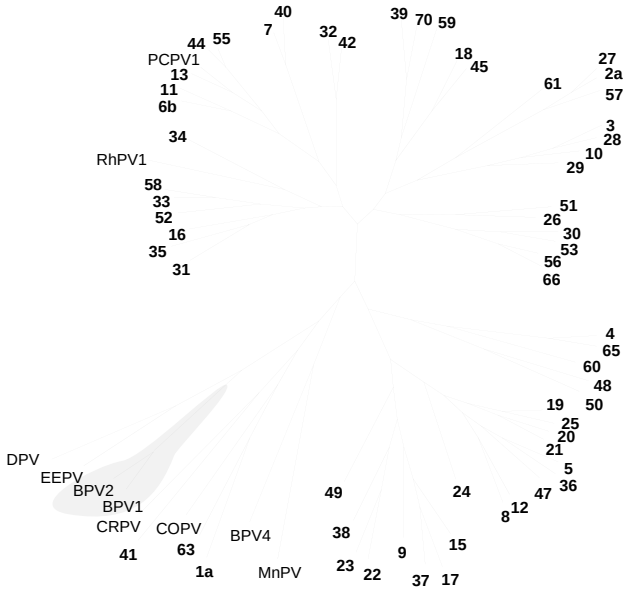
# Group C1 Sequences

**BPV1 BPV2**




## INTRODUCTION

Papillomaviruses infect a wide range of hosts including ungulates, birds, rodents, dogs, marsupials and primates. However, only a subset of these animal papillomavirus types have been cloned and characterized, while an even smaller number have been sequenced over the entire genome. Group I of last year's compendium included those animal types whose complete genomes have been sequenced: COPV, CRPV, EEPV, DPV, BPV-1, BPV-2, BPV-4, PCPV-1, MnPV, and RhPV. This year, we have divided the animal papillomaviruses into Groups C1, C2, D1, and E. The bovine papillomaviruses can be classified into two groups, C1 composed of BPV-1 and BPV-2, and D1 which comprises BPV-3, BPV-4 and BPV-6, based on the tissues they infect. (BPV-5 is an isolated lineage of probable group rank within the C supergroup.) In addition to differences in host tissue restriction, several other characteristics distinguish the groups of the bovine papillomaviruses. First, group C1 viruses have larger genomes ($\approx$7.9 kB) than group D1 viruses ($<$7.2 kB). Second, the analogous position of the group C1 E6 ORF is occupied by the group D1 E8 ORF [1]. This coding region encodes a protein which strongly resembles the E5 transforming protein of the group C1 viruses [1].

Distinctive clinical pathologies have been associated with the various categories of animal papillomaviruses. BPV-1 and BPV-2, which comprise Group C1, cause ungulate fibropapillomas. Group C1 viruses infect both dermal fibroblasts and squamous epithelial cells [2]. BPV-1, originally isolated from a Swedish cow, has been linked specifically to frond-like fibropapillomas which occur on the teats, penis, and nose. It also occurs in equine sarcoida, a benign, naturally occurring fibroblastic tumor in horses [2, 3], and with sarcoid tumours in donkeys [4]. BPV-2 is associated with fibropapillomas of the head, neck, and alimentary canal [2]. "Rice grain" lesions of the teat and the udder are characteristic of BPV-5 [2].

