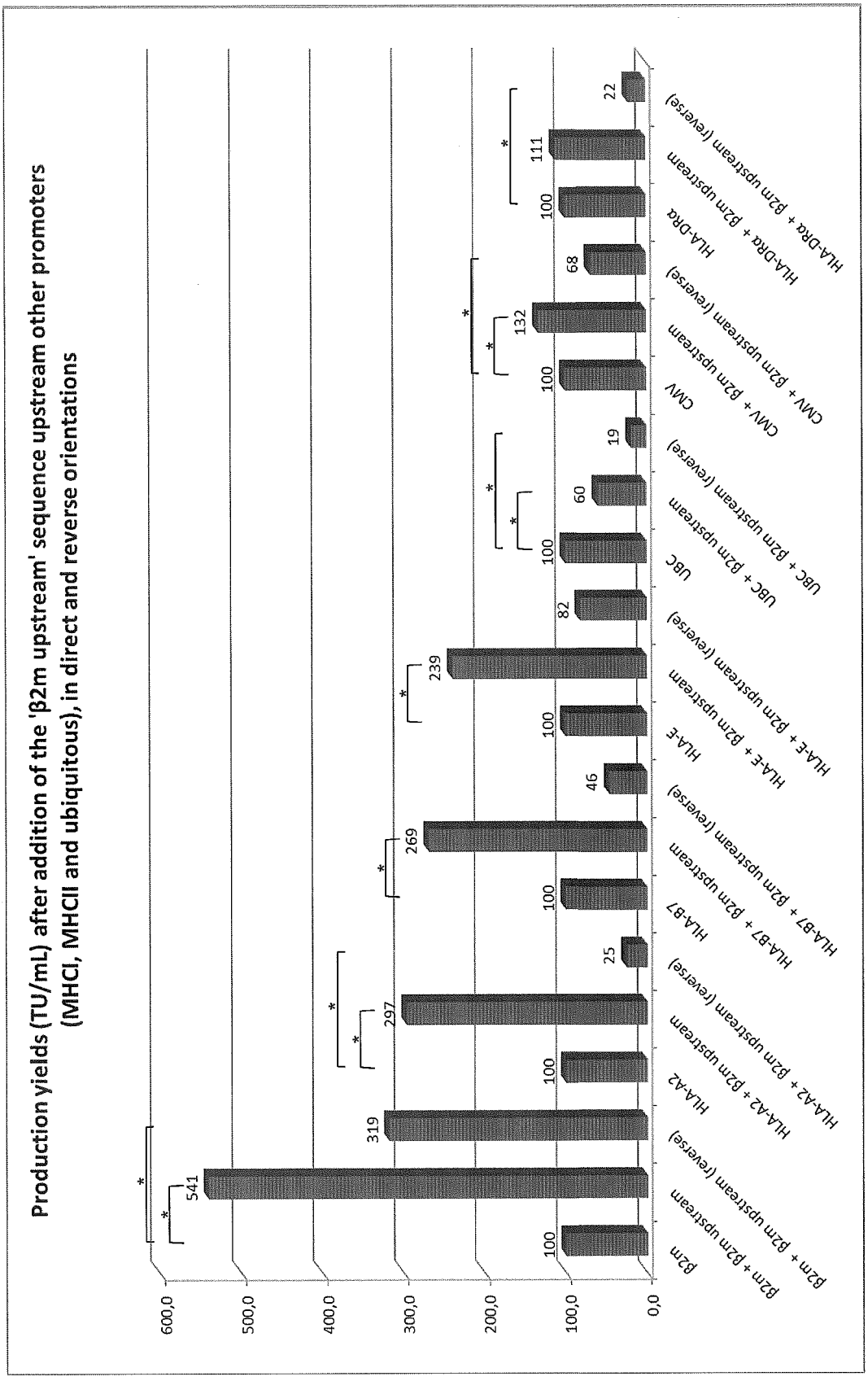

Production yields (TU/mL) after addition of the 'β2m upstream' sequence upstream other promoters (MHCI, MHCII and ubiquitous), in direct and reverse orientations
600,0
500,0
400,0
300,0
200,0
100,0
0,0
β2m
β2m + β2m upstream (reverse)
HLA-A2
HLA-A2 + β2m upstream (reverse)
HLA-B7
HLA-B7 + β2m upstream (reverse)
HLA-E
HLA-E + β2m upstream (reverse)
UBC
UBC + β2m upstream (reverse)
CMV
CMV + β2m upstream (reverse)
HLA-DRα
HLA-DRα + β2m upstream
HLA-DRα + β2m upstream (reverse)
100
541
319
100
297
100
25
269
100
46
239
100
82
100
60
19
100
132
68
100
111
22
*

