# Comparative analysis of oncogenic properties and nuclear factor-κB activity of latent membrane protein 1 natural variants from Hodgkin's lymphoma's Reed-Sternberg cells and normal B-lymphocytes

Nathalie Faumont,[1,2,3] Aurélie Chanut,[3] Alan Benard,[1,2] Nadine Cogne,[3] Georges Delsol,[1,2] Jean Feuillard,[3] and Fabienne Meggetto[1,2]

[1]INSERM, U563, Centre de Physiopathologie de Toulouse Purpan, Toulouse, France; [2]Université Toulouse III Paul Sabatier, Institut Claude de Préval, Toulouse, France and [3]Centre National de la Recherche Scientifique, Unité Mixte de Recherche 6101, Centre Hospitalier Universitaire Dupuytren, Université de Limoges, Laboratoire d'Hématologie, Limoges, France

*Citation: Faumont N, Chanut A, Benard A, Cogne N, Delsol G, Feuillard J, and Meggetto F. Comparative analysis of oncogenic properties and nuclear factor-kB activity of latent membrane protein 1 natural variants from Hodgkin's lymphoma's Reed-Sternberg cells and normal B-lymphocytes. Haematologica 2009; 94:355-363. doi:10.3324/haematol.13269*

*See the pdf.*

Online Supplementary Figure S1. Nucleotide sequence patterns identified in the *LMP1-BNLF1* genes coding for LMP1 natural variants from Reed-Sternberg cells (RS1 to RS5-LMP1-variants), non-tumor B-cells of Hodgkin's lymphomas (NT1, NT4, and NT6-LMP1-variants) and from B-cells of benign reactive lymph nodes (RN1 to RN4-LMP1-variants). The sequence of the prototype *B95.8-BNLF1* gene is numbered on the basis of published sequences (GenBank accession number X01995). Nucleotide differences from the *B95.8-BNLF1* sequence are underlined in gray. Hyphens specify absence of nucleotides such as del15bp (nucleotides 168.496 to 168.482) and del30bp (nucleotides 168.286 to 168.257). The *B95.8-BNLF1* sequence in italics, underlined with one or two lines indicate the N-terminal region (nucleotides 169.475 to 169.406), the six transmembrane spanning hydrophobic domains (nucleotides 169.406 to 168.764) and the cytoplasmic C-terminal region (nucleotides 168.763 to 168.161), respectively. Sequences boxed represent the two intronic segments (nucleotides 169.207 to 169.130 and 169.043 to 168.967). Sequences in bold are the two functional domains, CTAR1 (nucleotides 168.743 to 168.626) and CTAR2 (nucleotides 168.271 to 168.164). The 33 bp repeat units are indicated by dotted boxes (nucleotides 168.574 to 168.428). Asterisks indicate nucleotide sequence identity between all the *LMP1-BNLF1* genes.