### BPV-1 Molecular Biology

BPV-1 plasmid replication is dependent upon the expression of most of the early orfs (only E3 and E4 do not appear to play a role) [5]. Molecular regulation is highly complex: thus far, seven promoters, several complicated splice patterns, and eighteen distinct mRNA species have been identified. Six of the seven promoters, $P_{89}$, $P_{890}$, $P_{2443}$, $P_{3080}$, $P_{7185}$, and $P_{794}$, are active in transformed cells [5]. Conversely, the major late promoter, $P_{7250}$, is active only in differentiating keratinocytes of a fibropapilloma or papilloma [5]. Transcription of the structural proteins origininates at P7250. Multiple interacting elements encoded in the E2 region act to regulate transcription. (The use of the E2 protein to regulate transcription is a characteristic feature of papillomaviruses.) Three E2 regulatory proteins have been identified: two transcription repressors, E2-TR and the E2^E8 fusion product, and the full length E2 transactivator. (The E8 orf of BPV1 is contained within the E1 orf, although in another frame.) These proteins bind the motif $\texttt{ACCN}_6\texttt{GGT}$, which exists in many copies in the genome, particularly in the LCR. E2 responsive elements 1 (E2RE1) and 2 (E2RE2), expression enhancers, are activated by the E2 transactivator [5]. Lambert et al. suggest that the relative abundance of the positive- and negative-acting E2 proteins determines the level of viral gene expression [5].

The capacity of BPV-1 to transform rodent cells in culture has primarily been attributed to the proteins encoded by the E5 and E6 orfs. The putative E5 transformation pathway involves binding

of E5 to a 16-kDa cellular protein and the subsequent loss of cell-cycle control [6]. It is possible that the E6 mechanism of transformation may be linked to the alteration of gene expression through nucleic acid binding [6].

## What's new?

While no new sequences in Group C1 were released during 1995, we have compiled a revised sequence of BPV-1, called BPV-1R that is presented on the following pages. The sequence of BPV-2 was published in *Human Papillomaviruses 1994* pp. I-I-28.

**References**


[1] Jackson, M.E., Pennie, W.D., McCaffery, R.E., Smith, K.T., Grindlay, G.J., and Campo, M.S. The B subgroup bovine papillomaviruses lack an identifiable E6 open reading frame. *Molecular Carcinogenesis* **4**: 382–387 (1991)

[2] Coggins, L.W., Ma, J.Q., Slater, A.A., and Campo, M.S. Sequence homologies between bovine papillomavirus genomes mapped by a novel low-stringency heteroduplex method. *Virology* **143**: 603–611 (1985)

[3] Amtmann, E., Muller, H., and Sauer, G. Equine connective tissue tumors contain unintegrated bovine papilloma virus DNA. *J Virol* **35**: 962–964 (1980)

[4] Reid,S.W.J., Smith,K.T. and Jarrett,W.F.H. Detection, cloning and charcaterization of papillomaviral DNA present in sarcoid tumours of Equus asinus. *The Veterinary Record* **135**: 430-32 (1994)

[5] Lambert, P.F., Baker, C.C., and Howley, P.M. The genetics of bovine papillomavirus type 1. *Annu. Rev. Genet.* **22**: 235–258 (1988)

