NR1 motif as discussed herein, and S represents an optional spacer. When two or more NR1 motifs are present, they can be identical NR1 or they can be different to one another Further, when a spacer is present, it can have any sequence and be of any suitable length. For example, each spacer can be independently from 2 to 50 nucleotides in length. In some embodiments, each spacer is from 3 to 40, from 4 to 30, from 5 to 20, from 6 to 10, or from 7 to 9 nucleotides in length. In some embodiments, each spacer is independently, 5, 6, 7, 8, 9, 10 or 11 nucleotides in length.

[00156] In some embodiments of any one of the aspects described herein, the NR1 motif comprises the nucleotide sequence $[TGTACTTTCCTGACCN\text{-}S\text{-}]_n$ (**SEQ ID NO: 8**), or $[CTGTACTTTCCTGACCN\text{-}S\text{-}]_n$ (**SEQ ID NO: 9**), wherein N is any nucleotide, n is an integer from 1 to 10, and S is absent or a spacer.

[00157] In some embodiments, n is an integer from 1 to 6. For example, n is an integer from 2 to 4. In some embodiments, n is selected from 2, 3, or 4. For example, n is 1, 2 or 3. In some embodiments, n is 1. In some other embodiments, n is 2. In yet some other embodiments, n is 3.

[00158] When present, each spacer, S, can be independently from 2 to 50 nucleotides in length. In some embodiments, each spacer, S, is from 3 to 40, from 4 to 30, from 5 to 20, from 6 to 10, or from 7 to 9 nucleotides in length. In some embodiments, each spacer, S, is independently, 5, 6, 7, 8, 9, 10 or 11 nucleotides in length.

[00159] In some embodiments of any one of the aspects described herein, n is 2 or 3. For example, the functional variant of a PBREM motif comprises the nucleotide sequence:

TGTACTTTCCTGACCN-S-TGTACTTTCCTGACCN (**SEQ ID NO: 10**) ("TGTACTTTCCTGACCN" disclosed as SEQ ID NO: 6);

TGTACTTTCCTGACCN-S-TGTACTTTCCTGACCN-S-TGTACTTTCCTGACCN (**SEQ ID NO: 11**) ("TGTACTTTCCTGACCN" disclosed as SEQ ID NO: 6);

CTGTACTTTCCTGACCN-S-CTGTACTTTCCTGACCN (**SEQ ID NO: 12**) ("CTGTACTTTCCTGACCN" disclosed as SEQ ID NO: 7);

CTGTACTTTCCTGACCN-S-CTGTACTTTCCTGACCN-S-CTGTACTTTCCTGACCN (**SEQ ID NO: 13**) ("CTGTACTTTCCTGACCN" disclosed as SEQ ID NO: 7);

NCTGTACTTTCCTGACCNTG-S-NCTGTACTTTCCTGACCNTG (**SEQ ID NO: 14**) ("NCTGTACTTTCCTGACCNTG" disclosed as SEQ ID NO: 73); or

NCTGTACTTTCCTGACCNTG-S-NCTGTACTTTCCTGACCNTG-S-NCTGTACTTTCCTGACCNTG (**SEQ ID NO: 15**) ("NCTGTACTTTCCTGACCNTG" disclosed as SEQ ID NO: 73),

wherein N is any nucleotide, and S is absent or a spacer.

[00160] In some embodiments of any one of the aspects described herein, n is 3. For example, the functional variant of a PBREM motif comprises the nucleotide sequence:TCTGTACTTTCCTGACCTTG-S-TCTGTACTTTCCTGACCTTG-S-TCTGTACTTTCCTGACCTTG (**SEQ ID NO: 16**) ("TCTGTACTTTCCTGACCTTG" disclosed as SEQ ID NO: 74); or

ACTGTACTTTCCTGACCCTG-S-ACTGTACTTTCCTGACCCTG-S-ACTGTACTTTCCTGACCCTG (**SEQ ID NO: 17**) ("ACTGTACTTTCCTGACCCTG" disclosed as SEQ ID NO: 75),

wherein N is any nucleotide, and S is absent or a spacer.