Figure 3

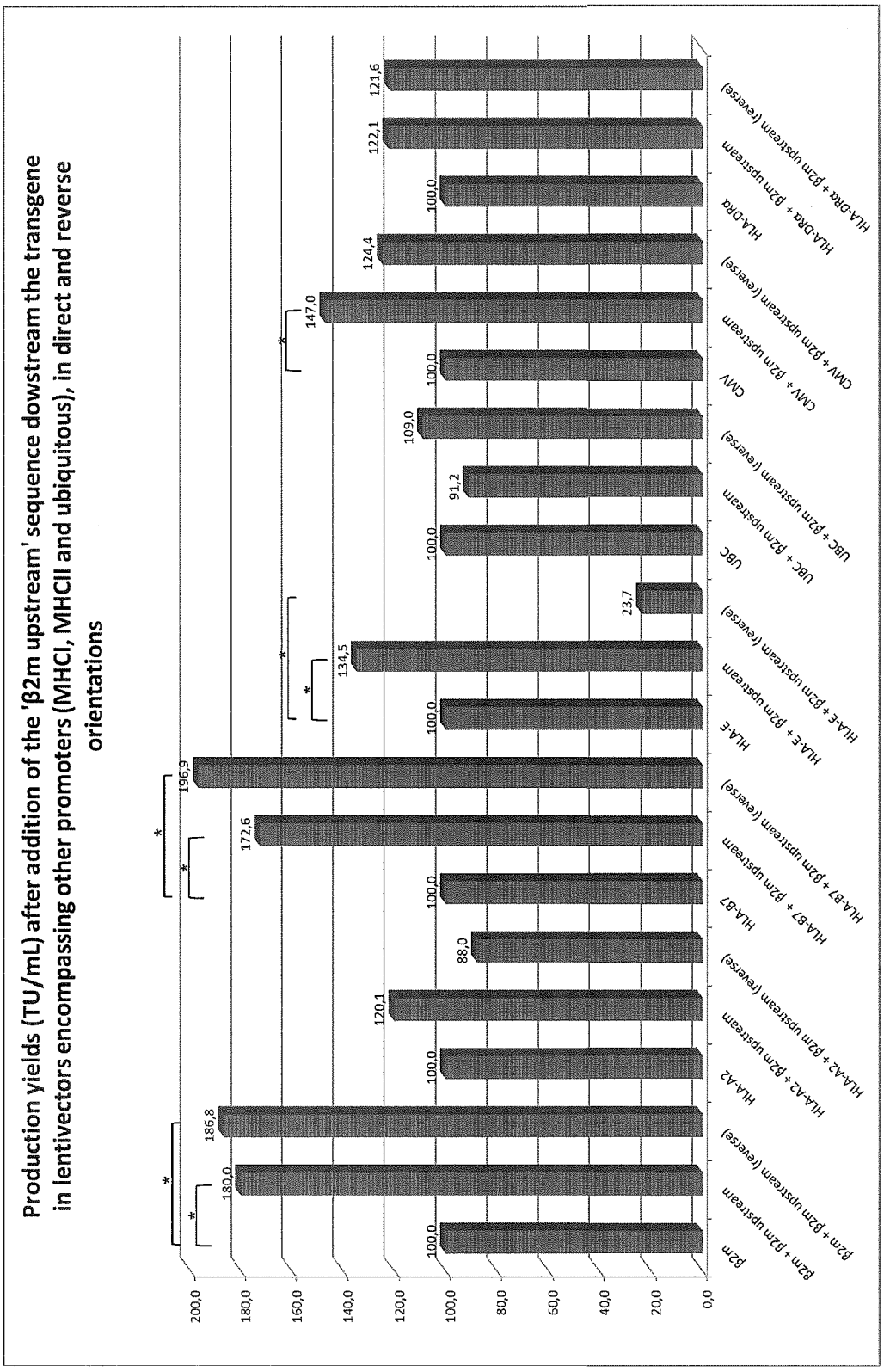

Production yields (TU/mL) after addition of the 'β2m upstream' sequence dowstream the transgene in lentivectors encompassing other promoters (MHCI, MHCII and ubiquitous), in direct and reverse orientations
200,0
180,0
160,0
140,0
120,0
100,0
80,0
60,0
40,0
20,0
0,0
100,0
180,0
186,8
100,0
120,1
88,0
100,0
172,6
196,9
100,0
134,5
100,0
23,7
100,0
91,2
109,0
100,0
147,0
124,4
100,0
122,1
121,6
β2m
β2m + β2m upstream (reverse)
HLA-A2
HLA-A2 + β2m upstream
HLA-A2 + β2m upstream (reverse)
HLA-B7
HLA-B7 + β2m upstream
HLA-B7 + β2m upstream (reverse)
HLA-E
HLA-E + β2m upstream
HLA-E + β2m upstream (reverse)
UBC
UBC + β2m upstream
UBC + β2m upstream (reverse)
CMV
CMV + β2m upstream
CMV + β2m upstream (reverse)
HLA-DRα
HLA-DRα + β2m upstream
HLA-DRα + β2m upstream (reverse)