```
B95.8   169.475  ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC 169.416
RS1              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
RS2              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
RS3              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
RS4              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
RS5              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
NT1              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
NT4              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
NT6              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
RN1              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
RN2              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
RN3              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
RN4              ATGGAACACGACCTTGAGAGGGGCCCACCGGGCCCGCGACGGCCCCCTCGAGGACCCCCC
                 ************************************************************

B95.8            CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTGGCGCTACTGTTTTGGCTG 169.356
RS1              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTGGCGCTACTGTTTTGGCTG
RS2              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTTGCGCTACTGTTTTGGCTG
RS3              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTGGCGCTACTGTTTTGGCTG
RS4              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTTGCGCTACTGTTTTGGCTG
RS5              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTGGCGCTACTGTTTTGCCTG
NT1              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTGGCGCTACTGTTTTGGCTG
NT4              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTTGCGCTACTGTTTTGGCTG
NT6              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTGGCGCTACTGTTTTGGCTG
RN1              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTGGCGCTACTGTTTTGGCTG
RN2              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTGGCGCTACTGTTTTGGCTG
RN3              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTGGCGCTACTGTTTTGGCTG
RN4              CTCTCCTCTTCCCTAGGCCTTGCTCTCCTTCTCCTCCTCTTGGCGCTACTGTTTTGGCTG
                 ***************************************** ************** ***

B95.8            TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC 169.296
RS1              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCCTGTCCTCTATTCCTTTGCTCTC
RS2              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC
RS3              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC
RS4              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC
RS5              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC
NT1              TACATCGTTATGAGTGACTGGACTGGAGGAGTCCTCCTTGTCCTCTATTCCTTTGCTCTC
NT4              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC
NT6              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC
RN1              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC
RN2              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC
RN3              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC
RN4              TACATCGTTATGAGTGACTGGACTGGAGGAGCCCTCCTTGTCCTCTATTCCTTTGCTCTC
                 ******************************* ***** **********************

B95.8            ATGCTTATAATTATAATTTTGATCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT 169.236
RS1              ATGCTTATAATTATAATTTTGATCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT
RS2              ATGCTTATAATTATAATTTTGCTCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT
RS3              ATGCTTATAATTATAATTTTGATCATCTTTATCTTCAGGAGAGACCTTCTCTGTCCACTT
RS4              ATGCTTATAATTATAATTTTGCTCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT
RS5              ATGCTTATCATTATCATTTTGATCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT
NT1              ATGCTTATAATTATAATTTTGATCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT
NT4              ATGCTTATAATTATAATTTTGATCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT
NT6              ATGCTTATAATTATAATTTTGATCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT
RN1              ATGCTTATAATTATAATTTTGATCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT
RN2              ATGCTTATAATTATAATTTTGATCATCTTTATCTTCAGGAGAGACCTTCTCTGTCCACTT
RN3              ATGCTTATAATTATAATTTTGATCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT
RN4              ATGCTTATAATTATAATTTTGATCATCTTTATCTTCAGAAGAGACCTTCTCTGTCCACTT
                 ******** ***** ****** **************** *********************

B95.8            GGAGCCCTTTGTATACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT 169.176
RS1              GGAGCCCTTTGTCTACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT
RS2              GGAGCCCTTTGTCTACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACTCCCCCT
RS3              GGAGCCCTTTGTATACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT
RS4              GGAGCCCTTTGTCTACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT
RS5              GGAGCCCTTTGTCTACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT
NT1              GGAGCCCTTTGTATACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT
NT4              GGAGCCCTTTGTATACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT
NT6              GGAGCCCTTTGTCTACTCCTACTGATGAGTAAGTATTACACCCTTTGCCTCACACCCCCT
RN1              GGAGCCCTTTGTATACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT
RN2              GGAGCCCTTTGTATACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT
RN3              GGAGCCCTTTGTATACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT
RN4              GGAGCCCTTTGTATACTCCTACTGATGAGTAAGTATTACACCCTTTGCCCCACACCCCCT
                 ************ ************************************ *** ******

B95.8            TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC 169.116
```

```
RS1       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
RS2       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
RS3       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
RS4       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
RS5       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
NT1       CTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
NT4       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
NT6       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
RN1       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
RN2       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
RN3       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCAGTCACCCTCCTGCTC
RN4       TTCCCTTACTCTTCCTTCTCTAACGCACTTTCTCCTCTTTCCCCGGTCACCCTCCTGCTC
           ******************************************* ***************

B95.8     ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTTCCTTGGAATTGTGCTGTTCATCTTC 169.056
RS1       ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTACCTTGGAATTGTGCCGTTCATCTTC
RS2       ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTACCTTGGAATTGTGCTGTTCATCTTC
RS3       ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTTCCTTGGAATTGTGCTGTTCATCTTC
RS4       GTCGCTCTCTGGAATTTGCACGGACAGGCATTGTACCTTGGAATTGTGCTGTTCATCTTC
RS5       ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTACCTTGGAATTGTGCTGTTCATCTTC
NT1       ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTTCCTTGGAATTGTGCTGTTCATCTTC
NT4       ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTTCCTTGGAATTGTGCTGTTCATCTTC
NT6       ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTACCTTGGAATTGTGCTGTTCATCTTC
RN1       ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTTCCTTGGAATTGTGCTGTTCATCTTC
RN2       ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTTCCTTGGAATTGTGCTGTTCATCTTC
RN3       ATCGCTCTCTGGAATTTGCACGGACAGGCATCGTTCCTTGGAATTGTGCTGTTCATCTTC
RN4       ATCGCTCTCTGGAATTTGCACGGACAGGCATTGTTCCTTGGAATTGTGCTGTTCATCTTC
           ****************************** ** ************** **********

B95.8     GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT 168.996
RS1       GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT
RS2       CGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT
RS3       GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT
RS4       GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT
RS5       GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT
NT1       GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT
NT4       GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATCATTTACCACACCCCCACTTTT
NT6       GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT
RN1       GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT
RN2       GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT
RN3       GGGTGCTTACTTGGTAAGATCTAACATTCCCTAGGAATTATTTACCACACCCCCACTTTT