[00161] In some embodiments of any one of the aspects described herein, the functional variant of a PBREM motif comprises the nucleotide sequence:

gatcTCTGTACTTTCCTGACCTTGgatcgatcTCTGTACTTTCCTGACCTTGgatcgatcTCTGTACTTTCCTGACCTTGgatc (**SEQ ID NO: 18**); or

gatcACTGTACTTTCCTGACCCTGgatcgatcACTGTACTTTCCTGACCCTGgatcgatcACTGTACTTTCCTGACCCTGgatc (**SEQ ID NO: 19**).

NF1

[00162] Generally, the NF1 motif comprises a nucleotide sequence that varies by 7 or fewer nucleotides (e.g., 6, 5, 4, 3, 2, or 1 nucleotides) from nucleotides 19 to 31 of SEQ ID NO: 1 or SEQ ID NO: 2. For example, the NF1 motif comprises the nucleotide sequence TGGCACAGTGCCA (**SEQ ID NO: 20**) or TGAAGAGGTGGCA (**SEQ ID NO: 21**), or a nucleotide sequence that varies no more than 7 nucleotides from **SEQ ID NO: 20 or SEQ ID NO: 21**. In some embodiments of any one of the aspects described herein, the NF1 motif comprises a nucleotide sequence that varies by no more than 1 to 6 nucleotides from **SEQ ID NO: 20 or SEQ ID NO: 21**. For example, the NF1 motif comprises a nucleotide sequence that varies by no more than 1, 2, 3, 4 or 5 nucleotides from **SEQ ID NO: 20 or SEQ ID NO: 21**. In some embodiments of any one of the aspects described herein, the NF1 motif comprises a nucleotide sequence that varies by no more than 1 or 2 nucleotides from **SEQ ID NO: 20 or SEQ ID NO: 21**.

[00163] In some embodiments of any one of the aspects described herein, the NF1 motif comprises the nucleotide sequence TGNNNNNGTGNCA, where N is any nucleotide.

[00164] In some embodiments of any one of the aspects described herein, the NF1 motif consists of **SEQ ID NO: 20 or SEQ ID NO: 21**.

NR2 motif

[00165] Generally, the NR2 motif comprises a nucleotide sequence that varies by 5 or fewer nucleotides (e.g., 4, 3, 2, or 1 nucleotides) from nucleotides 35 to 50 of SEQ ID NO: 1 or SEQ ID NO: 2. For example, the NR2 motif suitably comprises the nucleotide sequence TCAACTTGCCTGACAC (**SEQ ID NO: 23**) or TGGACTTTCCTGAACC (**SEQ ID NO: 24**), or a nucleotide sequence that varies by no more than by 5 nucleotides from **SEQ ID NO: 23 or SEQ**

independently from 15 to 25 nucleotides in length. In some embodiments, each spacer, L, is independently 18, 19, 20, 21 or 22 nucleotides in length. A spacer of approximately 20 nucleotides in length has been found to be particularly suitable. In some non-limiting examples, each spacer, L, is a multiple of 5 nucleotides in length.

[00182] In some embodiments of any one of the aspects described herein, the CRM comprises the nucleotide sequence:

NCTGTACTTTCCTGACCNTGNNNNNGTGNCANCATNNACTTNCCTGANNCN-L-NCTGTACTTTCCTGACCNTGNNNNNGTGNCANCATNNACTTNCCTGANNCN (**SEQ ID NO: 28**) ("NCTGTACTTTCCTGACCNTGNNNNNGTGNCANCATNNACTTNCCTGANNCN" disclosed as SEQ ID NO: 26); or

NCTGTACTTTCCTGACCNTGNNNNNGTGNCANCATNNACTTNCCTGANNCN-L-NCTGTACTTTCCTGACCNTGNNNNNGTGNCANCATNNACTTNCCTGANNCN-L-NCTGTACTTTCCTGACCNTGNNNNNGTGNCANCATNNACTTNCCTGANNCN (**SEQ ID NO: 29**) ("NCTGTACTTTCCTGACCNTGNNNNNGTGNCANCATNNACTTNCCTGANNCN" disclosed as SEQ ID NO: 26),

wherein N is any nucleotide and L is absent or a spacer.