Figure 4

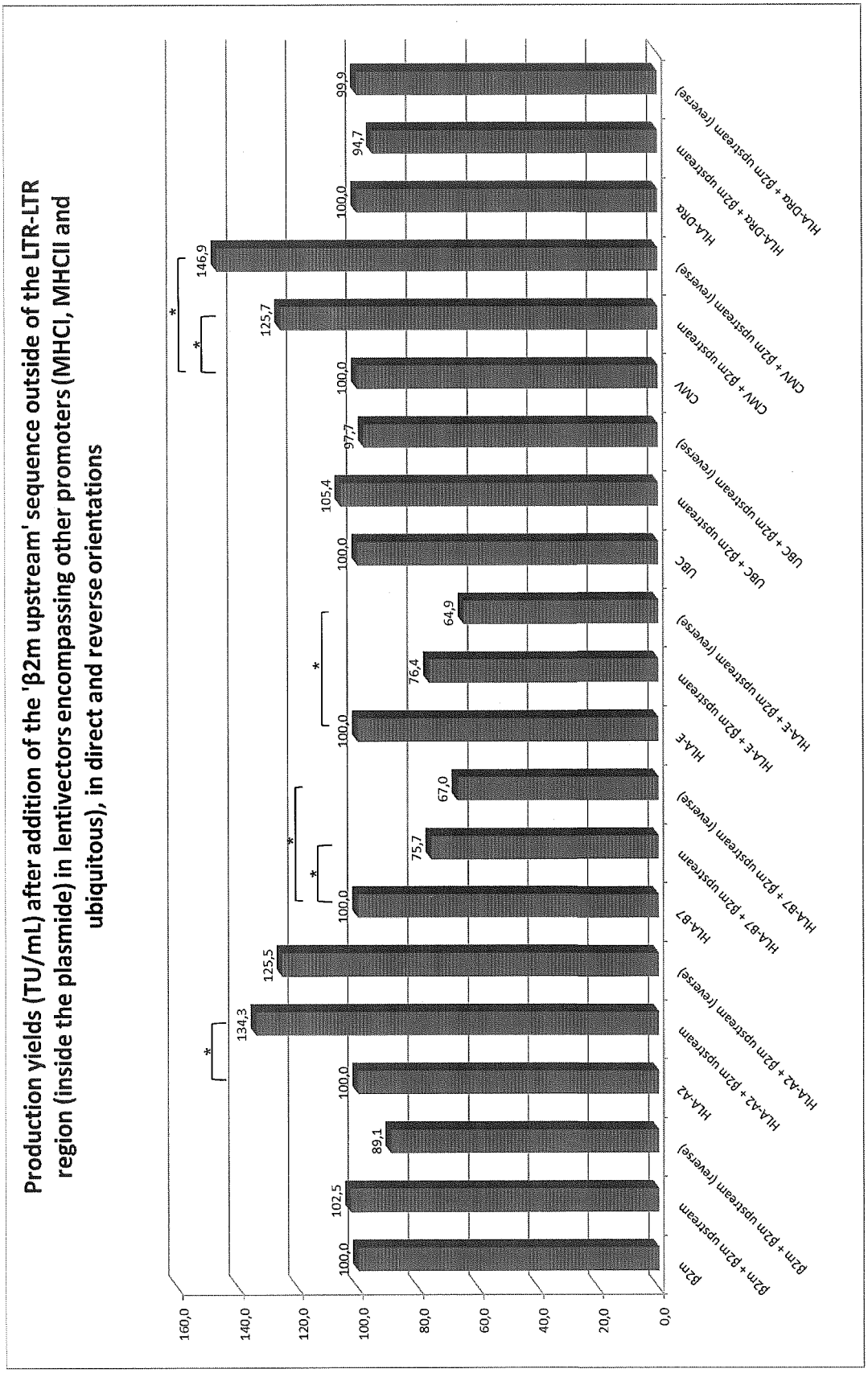

Production yields (TU/mL) after addition of the 'β2m upstream' sequence outside of the LTR-LTR region (inside the plasmide) in lentivectors encompassing other promoters (MHCI, MHCII and ubiquitous), in direct and reverse orientations
160,0
140,0
120,0
100,0
80,0
60,0
40,0
20,0
0,0
100,0
102,5
89,1
100,0
134,3
125,5
100,0
75,7
67,0
100,0
76,4
64,9
100,0
105,4
100,0
97,7
100,0
125,7
146,9
100,0
94,7
99,9
*
*
*
*
*
β2m
β2m + β2m upstream
β2m + β2m upstream (reverse)
HLA-A2
HLA-A2 + β2m upstream
HLA-A2 + β2m upstream (reverse)
HLA-B7
HLA-B7 + β2m upstream
HLA-B7 + β2m upstream (reverse)
HLA-E
HLA-E + β2m upstream
HLA-E + β2m upstream (reverse)
UBC
UBC + β2m upstream
UBC + β2m upstream (reverse)
CMV
CMV + β2m upstream
CMV + β2m upstream (reverse)
HLA-DRα
HLA-DRα + β2m upstream
HLA-DRα + β2m upstream (reverse)