RN4       GGGTGCTTACTTGGTAAGATCTAACATTCCCAAGGAATTATTTACCACACCCCCACTTTT
          ******************************* ****** *********************

B95.8     CCAACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTATCTGGATCTACTTATTGGAGAT 168.936
RS1       CCCACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTCTCTGGATCTACTTATTGGAGAT
RS2       CCCACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTCTCTGGATCTACTTATTGGAGAT
RS3       CCAACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTATCTGGATCTACTTATTGGAGAT
RS4       CCCACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTCTCTGGATCTACTTATTGGAGAT
RS5       CCAACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTCTCTGGATCTACTTATTGGAGAT
NT1       CCAACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTATCTGGATCTACTTATTGGAGAT
NT4       CCAACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTATCTGGATCTACTTATTGGAGAT
NT6       CCAACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTGTCTGGATCTACTTATTGGAGAT
RN1       CCAACCCTAACACTCTTTTTTCAACGCAGTCTTAGGCATCTGGATCTACTTATTGGAGAT
RN2       CCAACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTATCTGGATCTACTTATTGGAGAT
RN3       CCAACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTATCTGGATCTACTTATTGGAGAT
RN4       CCAACCCTAACACTCTTTTTTCAACGCAGTCTTAGGTATCTGGATCTACTTATTGGAGAT
          ** *********************************  **********************

B95.8     GCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT 168.876
RS1       TCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT
RS2       TCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT
RS3       GCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT
RS4       TCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT
RS5       TCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT
NT1       GCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT
NT4       GCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT
NT6       GCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT
RN1       GCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCCTCTTCCT
RN2       GCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT
RN3       GCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCTTCTTCCT
RN4       GCTCTGGCGACTTGGTGCCACCATCTGGCAGCTTTTGGCCTTCTTCCTAGCCCTCTTCCT
           *************************************************** *******
```

```
B95.8           AGACCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT 168.816
RS1             AGACCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
RS2             AGACCTCATCCTGCCCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
RS3             AGACCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
RS4             AGACCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
RS5             AGACCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
NT1             AGACCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
NT4             AGACCTCATCCCGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
NT6             AGACCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
RN1             AGACCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
RN2             AGGCCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
RN3             AGACCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
RN4             AGACCTCATCCTGCTCATTATTGCTCTCTATCTACAACAAAACTGGTGGACTCTATTGGT
                ** ******** ** *********************************************

B95.8           TGATCTCCTTTGGCTCCTCCTGTTTCTGGCGATTTTAATCTGGATGTATTACCATGGACA 168.756
RS1             TGATCTCCCTTGGCTCCTCCTGTTTCTGGCGATTTTAATCTGGATGTATTACCATGGACA
RS2             TGATCTCCTTTGGCTCCTCCCGTTTCTGGCGATTTTAATCTGGATGTATTACCATGGACA
RS3             TGATCTCCTTTGGCTCCTCCTGTTTCTGGCGATTTTAATCTGGATGTATTACCATGGACA
RS4             TGATCTCCTTTGGCTCCTCCTGTTTCTGGCGATTTTAATCTGGATGTATTACCATGGACA
RS5             TGATCTCCTTTGGCTCCTCCTGTTTCTGGCCATTTTAATCTGGATGTATTATCATGGACC
NT1             TGATCTCCTTTGGCTCCTCCTGTTTCTGGCGATTTTAATCTGGATGTATTACCATGGACA
NT4             TGATCTCCTTTGGCTCCTCCTGTTTCTGGCGATTTTAATCTGGATGTATTACCATGGACA
NT6             TGATCTCCTTTGGCTCCTCCTGTTTCTGGCGATTTTAATCTGGATGTATTACCGTGGACA
RN1             TGATCTCCTTTGGCTCCTCCTGTTTCTGGCGGTTTTAATCTGGATGTATTACCATGGACA
RN2             TGATCTCCTTTGGCTCCTCCTGTTTCTGGCGATTTTAATCTGGATGTATTACCATGGACA
RN3             TGATCTCCTTTGGCTCCTCCTGTTTCTGGCGATTTTAATCTGGATGTATTACCATGGACA
RN4             TGATCTCCTTTGGCTCCTCCTGTTTCTGGCGATTTTAATCTGGATGTATTACCATGGACA