[00183] In some embodiments of any one of the aspects described herein, the CRM comprises a nucleotide sequence having at least 60% identity to the nucleotide sequence:

TCTGTACTTTCCTGACCTTGGCACAGTGCCACCATCAACTTGCCTGACACC-L-TCTGTACTTTCCTGACCTTGGCACAGTGCCACCATCAACTTGCCTGACACC (**SEQ ID NO: 30**) ("TCTGTACTTTCCTGACCTTGGCACAGTGCCACCATCAACTTGCCTGACACC" disclosed as SEQ ID NO: 1);

TCTGTACTTTCCTGACCTTGGCACAGTGCCACCATCAACTTGCCTGACACC-L-TCTGTACTTTCCTGACCTTGGCACAGTGCCACCATCAACTTGCCTGACACC-L-TCTGTACTTTCCTGACCTTGGCACAGTGCCACCATCAACTTGCCTGACACC (**SEQ ID NO: 31**) ("TCTGTACTTTCCTGACCTTGGCACAGTGCCACCATCAACTTGCCTGACACC" disclosed as SEQ ID NO: 1);

ACTGTACTTTCCTGACCCTGAAGAGGTGGCAGCATGGACTTTCCTGAACCA-L-ACTGTACTTTCCTGACCCTGAAGAGGTGGCAGCATGGACTTTCCTGAACCA-L-ACTGTACTTTCCTGACCCTGAAGAGGTGGCAGCATGGACTTTCCTGAACCA (**SEQ ID NO: 32**)

("ACTGTACTTTCCTGACCCTGAAGAGGTGGCAGCATGGACTTTCCTGAACCA" disclosed as SEQ ID NO: 2); or

ACTGTACTTTCCTGACCCTGAAGAGGTGGCAGCATGGACTTTCCTGAACCA-L-ACTGTACTTTCCTGACCCTGAAGAGGTGGCAGCATGGACTTTCCTGAACCA (**SEQ ID NO: 33**)

("ACTGTACTTTCCTGACCCTGAAGAGGTGGCAGCATGGACTTTCCTGAACCA" disclosed as SEQ ID NO: 2),

wherein L is absent or a spacer.

[00184] For example, the CRM comprises a nucleotide sequence that is at least 65%, 70%, 75%, 80%, 85%, or 90% identical to one of **SEQ ID NO: 30-33**. In some embodiments of any one of the aspects described herein, the inducible promoter comprises a nucleotide sequence having at least 95% identity to one of **SEQ ID NO: 30-33**. For example, the inducible promoter comprises

ACGCCATCCACGCTGTTTTGACCTCCATAGAAGATCGCCACCC (**SEQ ID NO: 53**, PB1-1-CMV);

TCTGTACTTTCCTGACCTTGGCACAGTGCCACCATCAACTTGCCTGACACCCA
TTACTCGCATCCATTCTCTCTGTACTTTCCTGACCTTGGCACAGTGCCACCATC
AACTTGCCTGACACCGCACTGAAGGTCCTCAATCGTCTGTACTTTCCTGACCT
TGGCACAGTGCCACCATCAACTTGCCTGACACCGCTGGGAGTTCGTAGACGG
A**GCGATTAATCCATATGCAGGTCTATATAAGCAGAGCTCGTTTAGTGAAC**
CGTCAGATCGCCTAGATACGCCATCCACGCTGTTTTGACCTCCATAGAAG
ATCGCCACCC (**SEQ ID NO: 54**, PB1-2-CMV);

TCTGTACTTTCCTGACCTTGGCACAGTGCCACCATCAACTTGCCTGACACCCA
TTACTCGCATCCATTCTCTCTGTACTTTCCTGACCTTGGCACAGTGCCACCATC
AACTTGCCTGACACCGCACTGAAGGTCCTCAATCGTCTGTACTTTCCTGACCT
TGGCACAGTGCCACCATCAACTTGCCTGACACCCTGACCTCCTGCCAGCAATA
TCTGTACTTTCCTGACCTTGGCACAGTGCCACCATCAACTTGCCTGACACCGC
TGGGAGTTCGTAGACGGA**GCGATTAATCCATATGCAGGTCTATATAAGCA**
GAGCTCGTTTAGTGAACCGTCAGATCGCCTAGATACGCCATCCACGCTG
TTTTGACCTCCATAGAAGATCGCCACCC (**SEQ ID NO: 55**, PB1-3-CMV);