Figure 5

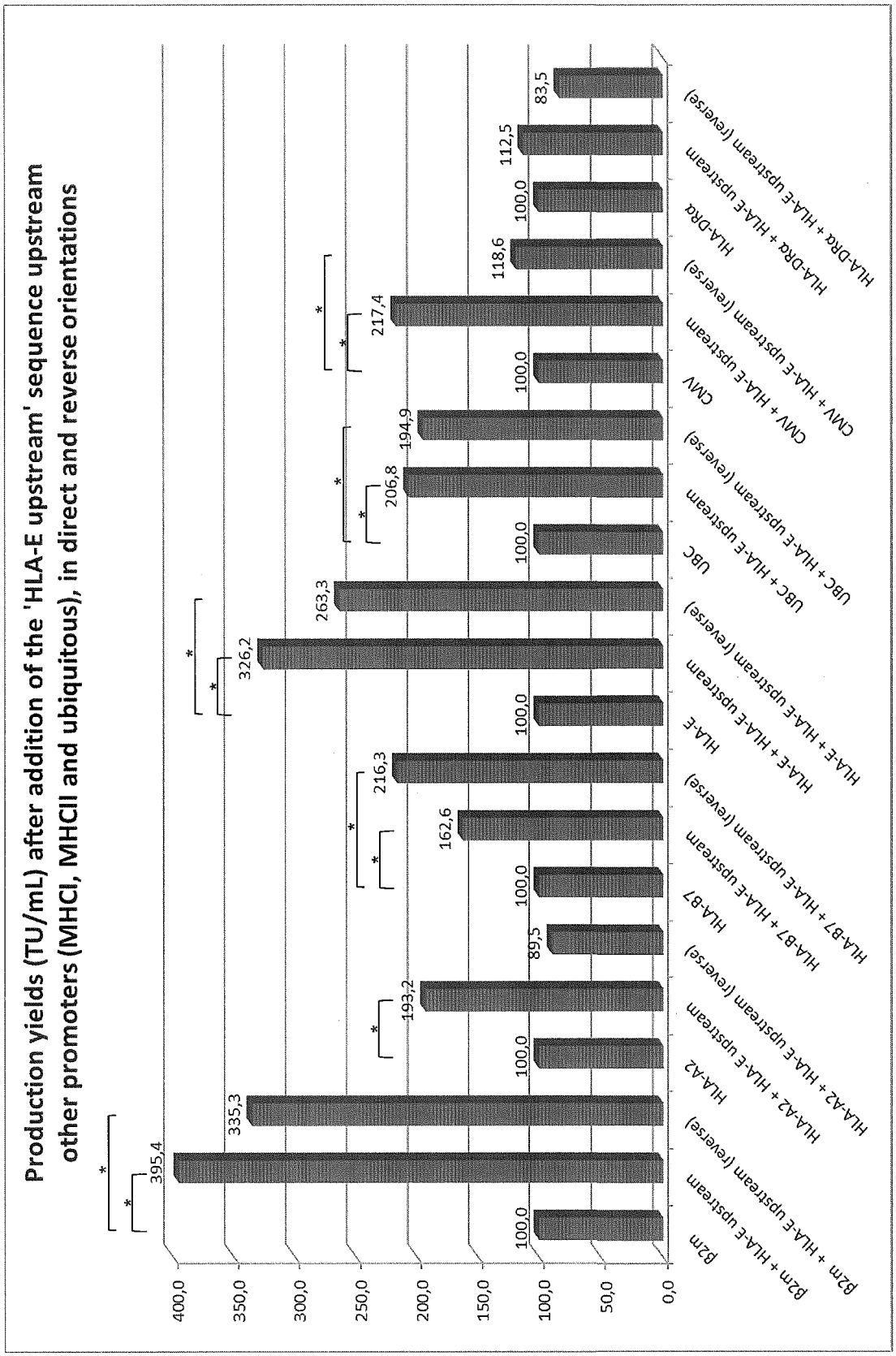

Production yields (TU/mL) after addition of the 'HLA-E upstream' sequence upstream other promoters (MHCI, MHCII and ubiquitous), in direct and reverse orientations
400,0
350,0
300,0
250,0
200,0
150,0
100,0
50,0
0,0
β2m
β2m + HLA-E upstream (reverse)
HLA-A2
HLA-A2 + HLA-E upstream
HLA-A2 + HLA-E upstream (reverse)
HLA-B7
HLA-B7 + HLA-E upstream
HLA-B7 + HLA-E upstream (reverse)
HLA-E
HLA-E + HLA-E upstream
HLA-E + HLA-E upstream (reverse)
UBC
UBC + HLA-E upstream
UBC + HLA-E upstream (reverse)
CMV
CMV + HLA-E upstream
CMV + HLA-E upstream (reverse)
HLA-DRα
HLA-DRα + HLA-E upstream
HLA-DRα + HLA-E upstream (reverse)
100,0
395,4
100,0
335,3
100,0
193,2
89,5
100,0
162,6
100,0
216,3
100,0
326,2
100,0
263,3
100,0
206,8
194,9
100,0
217,4
118,6
100,0
112,5
83,5

