WHO
International Nonproprietary Names Programme

7/2020

11480

Schematic

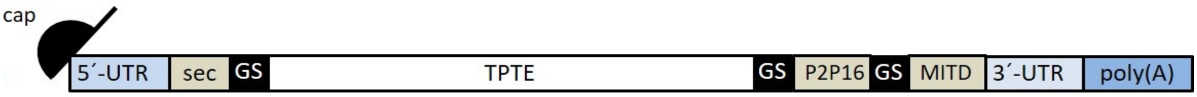


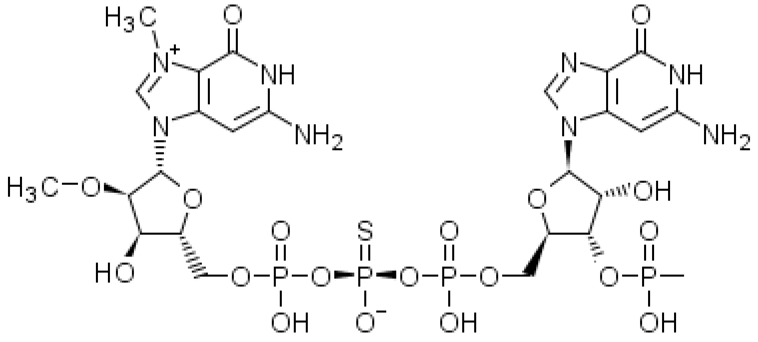
Table of features

Element	Description	Position
5´cap	A specific capping structure at the 5´-end for improved RNA stability and translational efficiency.	1-2
5'-UTR (hAg-Kozak)	The 5´-UTR sequence has been derived from the human alpha-globin RNA with an optimized "Kozak sequence".	3-53
sec	The secretory signal peptide "sec" derived from the sequence encoding the human MHC Class I complex alpha chain "HLA-I, Cw*" is used as a fusion-protein tag, to improve antigen processing and presentation.	54-131
GS	Sequences that code for short GS-rich linker peptides generally consisting of the amino acids glycine and serine (usually GGSGGGGSGG).	132-161, 1812-1841 and 2037-2078
TPTE	Codon-optimized sequences encoding the target protein TPTE.	162-1811
P2P16	Sequence coding for tetanus toxoid-derived helper epitopes to break immunological tolerance.	1842-2036
MITD	MITD corresponds to the transmembrane and cytoplasmic domain of the MHC class I molecule and is used as a fusion-protein tag, improve antigen processing and presentation.	2079-2249
3'-UTR (FI element)	The 3´-UTR is a combination of two sequence elements derived from the AES mRNA (called F) and the mitochondrial encoded 12S ribosomal RNA (called I) to confer RNA stability and highest total protein expression.	2250-2566
Poly(A)	A poly(A)-tail measuring 110 nucleotides in length, consisting of a stretch of 30 adenosine residues, followed by a 10-nucleotide linker sequence and another 70 adenosine residues.	2567-2676

Abbreviations: AES = amino terminal enhancer of split; GS = glycine and serine;

HLA = human leukocyte antigen, MHC = major histocompatibility complex; MITD = MHC class I transmembrane domain; UTR = untranslated region.

5‘- capping structure = G^1G^2: m^7Guo^+2'*O*Me-5'-p-(*R*)p^S-p-5'-G



1-2 : cap m^7Guo^+2'*O*Me-5'-p-(*R*)p^S-p-5'-G; *3-53* : 5'UTR; **54-131** : sec; **132-161** : $G_2SG_4SG_2$ linker; 162-1811 : TPTE; **1812-1841** : $G_2SG_4SG_2$ linker; **1842-2036** : P2P16 tetanustoxoid-derived helper epitopes; **2037-2078** : $GS_2G_4SPG_3S_2$ linker; **2079-2249** : MITD; *2250-2566* : FI element (3' UTR); **2567-2676** : A30L70 polyA tail.