ACTGTACTTTCCTGACCCTGAAGAGACTGTACTTTCCTGACCCTGAAGAGACT
GTACTTTCCTGACCCTGAAGAGGATCCGGCCCCGCCCAGCGTCTTGTCATTGG
CGAATTCGAACACGCAGATGCAGTCGGGGCGGCGCGGTCCGAGGTCCAC**TTC**
GCATATTAAGGTGACGCGTGTGGCCTCGAACACCGAGCGACCCTGCAGC
GACCCGCTTAACAGCGTCAACAGCGTGCCGCAGATCTCGAGGAGCTTGGCG
AGATTTTCAGGAGCT (SEQ ID NO: 49, human NR1x3-MinTK);
ACTGTACTTTCCTGACCCTGAAGAGGTGGCAGCATGGACTTTCCTGAACCAGA
TCCGGCCCCGCCCAGCGTCTTGTCATTGGCGAATTCGAACACGCAGATGCAGT
CGGGGCGGCGCGGTCCGAGGTCCAC**TTCGCATATTAAGGTGACGCGTGTG**
GCCTCGAACACCGAGCGACCCTGCAGCGACCCGCTTAACAGCGTCAACAG
CGTGCCGCAGATCTCGAGGAGCTTGGCGAGATTTTCAGGAGCTAAGGAAGCT
AAACATGGAAGATGCCAAAAACATTAAG (**SEQ ID NO: 56**, human PBREM-MinTK);

AACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATCGCTGACTAATTTTTT TTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAA GTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTTGGCA TTCCGGTACTGTTGGTAAAGCCACCC (**SEQ ID NO: 61**, hPB-SV40);

TCTGTACTTTCCTGACCTTGAAGAGGTGGCACCATCAACTTGCCTGACACCGC TGGGAGTTCGTAGACGGACTAGCCCGGGCTCGAGATCTGCGATCTGCATCTC AATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTAAC TCCGCCCAGTTCCGCCCATTCTCCGCCCCATCGCTGACTAATTTTTTTTATTTA TGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGA GGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTTGGCATTCCGGTACTGTT GGTAAAGCCACCC (**SEQ ID NO: 62**, MHM-SV40);

ACTGTACTTTCCTGACCCTGAAGAGGTGGCAGCATGGACTTTCCTGAACCACA TTACTCGCATCCATTCTCACTGTACTTTCCTGACCCTGAAGAGGTGGCAGCAT GGACTTTCCTGAACCAGCTGGGAGTTCGTAGACGGACTAGCCCGGGCTCGAG ATCTGCGATC**TGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACT CCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCA TCGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCT CTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTT TTGCAAA**AAGCTTGGCATTCCGGTACTGTTGGTAAAGCCACCC (**SEQ ID NO: 63**, 2xhPB SV40);

TCTGTACTTTCCTGACCTTGAAGAGGTGGCACCATCAACTTGCCTGACACCCA TTACTCGCATCCATTCTCTCTGTACTTTCCTGACCTTGAAGAGGTGGCACCATC AACTTGCCTGACACCGCTGGGAGTTCGTAGACGGAGATCCGGCCCCGCCCAG CGTCTTGTCATTGGCGAATTCGAACACGCAGATGCAGTCGGGGCGGCGCGGT CCGAGGTCCAC**TTCGCATATTAAGGTGACGCGTGTGGCCTCGAACACCGA GCGACCCTGCAGCGACCCGCTTAA**CAGCGTCAACAGCGTGCCGCAGATCTC GAGGAGCTTGGCGAGATTTTCAGGAGCTAAGGAAGCTAAAC (**SEQ ID NO: 64**, 2xMHM MinTK);

TCTGTACTTTCCTGACCTTGAAGAGGTGGCACCATCAACTTGCCTGACACCCA TTACTCGCATCCATTCTCTCTGTACTTTCCTGACCTTGAAGAGGTGGCACCATC AACTTGCCTGACACCGCTGGGAGTTCGTAGACGGACTAGCCCGGGCTCGAG