Figure 6

```
                    1                                                                                                  100
   Upstream B2m    (1) AGAAGTTCTCCTTCTGCTAGGTAGCATTCAAAGATCTTAATCTTCTGGGTTTCCGTTTTCTCGAATGAAAAATGCAGGTCCGAGCAGTTAACTGGCGGGG
 Upstream HLA-E    (1) ------------------------CTGGAGGGCAATGGCACGATCTTGGCTCACCGCAACCTCCTCCTCCTGGGTTCAAGTGATTCTCCTGC-CTCAGCC
Upstream HLA-B7    (1) --------------------ACTCTCTGGCATCAAGTTCCCCGTGCTCAGTTTCCCTACACAAGAGTCCAAG-AGGAGAGGTAAGGAGTGGGA-GGCAGGG
 Upstream HLA-C    (1) ---------CAAGGGGAGAGGTAAGTGTCCTTTATTTTGCTGGATGTAGTTTAATATTACCTGAGGT---A-AGGTAAGGCAAAGAGTGGGA-GGCAGGG
 Upstream HLA-F    (1) ----------------TTCATTGTCTGGCACCAAGCTCCTTGGGGTGAATTTTCTTCCAAAAGAGTCCGGGGAGTCCAGGTATGGAATGGGA-GGCAGAA
 Upstream HLA-G    (1) ---------------GCTCACTCTCTGGCAACAAGCTCCCTGGGGTGATTTTTCTTCTAGAAGAGTACAGG-AGGACAGGCAAGGAGTGGGA-GGCAGGG
Upstream HLA-A2    (1) ---------------GCTTACTCTCTGGCACCAAACTCCATGGGATGATTTTTCTTCTAGAAGAGTCCAGG-TGGACAGGTAAGGAGTGGGA-GTCAGGG
      Consensus    (1)                G T A T TCTGGCA CAA CTCC TGGG TGAGTTT CTTCTACAAGAGTCCA G AGGACAGGTAAGGAGTGGGA GGCAGGG

                    101                                                                                                200
   Upstream B2m  (101) GCACCATTAGCAAGTCACTTAGCATCTCTGGGGCCAGTCTGCAAAGCGAGGGGGCAG---CCTTAATGTGCCTCCAGCCTGAAGTCCTAGAATGAGCGCC
 Upstream HLA-E   (76) TCCCAAGTAGCCAGGATTACAGCCATGCGCCACCACGCCGGCTAATTTTTTGGACTTTTAGTAGAGACAGGGTTTCTCCATA--TTGGTCGGGCTGGTCT
Upstream HLA-B7   (80) AGTCCAGTT-C-AGGG--ACAGGGATTCCAGGACGAGAAGTGAAGGGGAAGGGGCTGGGCGCAGCCTGGGGGTCTCTCCCTGGTTTCCACAGACAG--AT
 Upstream HLA-C   (87) AGTCCAGTT-C-AGGG--ACGGGGATTCCAGGA---GAAGTGAAGGGGAAGGGGCTGGGCGCAGCCTGGGGGTCTCTCCCTGGTTTCCACAGACAG--AT
 Upstream HLA-F   (84) AGTTCAAT--CAAGGG--ACTGGGATTTCGGAATGAATAATGAAGGGAGATGGACTGGGTCCATGCCGAAGGTTTCTCCCTGGTTTCT-CAGCC------
 Upstream HLA-G   (84) AGTCCAGTT-C-AGGG--ACAGGGATTCCGGGATGAAAAGTGAAGGGAGAGGGCCAGGGACCTTGCCGAGGGTTTCTCCCTGGTTTCT-CAGACAG--CT
Upstream HLA-A2   (84) AGTCCAGTT-CCAGGG--ACAGAGATTACGGGATAAAAAGTGAAAGGAGAGGGACGGGGCCCATGCCGAGGGTTTCTCCCTTGTTTCT-CAGACAG--CT
      Consensus  (101) AGTCCAGTT C AGGG  ACAGGGATTCCGGGA  AGAAGTGAAGGG  AGGG CTGGG CCAT C GAGGGTTTCTCCCTGGTTTCT CAGACAG  CT

                    201                                                                                                300
   Upstream B2m  (198) CGGTGTCCCAAGCTGGGGCGCGCACCC---CAGATC---GGAGGGCGCCGA-TGTACAGA---CAGCAAACTCACCCAGT--CTAGTGCATGCCTTCTTA
 Upstream HLA-E  (174) CGAACTCCCAACCTCAGGTGATCAGCCCGCCTTGGCCTCCCAAAGTGCTGAGATTACAGGCGTGAGCCACCGCGCCCAG---C-CAGGACTAATTTCTAA
Upstream HLA-B7  (174) CCTTGTCCAGGACTCAGGCAGACAGTGTGACAAAGA-G-GCTTGGTGTAGG-AGAAGAGGGATCAGGACGAAGTCCCAGGTCC-CGGACGG-GGCTCTCA
 Upstream HLA-C  (178) CCTTGGCCAGGACTCAGGCACACAGTGTGACAAAGA-T-GCTTGGTGTAGG-AGAAGAGGGATCAGGACGAAGTCCCAGGTCC-CGGGCGG-GGTTCTCA
 Upstream HLA-F  (173) CCCGGGCGAAGACTCAGGGAGACATTGAGACACACCCT-GCACAGGAGGGGGAGGGGGAGGGGGAGGGCAAAGTCCCAGGGCCCCAGGAGT-GGCTCTCA
 Upstream HLA-G  (177) CCTGGGCCAAGACTCAGGGAGACACTGAGACAGAAC---GCTTGGCACAAG-AGTAGCGGGGTCAGGGCGAAGTCCCAGGGCCTCAAGCGT-GGCTCTCA
Upstream HLA-A2  (178) CTTGGGCCAAGACTCAGGGAGACATTGAGACAGAGC---GCTTGGCACAGA-AGCAGAGGGGTCAGGGCGAAGTCC-AGGGCCCCAGGCGTTGGCTCTCA
      Consensus  (201) CCT GGCCAAGACTCAGG AGACA TG GACA AGC   GCTTGG GCAGG AG AGAGGGGTCAGG CGAAGTCCCAGG CC CAGGCGT GGCTCTCA

                    301                              335
   Upstream B2m  (286) AACA-TCACGAGACTC--------------------  (SEQ ID NO:1)
 Upstream HLA-E  (270) GAGTGTGCAGAGATACCGAAACCTAAAAGTT----  (SEQ ID NO:2)
Upstream HLA-B7  (269) GGGTCTC---AGGCTCCGAGGGCCGCGTCTGCAAT  (SEQ ID NO:3)
 Upstream HLA-C  (273) GGGTCTC---AGGCTCCAAGGGCCGTGTCTG----  (SEQ ID NO:4)
 Upstream HLA-F  (271) AGGGCTC---AGGCCCCG-AGGCGGTGTCTGGGG-  (SEQ ID NO:5)
 Upstream HLA-G  (272) GGGTCTC---AGGCCCCACAGGCGGTGTATGG---  (SEQ ID NO:6)
Upstream HLA-A2  (273) GGGTCTC---AGGCCCCGAAGGCGGTGTATG----  (SEQ ID NO:7)
      Consensus  (301) GGGTCTC   AGGC CCGAAGGC GTGT TG       (SEQ ID NO:8)
```

Figure 7

HLA-A2+Short
HLA-B7+Short
HLA-E+short
B2m+Short
HLA-DRa+Short
κB2
κB1
ISRE
S
X1 X2
E box
Ets/ISRE
κB