Sequence / Séquence / Secuencia

GG_GGCGAACU AGUAUUCUUC UGGUCCCCAC AGACUCAGAG AGAACCCGCC_ 50
ACC**AUGAGAG UGAUGGCCCC CAGAACCCUG AUCCUGCUGC UGUCUGGCGC** 100
CCUGGCCCUG ACAGAGACAU GGGCCGGAAG CGGCGGCUCU GGAGGAGGCG 150
GCUCCGGAGG CAUGAACGAG AGCCCCGACC CUACAGAUCU GGCCGGCGUG 200
AUCAUCGAGC UGGGACCCAA CGAUAGCCCU CAGACCAGCG AGUUCAAGGG 250
GGCCACAGAG GAAGCCCCUG CCAAAGAGAG CCCCCACACC UCCGAGUUUA 300
AGGGCGCUGC UCGGGUGUCC CCUAUCAGCG AGAGCGUGCU GGCCCGGCUG 350
AGCAAGUUCG AGGUGGAGGA CGCCGAGAAC GUGGCCAGCU ACGACAGCAA 400
GAUCAAGAAA AUCGUGCACA GCAUCGUGUC CAGCUUCGCC UUCGGCCUGU 450
UCGGCGUGUU CCUGGUGCUG CUGGACGUGA CACUGAUCCU GGCCGACCUG 500
AUCUUCACCG ACAGCAAGCU GUACAUCCCC CUGGAAUACC GGUCCAUCAG 550
CCUGGCCAUU GCCCUGUUCU UUCUGAUGGA CGUGCUGCUG CGGGUGUUCG 600
UGGAGCGGCG GCAGCAGUAC UUCAGCGACC UGUUCAACAU CCUGGACACC 650
GCCAUCAUCG UGAUUCUGCU GCUGGUGGAU GUGGUGUACA UCUUCUUCGA 700
CAUCAAGCUG CUGAGAAACA UCCCCCGGUG GACCCAUCUG CUGCGGCUGC 750
UGAGACUGAU CAUCCUGCUG CGGAUCUUCC ACCUGUUCCA CCAGAAGCGG 800
CAGCUGGAAA AGCUGAUCAG ACGGCGGGUG UCCGAGAACA AGCGGCGGUA 850
CACCAGGGAC GGCUUCGACC UGGACCUGAC CUACGUGACC GAGCGGAUCA 900
UUGCCAUGAG CUUCCCCAGC AGCGGCAGAC AGAGCUUCUA CCGGAACCCC 950
AUCAAAGAAG UGGUGCGGUU CCUGGACAAG AAGCACCGGA ACCACUACCG 1000
GGUGUACAAC CUGUGCAGCG AGCGGGCCUA CGACCCCAAG CACUUCCACA 1050
ACCGGGUGGU GCGGAUCAUG AUCGACGACC ACAACGUGCC CACCCUGCAC 1100

CAGAUGGUGG UGUUCACCAA AGAAGUGAAC GAGUGGAUGG CCCAGGACCU 1150
GGAAAACAUC GUGGCCAUCC ACUGCAAGGG CGGCACCGAC AGAACCGGCA 1200
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CUGUUCAUCA AGCACUUCAU CAUCUACAGC AUCCCCAGAU ACGUGCGGGA 1450
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AUCGACGUGU UCGACGGCCU GCCCCUGUAC GACGACGUGA AGGUGCAGUU 1600
CUUCUACAGC AACCUGCCCA CCUACUACGA CAAUUGCAGC UUCUACUUCU 1650
GGCUGCACAC CAGCUUCAUC GAGAACAACA GGCUGUACCU GCCCAAGAAC 1700
GAGCUGGACA ACCUGCACAA GCAGAAGGCC AGAAGAAUCU ACCCCAGCGA 1750
CUUCGCCGUG GAGAUCCUGU UUGGCGAGAA GAUGACCAGC AGCGACGUGG 1800
UGGCCGGCAG C**GGAGGAUCC GGUGGUGGCG GCAGCGGCGG CAAGAAGCAG** 1850
UACAUCAAGG CCAACAGCAA GUUCAUCGGC AUCACCGAGC UGAAGAAGCU 1900
GGGAGGGGGC AAACGGGGAG GCGGCAAAAA GAUGACCAAC AGCGUGGACG 1950
ACGCCCUGAU CAACAGCACC AAGAUCUACA GCUACUUCCC CAGCGUGAUC 2000
AGCAAAGUGA ACCAGGGCGC UCAGGGCAAG AAACUGGGCU CUAGCGGAGG 2050
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UGGCAGUGCU GGCCGUGGUG GUGAUCGGAG CCGUGGUGGC UACCGUGAUG 2150
UGCAGACGGA AGUCCAGCGG AGGCAAGGGC GGCAGCUACA GCCAGGCCGC 2200
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*CGCUAGCCGC GUCGCU***AAAA AAAAAAAAAA AAAAAAAAAA AAAAAAGCAU** 2600
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AAAAAAAAAA AAAAAAAAAA AAAAAA 2676