                ******** *********** *********  ******************* * ***** 

B95.8           ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA 168.696
RS1             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
RS2             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
RS2             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
RS3             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
RS4             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
RS5             ACGACACACTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
NT1             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
NT4             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
NT6             ACGACACAGTGATGAGCACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCCA
RN1             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
RN2             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
RN3             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
RN4             ACGACACAGTGATGAACACCACCACGATGACTCCCTCCCGCACCCTCAACAAGCTACCGA
                ******** ****** ****************************************** *

B95.8           TGATTCTGGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTCGTGAG 168.636
RS1             TGATTCTAGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCGCCTGCTCGTGAC
RS2             TGATTCTAGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTCGTGAC
RS3             TGATTCTGGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTTGTGAG
RS4             TGATTCTGGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTCGTGAG
RS5             CGATTCTAGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTCGTGAG
NT1             TGATTCTGGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTCGTGAG
NT4             TGATTCTGGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTCGTGAG
NT6             TGATTCTAGCAATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTCGTGAG
RN1             TGATTCTGGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTCGTGAG
RN2             TGATTCTGGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTTGTGAG
RN3             TGATTCTGGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTCGTGAG
RN4             TGATTCTGGCCATGAATCTGACTCTAACTCCAACGAGGGCAGACACCACCTGCTCGTGAG
                 ****** ** ************************************ ****** **** 

B95.8           TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC 168.576
RS1             TGGAGCCGGCAACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
RS2             TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
RS3             TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
RS4             TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
RS5             TGGGGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
NT1             TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
NT4             TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
NT6             TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTGGGCGCACCTGGAGGTGGTCC
RN1             TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
RN2             TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
RN3             TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
RN4             TGGAGCCGGCGACGGACCCCCACTCTGCTCTCAAAACCTAGGCGCACCTGGAGGTGGTCC
                *** ****** **************************** ********************

B95.8           TGACAATGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAA 168.516
RS1             TGACAATACCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAA
```

```
RS2       TGACAATGGCCCACAGGACCCTGACAACACTGATGACAATGACCCACAGGGCCCTGACAA
RS3       TGACAATGGCCCACAGGACCCTGACAACACTGATGACAGTGGCCCACAGGACCCTGACAA
RS4       TGACAATGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAA
RS5       TGACAATGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAA
NT1       TGATAATGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAA
NT4       TGACAATGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAA
NT6       TGACAATGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAA
RN1       TGACAATGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAA
RN2       TGACAATGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGGCCCTGACAA
RN3       TGACAATGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAA
RN4       TGACAATGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAA
          *** ***  ***************************** ** ******** *********

B95.8     CACTGATGACAATGGCCCACATGACCCGCTGCCTCAGGACCCTGACAACACTGATGACAA 168.456
RS1       CACTGATGACAATGGCCCA---------------CAGGACCCTGACAACACTGATGACAA
RS2       CACTGATGACAATGGCCCA---------------CAGGGCCCTGACAACACTGATGACAA
RS3       CACTGATGACAATGGCCCACACGACCCGCTGCCTCAGGACCCTGACAACACTGATGACAA
RS4       CACTGATGACAATGGCCCACATGACCCGCTGCCTCAGGACCCTGACAACACTGATGACAA
RS5       CACTGATGACAATGGCCCA---------------CAGGACCCTGACAACACTGATGACAA
NT1       CACTGATGACAATGGCCCA---------------CAGGGCCCCGACAACACTGATGACAA
NT4       CACTGATGACAATGGCCCACATGACCCGCTGCCTCAGGACCCTGACAACACTGATGACAA
NT6       CACTGATGACAATGGCCCACATGACCCGCTGCCTCAGGACCCTGACAACACTGATGACAA
RN1       CACTGATGACAATGGCCCACATGACCCGCTGCCTCAGGACCCTGACAACACTGATGACAA
RN2       CACTGATGACAATGGCCCACATGACCCGCTGCCTCAGGACCCTGACAACACTGATGACAG
RN3       CACTGATGACAATGGCCCACATGACCCGCTGCCTCAGGACCCTGACAACACTGATGACAA
RN4       CACTGATGACAATGGCCCACATGACCCGCTGCCTCAGGACCCTGACAACACTGATGACAA
          *******************               **** *** ****************

B95.8     TGGCCCACAGGACCCTGACAACACTGAT-------------------------------- 168.428
RS1       TGGCCCACAGGGCCCTGACAACACTGATGACAATGGCCCACAGGGCCCTGACAACACTGA
RS2       TGGCCCACAGGGCCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAACACTGA
RS3       TGGCCCACAGGACCCTGACAACACTGAT--------------------------------
RS4       TGGCCCACAGGACCCTGACAACACTGAT--------------------------------
RS5       TGGCCCACAGGACCCTGACAACACTGATGACAATGGCCCACAGGACCCTGACAACACTGA
NT1       TGGCCCACAGGACCCTGACAACACTGAT--------------------------------
NT4       TGGCCCACAGGACCCTGACAACACTGAT--------------------------------
NT6       TGGCCCACAGGACCCTGACAACACTGAT--------------------------------
RN1       TGGCCCACAGGACCCTGACAACACTGAT--------------------------------
RN2       TGGCCCACAGGACCCTGACAACACTGAT--------------------------------
RN3       TGGCCCACAGGACCCTGACAACACTGAT--------------------------------
RN4       TGGCCCACAGGACCCTGACAACACTGAT--------------------------------
          *********** ****************

B95.8     ------------------------------------------------------------
RS1       T-----------------------------------------------------------
RS2       TGACAATGGCCCACAGGGCCCTGACAACACTGATGACAATGGCCCACAGGGCCCTGACAA
RS3       ------------------------------------------------------------
RS4       ------------------------------------------------------------
RS5       T-----------------------------------------------------------
NT1       ------------------------------------------------------------
NT4       ------------------------------------------------------------
NT6       ------------------------------------------------------------
RN1       ------------------------------------------------------------
RN2       ------------------------------------------------------------
RN3       ------------------------------------------------------------
RN4       ------------------------------------------------------------

B95.8     -------GACAATGGCCCACATGACCCGCTGCCTCATAGCCCTAGCGACTCTGCTGGAAA 168.375
RS1       -------GACAATGGCCCACATGACCCGCTGCCTCATAACCCTAGCGACTCTGCTGGAAA
RS2       CACTGATGACAATGGCCCACATGACCCGCTGCCTCATAACCCTAGCGACTCTGCTGGAAA
RS3       -------GACAATGGCCCACATGACCCGCTGCCTCATAGCCCTAGCGACTCTGCTGGAAA
RS4       -------GACAATGGCCCACATGACCCGCTGCCTCATAGCCCTAGCGACTCTGCTGGAAA
RS5       -------GACAATGGCCCACATGACCCGCTGCCTCATAACCCTAGCGACTCTGCTGGAAA
NT1       -------GACAATGGCCCACATGACCCGCTGCCTCATAACCCTAGCGACTCTGCTGGAAA
NT4       -------GACAATGGCCCACATGACCCGCTGCCTCATAGCCCTAGCGACTCTGCTGGAAA
NT6       -------GACAATGGCCCACATGACCCGCTGCCTCATAGCCCTAGCGACTCTGCTGGAAA
RN1       -------GACAATGGCCCACATGACCCGCTGCCTCATAGCCCTAGCGACTCTGCTGGAAA
RN2       -------GACAATGGCCCACACGACCCGCTGCCTCATAGCCCTAGCGACTCTGCTGGAAA
RN3       -------GACAATGGCCCACATGACCCGCTGCCTCATAGCCCTAGCGACTCTGCTGGAAA
RN4       -------GACAATGGCCCACATGACCCGCTGCCTCATAGCCCTAGCGACTCTGCTGGAAA
                 ************** **************** *********************
```

```
B95.8           TGATGGAGGCCCTCCACAATTGACGGAAGAGGTTGAAAACAAAGGAGGTGACCAGGGCCC 168.315
RS1             TGATGGAGGCCCTCCAGAATTGACGGAAGAGGTTGAAAACAAAGCAGGTGCCCGGGGCCC
RS2             TGATGGAGGCCCTCCAGAATTGACGGAAGAGGTTGAAAACAAAGGAGGTGACCAGCGCCA
RS3             TGATGGAGGCCCTCCACAATTGACGGAAGAGGTTGAAAACAAAGGAGGTGACCAGGGCCC
RS4             TGATGGAGGCCCTCCACAATTGACGGAAGAGGTTGAAAACAAAGGAGGTGACCAGGGCCC