Figure 8A

```
Y
CCAGTTCTCACTCCC+ATTGGGTGTCGGGTTTCCAGAGAAGCCAATCAGTGTCGTCGCGG-TCGCGGTTCTAAAGTCCGCACGCACCCACCGGGACTCA-GATTCTCCCCAGACGCCCGAGG SEQ ID NO:37
CCACTTCCCACTCCC+ATTGGGTATTGGATATCTAGAGAAGCCAATCAGCGTCGCCGCGG-TCCCAGTTCTAAAGTCCCCACGCACCCACCCGGACTCA-GAG               SEQ ID NO:38
TCAGTTCTCATTCCC+AATGGGTGTCGGGTTTCTAGAGAAGCCAATCAGCGTCGCCACGACTCCCGACTATAAAGTCC----------CCATCCGGACTCAAGAAGTTCTCAGGACTCAGAGG SEQ ID NO:39

TGCGGGCCTTGTCCTCATTGGCTGGCCACGCGTTTAATATAAGTGGAGGCGTCGCGCTGGCGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAG                        SEQ ID NO:40

TCAAAATATTTTTCTCATTGGCCAAAGAGTAATTGATTTGCATTTTAATGGTCAGACTCTATTACACCCCACATTCTCTTTTCTTTTTATTCTTGTCTGTTCTGCCTCACTCCCGAGCT   SEQ ID NO:41
```

Figure 8B

```
HLA-A2+Long       ----------------------------------------------------------------------------------------------------
HLA-B7+Long       ----------------------------------------------------------------------------------------------------
HLA-E+Long        TTTTTTCCCCCTAGACATCTCACTCTGTCGCCCAGGCTGGAGTGCAGTGGTGTGATCTCGGCTCACTGCAACCACCACCTCTCGGGTTCAAGCAATTCTCCTATCTCAGCC

B2m+Long          CTTCCAAGATCTCTGCCCCTCCCCATCGCCATGGTCCACTTCCTCTTCTCACTGTTCCTCTT-AGAAAAGATCTGTGGACTCCACCACCACGAAATGGCGGCACCTTATTT

HLA-DRa+Long      ----------------------------------------------------------------------------------------------------

----------------------------------------------------------------------------------------------------
----------------------------------------------------------------------------------------------------
TCCAGAGTTGCTGGAATTACAGGCGCGCACCACCACACCCGGCTAATTTTTGTATTGTTAGTAGAGACAGGGTTTCATCATGTTGGCCAGGTTAGTCTTGAACTCCTGACCTCGTGATCTGCCTGCCTC

ATGGTCACTTTAGAGGGTAGGTTTTCTTAATGGGTCTGCCTGTCATGTTTAACGTCCTTGGCTGGGTCCAAGGCAGATGCAGTCCAAACTCTCACTAAAATTGCCGAGCCCTTTGTCTTCCAGTGTCTA

----------------------------------------------------------------------------------------------------

----------------------------------------------------------------------------------------------------
----------------------------------------------------------------------------------------------------
G-GCCTACCAAAATGCTGCGATTACAGGCGTGAGCCACCGTTCCCGGCCTATACGTTGTTTATTTTGGAAAAATTAAAAATTAAGTTTTTTTTCATTAAAGATATGTTATTTCCGATCAAGAGATCAAG

AAATATTAATGTCAATGGAATCAGGCCAGAGTTTGAATTCTAGTCTCTTAGCCTTTGTTTC—CCCTGTCCATAAAATGAATGGGGGTAATTCTTTCCTCCTACAGTTTATTTATATATTCACTAATTC

----------------------------------------------------------------------------------------------------

----------------------------------------------------------------------------------------------------
----------------------------------------------------------------------------------------------------
ACCATCCTGGCCAACATGGTGAAACCCCGTCTCTACTAAAAACACAAAAATTAGCTGGGTGTGGTGGCACACGCCTGTAGTTCCAGTTACTGGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCGGGAG

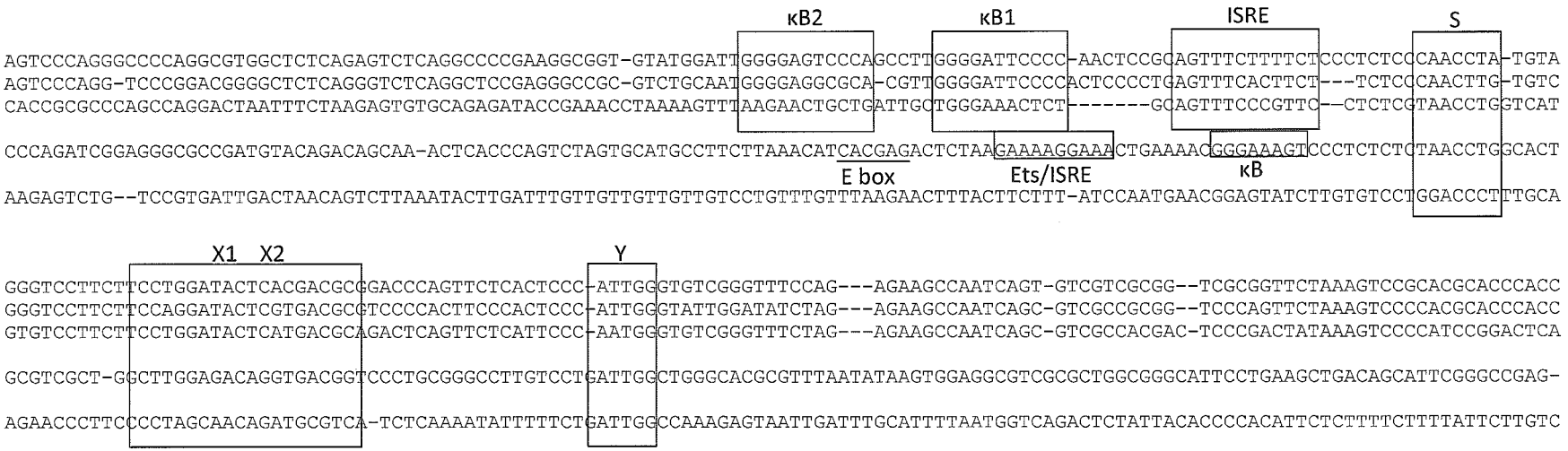
ATTCATT-CATCCATCCATTCGTTCATTCGGTTTACTGAGTACCTACTATGTGCCAGCCCCTGTTCTAGGGTGGAAACTAAGAGAATGATGTACCTAGAGGGCGCTGG-AAGCTCTAAAGCCCTAGCAG

----------TAGGCTTTGCCCATTATACTCTCTCATATTCATTGA
```

