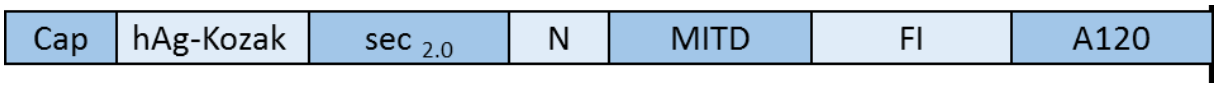
11177

Schematic



Element	Description
Cap	Beta-S-ARCA(D1) is utilized as a specific capping structure at the 5′-end for improved RNA stability and translational efficiency.
hAg-Kozak	The 5′-UTR sequence has been derived from human alpha-globin RNA. An optimized “Kozak sequence” has been added in order to increase translational efficiency.
$sec_{2.0}$	The secretory signal peptide “$sec_{2.0}$” derived from the sequence encoding human MHC Class I complex alpha chain “HLA-I, Cw*” is used as a fusion-protein tag to improve antigen processing and presentation.
N	Position of insertion of patient-specific sequences.
MITD	MITD corresponds to the transmembrane and cytoplasmic domains of the MHC class I molecule and is used as a fusion-protein tag to improve antigen processing and presentation.
FI	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). These were identified by performing an *ex vivo* selection process for sequences that confer RNA stability.
A120	A poly(A)-tail measuring 120 nucleotides (A120) is added to ensure high RNA stability and protein expression.

Abbreviations: AES = amino terminal enhancer of split; MHC = major histocompatibility complex; MITD = MHC class I transmembrane and cytoplasmic domains; UTR = untranslated region.

Cap structure

The 5'- capping structure beta-S-ARCA(D1) ($m_2^{7,2'\text{-}O}Gpp_spG$) used at the 5' end. The stereogenic P centre is *Rp*-configured in the "D1" isomer. Shown in red are the differences between beta-S-ARCA(D1) and the basic cap structure m^7GpppG; an -OCH3 group at the C2' position of the building block m^7G and substitution of a non-bridging oxygen at the beta-phosphate by sulphur. Owing to the presence of a stereogenic P center (labelled with *), the phosphorothioate cap analogue beta-S-ARCA exists as two diastereomers. Based on their elution order in reversed-phase high-performance liquid chromatography, these have been designated as D1 and D2.

Table of features

Feature		Position
Capping structure	phosphorothioate stabilized cap analogue	1-2
hAG-Kozak	Human α-globin Kozak region	3-53
$sec_{2.0}$	secretion signal sequence	54-131
N	indicates location of insertion of patient-specific sequences	132
MITD	transmembrane and cytoplasmic domains of MHC class I molecule	133-303
FI	sequence element derived of the amino terminal enhancer of split RNA (F) and from the mitochondrially encoded 12S RNA (I)	304-620
A120	poly A tail of 120 nucleotides	621-740

Sequence / Séquence / Secuencia

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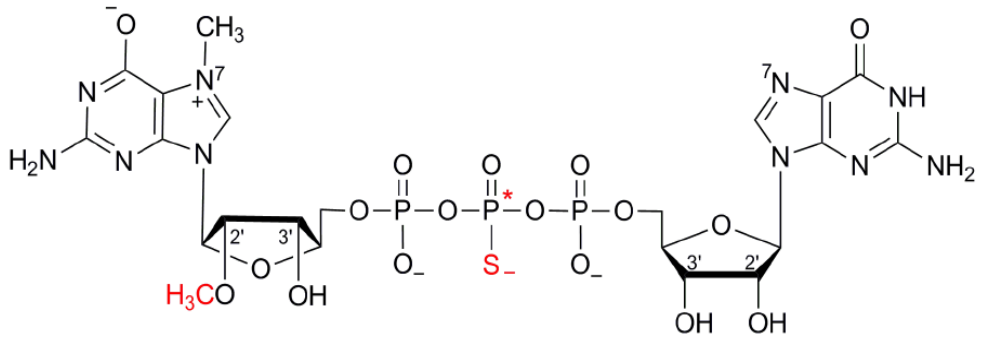

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CCGCCAGCUC UGAUAGCGCC CAGGGCAGCG ACGUGUCACU GACAGCCUAG    300
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CCUGGGUACC CCGAGUCUCC CCCGACCUCG GGUCCCAGGU AUGCUCCCAC    400
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