RS5             TGATGGAGGCCCTCCAAATTTGACGGAAGACGTTGAAAACAAAGGAGGTGACAGGAGCCC
NT1             TGATGGAGGCCCTCCAAATTTGACGGAAGAGGTTGAAAACAAAGGAGGTGACCGGGGCCC
NT4             TGATGGAGGCCCTCCACAATTGACGGAAGAGGTTGAAAACAAAGGAGGTGACCAGGGCCC
NT6             TGATGGAGGCCCTCCACAATTGACGGAAGAGGTTCAAAACAAAGGAGGTGACCAGGGCCC
RN1             TGATGGAGGCCCTCCACAATTGACGGAAGAGGTTGAAAACAAAGGAGGTGACCAGGGCCC
RN2             TGATGGAGGCCCTCCACAATTGACGGAAGAGGTTGAAAACAAAGGAGGTGACCAGGGCCC
RN3             TGATGGAGGCCCTCCACAATTGACGGAAGAGGTTGAAAACAAAGGAGGTGACCAGGGCCC
RN4             TGATGGAGGCCCTCCACAATTGACGGAAGAGGTTGAAAGCAAAGGAGGTGACCAGGGCCC
                **************** * *********** *** *** ***** ***** *  * ***

B95.8           GCCTTTGATGACAGACGGAGGCGGCGGTCATAGTCATGATTCCGGCCATGGCGGCGGTGA 168.255
RS1             GCCTTCGATGACAGACGGTGGCGGCGGTCATAGTCATGATTCCGGCCGTGGCGGCGGTGA
RS2             GCCTTCGATGACAGACGGTGGCGGCGGTCATAGTCATGATTCCGGCCGTGGCGGCGGTGA
RS3             GCCTTTGATGACAGACGGAGGCGGCGGTCATAGTCATGATTCCGGCCATGGCGGCGGTGA
RS4             GCCTTTGATGACAGACGGAGGCGGCGGTCATAGTCATGATTCCGGCCATGGCGGCGGTGA
RS5             GTCTTCGATGACAGACGGTGGCGGCGGT------------------------------GA
NT1             GCCTTCGATGACAGACGGTGGCGGCGGT------------------------------GA
NT4             GCCTTTGATGACAGACGGAGGCGGCGGTCATAGTCATGATTCCGGCCATGGCGGCGGTGA
NT6             GCCTTTGATGACAGACGGAGGCGGCGGTCATAGTCATGATTCCGGCCATGGCGGCGGTGA
RN1             GCCTTTGATGACAGACGGAGGCGGCGGTCATAGTCATGATTCCGGCCATGGCGGCGGTGA
RN2             GCCTTTGATGACAGACGGAGGCGGCGGTCATAGTCATGATTCCGGCCATGGCGGCGGTGA
RN3             GCCTTTGATGACAGACGGAGGCGGCGGCCATAGTCATGATTCCGGCCATGGCGGCGGTGA
RN4             GCCTTTGATGACAGACGGAGGCGGCGGTCATAGTCATGATTCCGGCCATGGCGGCGGTGA
                * *** ************ ********                               **

B95.8           TCCACACCTTCCTACGCTGCTTTTGGGTTCTTCTGGTTCCGGTGGAGATGATGACGACCC 168.195
RS1             TTCACACCTTCCTACACTGCTTTTGGGTACTTCTGGTTCCGGTGGAGATGATGACGACCC
RS2             TCCACACCTTCCTACACTGCTTTTGGGTACTTCTGGTTCCGGTGGAGATGATGACGACCC
RS3             TCCACACCTTCCTACGCTGCTTTTGGGTTCTTCTGGTTCCGGTGGGGATGATGACGACCC
RS4             TCCACACCTTCCTACGCTGCTTTTGGGTTCTTCTGGTTCCGGTGGAGATGATGACGACCC
RS5             TCCACACCTTCCTACGCTGCTTTTGGGTACTTCTGGTTCCGGTGGAGATGATGACGACCC
NT1             TCCACACCTTCCTACGCTGCTTTTGGGTACTTCTGGTTCCGGTGGAGATGATGACGACCC
NT4             TCCACACCTTCCTACGCTGCTTTTGGGTTCTTCTGGTTCCGGTGGAGATGATGACGACCC
NT6             CCCACACCTTCCTACGCTGCTTTTGGGTACTTCTGGTTCCGGTGGAGATGATGACGACCC
RN1             TCCACACCTTCCTACGCTGCTTTTGGGTTCTTCTGGTTCCGGTGGAGATGATGACGACCC
RN2             TCCACACCTTCCTACGCTGCTTTTGGGTTCTTCTGGTTCCGGTGGGGATGATGACGACCC
RN3             TCCACACCTTCCTACGCTGCTTTTGGGTTCTTCTGGTTCCGGTGGAGATGATGACGACCC
RN4             TCCACACCTTCCTACGCTGCTTTTGGGTTCTTCTGGTTCCGGTGGAGATGATGACGACCC
                  ************* ************ **************** **************

B95.8           CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA-------------------------- 168.161
RS1             CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
RS2             CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
RS3             CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
RS4             CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
RS5             CCACGGCCCAGTTCAGCTAAGCTACTATGACCAACCTTTCTTTACTTCTAGGCATTACCA
NT1             CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
NT4             CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
NT6             CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
RN1             CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
RN2             CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
RN3             CCACGGTCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
RN4             CCACGGCCCAGTTCAGCTAAGCTACTATGACTAA--------------------------
                ****** ************************ **

B95.8           ----------------------
RS1             ----------------------
RS2             ----------------------
RS3             ----------------------
RS4             ----------------------
RS5             TGTCATAGGCTTGCCTGACTGA
NT1             ----------------------
NT4             ----------------------
NT6             ----------------------
RN1             ----------------------
RN2             ----------------------
RN3             ----------------------
RN4             ----------------------
```