Figure 9A


----------GAGTCCTGTTGTAATGCTTTTGGACACATTTATACATTAAGG--GGCCAAAGT-CACATTTTTTACCTATTAGATTCCTGATCATTCAG-GGGTTACCAAGATTCTGCTACCCAC
----------GAGTTTAATTGTAATGC--TGTTTTGACACAGGTCTTTTACAAATTGGAATTCTAATCATTCAG-GGATTACCAATATTGTGCTACCTAC
AAGGAGGTTGCAGTGAGCCGAGATCATGCCACTGCACTCCAGCCTGGGGACAGAGCAAGACTCTGACTCAAAAAAAAAAAAAAGTTGTTTCTATTAACATGTAATGGGTTATTAATATTCTCTTAAATGA
TTACTGCTTTTACTATTAGTGGTCGTTTTTTTCTCCCCCCCGCCCCCCGACAAATCAACAGAACAAAGAAAATTACCTAA-ACAGCAAGGACATAGGGAGGAACTTCTTGGCACAGAACTTTCCAAACA
CCTGAATCCTCAA-ATGAGGTGTGTCCATTAGTCAACTCCAATCTCTTGTCATATA--TAAGATGGTAGAGATGAG-AAGAAGGTAGCTCCTTTACAGCCCACTATTTCCACTAACTACTACCTGTGTT
TGTAGTTAATAAACAAAGAGCAAATTGGTCTCTAT-------TCTGTCTCATGCACTCAGGCACAACTTTTCCGGATTAAAAACAAAAACAACAACAACAAAAATCTACACCT--CCATTC----CCAG
TGTA-TTAACAAACAAAAAGGAAACTGGTCTCTATGAGAATCCCTATGCGGTGCCTTCAGAGAAAACTTCACCAGGTTTAAAGAGAAAACCCCTGTC-------TCTACACCT--CCATTC----CCAG
ATTA-ATATTTTTAATATTTTGTTTTAATATCTTTTA--ATTTATATATGATAAAAATTGATACAA-TCCACAGAAACAAAATTTATTTGGGTCCTCACTAATTTCTTTTTTC--TTGTTG----CCCA
CTTTTTCCTGAAGGGATACAAGAAGCAAGAAAGGTACTCTT-TCACTAGGACCTTCTCTGAGCTGTCC----TCAGGATGCTTTTGGGACTATTTTTCTTA---CCCAGAGAATGGAGAAACCCTGCAG
TCAAGATACAGCCTTTCATCCTTCTCCAGTGTTGAGAGTGTTGAACCTCAGAGTTTCTCCTCTCATTTTCTCTAAATGAGATACAATGCCAGCCATCCCAAGCTCTTGGCCTGAGTTGTTCATCTTGAA
ATCAAGCTTACTCTCTGGCACCAAA---CTCCATGGGGTGATTTTTCTTCTAGAAGAGTCC--AGGTGGACAGGTAAGGAGTGGGAGTCAGGGAGTCCAGTTCAGGGACAGAGATAATGGGATGAAAAG
GGCGAGCTCACTCTCTGGCATCAAG---TTCCCCGTGCTCAGTTTCCCTACACAAGAGTCC--AAGAGGAGAGGTAAGGAGTGGGAGGCAGGGAGTCCAGTTCAGGGACAGGGATTCCAGGACGAGAAG
GGCTGGAGGGCAAT--GGCA-CGAT---CTTGGCTCACCGCAACCTCCTCCTCCTGGGTTC--AAGTGATTCTCCTGCCTCAGCCTCCCAAGTAGCCAGGATTACAGCCATG-CGCCACCACGCCGGC
GGAATTCCCAAGCTGTAGTTATAAACAGAAGTTCTCCTTCTG-CTAGGTAGCATTCAAAGATCTTAATCTTCTGGG TTTCCGTTTTCTCGAATGAAAAATGC--AGGTCCGAGCAGTTA-ACTGGCTG
GTCTAGGACTCCAAGAAGCATGAAAGAGCTTCTTTAGTGAAGCTATGTCCTCAGTACTGCCAAAATTCAGACAATCTCCATGGCCTGACAATTTACCTTCTATTTGGGTAATTTATTGTCCCTTACGCA
TGAAAGGAGAGGGACGGGGCCCATGCCGAGGGTTTCTCCCTTG-TTTCT-CAGACAGCTCCTGG--GCCAAGACTCAGGGAGACATTGAGACAGAGCG-CTTCGCACAGGAGCAGAGGGGTCAGGGCGA
TGAAGGGGAAGGGGCTGGGCGCAGCCTGGGGGTCTCTCCCTGG-TTTCCACAGACAGATCCTTG--TCCAGGACTCAGGCAGACAGTGTGACAAAGAGGCTTGGTGTAGGAGAAGAGGGATCAGGACGA
TAATTTTTTGGACTTTTAGTAGAGAC--AGGGTTTCTCCATA---TTGGTCGGGCTGGTCTCGAACTCCCAACCTCAGGTGATCAGCCCGCCTTGGCCTCCCA-AAGTGCTGAGATTACAGGCGTGAGC
GGGCACCATTAG----CAAGTCACTTAGCATCTCTGGGGCCAGTCTGCAAAGCGAGGGGGCAGCCTTAATGTGCCTCCAGCCTGAAGTCCTAG AATGAGCGCCCGGTGTCCCAAGCTGGGGCGCGCAC
AACTCTCCAGCTGTCATGGCACAGACATATGATCTGTATTTAGCTCTCACTTTAGGTGTTTCCA---TTGATTCTATTCTCACTAATGTGCTTCAGGTATATCCCTGTCTAGAAGTCAGATTGGGGTTA

Figure 9B



GGGA---CTCAGATTCTCCCCAGACGCCGAGG SEQ ID NO:42
CGGA---CTCAGAG------------------ SEQ ID NO:43
AGAAGTTCTCAGGACTCA--------------- SEQ ID NO:44

---------- SEQ ID NO:45

TGTTCTGCCTCACTCCCGAGCTC--------- SEQ ID NO:46

Figure 9C

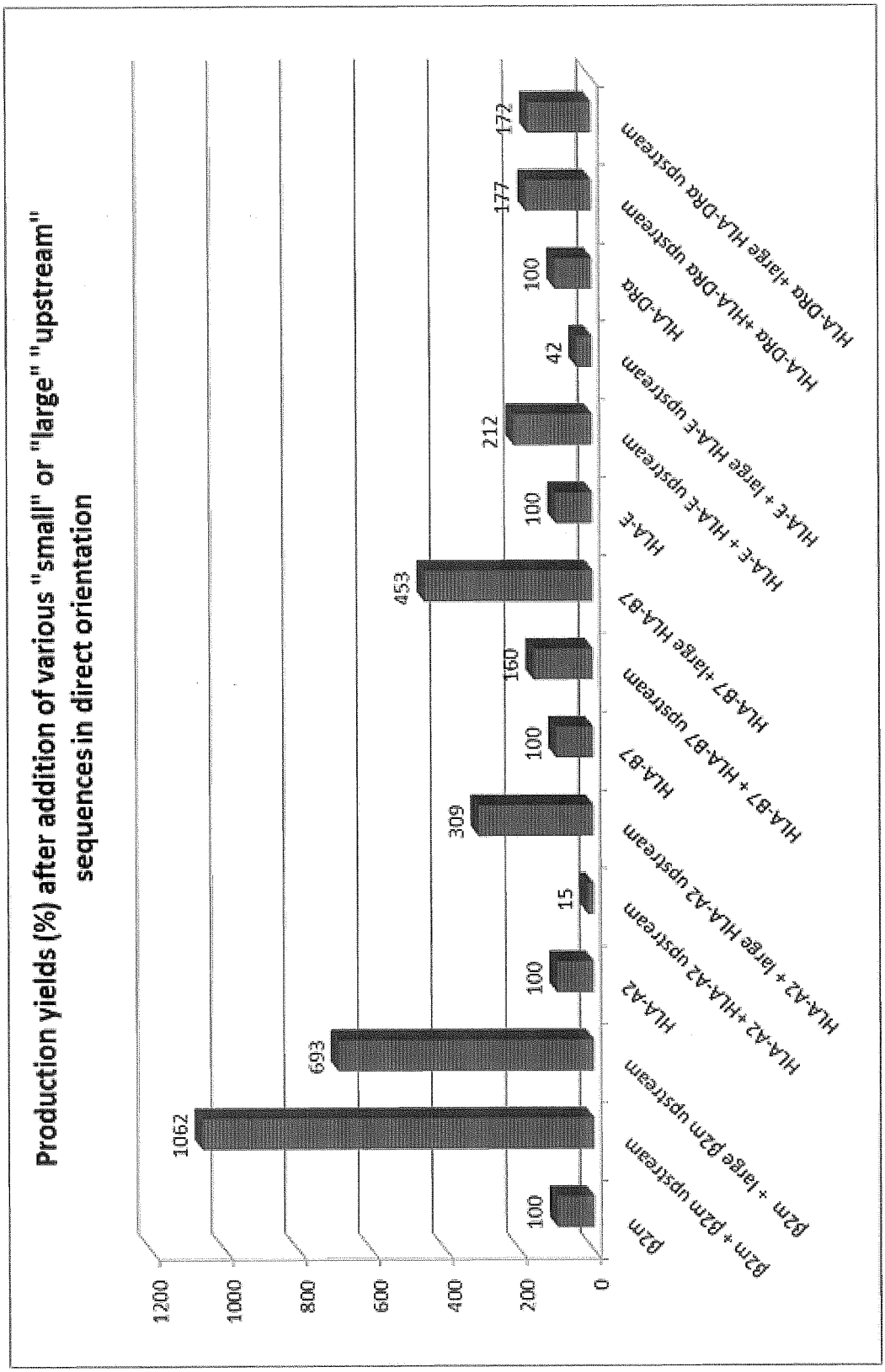

Production yields (%) after addition of various "small" or "large" "upstream" sequences in direct orientation
1200
1000
800
600
400
200
0
100
1062
693
100
15
309
100
160
453
100
212
42
100
177
172
β2m
β2m + β2m upstream
β2m + large β2m upstream
HLA-A2
HLA-A2 +HLA-A2 upstream
HLA-A2 + large HLA-A2 upstream
HLA-B7
HLA-B7 + HLA-B7 upstream
HLA-B7 +large HLA-B7
HLA-E
HLA-E + HLA-E upstream
HLA-E + large HLA-E upstream
HLA-DRα
HLA-DRα +HLA-DRα upstream
HLA-DRα +large HLA-DRα upstream

Figure 10