[6] Campo, S. Cell transformation by animal papillomaviruses. *J. Gen. Virol.* **73**: 217-222 (1992)

```
LOCUS       BPV1R        7946 bp ds-DNA   Circular  VRL       30-SEP-1988
DEFINITION  Bovine papillomavirus type 1 (BPV-1), complete genome.
ACCESSION   <not yet entered in GenBank>
KEYWORDS    complete genome; open reading frame.
SOURCE      Bovine papillomavirus type 1 DNA from cow, isolate 307.
REFERENCE   1  (bases 1 to 7946)
  AUTHORS   Chen,E.Y., Howley,P.M., Levinson,A.D. and Seeburg,P.H.
  TITLE     The primary structure and genetic organization of the bovine
            papillomavirus type 1 genome.
  JOURNAL   Nature 299, 529-534 (1982)
REFERENCE   2  (base 3445; revision)
  AUTHORS   Stenlund,A., Zabielski,J., Ahola,H., Moreno-Lopez,J.,
            and Pettersson,U.
  TITLE     Messenger RNAs from the transforming region of bovine papilloma
            virus type I.
  JOURNAL   J. Mol. Biol. 182, 541-554 (1985)
REFERENCE   3  (bases 7120 to 7399)
  AUTHORS   Baker,C.C., and Howley,P.M.
  TITLE     Differential promoter utilization by the bovine papillomavirus
            in transformed cells and productively infected wart tissues.
  JOURNAL   Embo J. 6, 1027-35 (1987)
REFERENCE   4  (bases 7306, 7588; revision)
  AUTHORS   Danos,O., Engel,L.W., Chen,E.T., Taniv,M., and Howley,P.M.
  TITLE     Comparative analysis of the human type 1a and bovine type
            1 papillomavirus genomes
  JOURNAL   J. Virology 46, 557-566 (1983)
REFERENCE   5  (base 7762; revision)
  AUTHORS   Spalholz,B.A., Lambert,P.F., Yee,C.L., and Howley,P.M.
  TITLE     Bovine papillomavirus transcriptional regulation: localization
            of the E2-responsive elements of the long control region.
  JOURNAL   J. Virol. 61, 2128-2137 (1987)
COMMENT     Full genomic sequences exist for BPV-1, BPV-2 and BPV-4,
            EEPV, DPV, and partial genomes for BPV-3, BPV-6 and RPV.
            The bovine papillomaviruses can be classified into two
            groups, subgroup A (BPV-1, BPV-2 and BPV-5) and subgroup
            B (BPV-3, BPV-4 and BPV-6), based on the tissues they
            infect (Jackson et al. Mol. Carc. 4: 382-387). The
            subgroup A viruses infect both dermal fibroblasts and
            squamous epithelial cells (Coggins et al. Vir. 143:
            603-611). BPV-1, isolated from a Swedish cow, has been
            linked specifically to frond-like fibropapillomas which
            occur on the teats, penis, and nose and equine sarcoida,
            a benign, naturally occurring fibroblastic tumor in horses
            (Coggins et al. Vir. 143: 603-611; Amtmann et
            al. J. Virol. 61: 3394-3400). In addition to differences
            in host tissue restriction, several other characteristics
            distinguish the subgroups of the bovine papillomaviruses.
            First, subgroup B viruses have smaller genomes (7.2 kB)
            than subgroup A viruses (7.9 kB).  Second, the analogous
            position of the subgroup A E6 ORF is occupied by the
            subgroup B E8 ORF (Jackson et al. Mol. Carc. 4: 382-387).
            This coding region encodes a protein which strongly
            resembles the E5 transforming protein of the subgroup A
            viruses (Jackson et al. Mol. Carc. 4: 382-387).

            Certain mRNA start sites are heterogeneous in BPV1, namely
            P_L, P_7940, P_890, P_2443, P_3880.

            The originally published sequence of [1] contained several
```

sequencing errors which have since been pointed out by other authors ([2]-[5]). These changes, which have been incorporated into the present entry, are as follows: insertion of ‘g’ at bp 3445; substitution of ‘c’ for ‘g’ at bp 7306; deletion of ‘g’ at bp 7588; insertion of ‘c’ at bp 7762 (nucleotide positions given in terms of the corrected sequence presented herein). The ’c’ to ’g’ change at bp 652 is a revision of an original typographical error.

```
BASE COUNT     2270 a   1714 c   1887 g   2075 t
ORIGIN      First base of Hpa I site
        1 gttaacaata atcacACCAT CACCGTTttt tcaagcggga aaaaaTAGcc agctaacTAT
                  E2 bind ->                    E6 orf start -> signal ->
         E1 binding <-/                          ori <-/
       61 AAAaagctgc tgacagaccc cggttttcac ATGgacctga aacctttgc aagaaccaat
                                      |-> mRNA start site from P(89) promoter
                                  E6 cds ->
      121 ccattctcag ggttggattg tctgtggtgc agagagcctc ttacagaagt tgatgctttt
      181 aggtgcatgg tcaaagactt tcatgttgta attcgggaag gctgtagata tggtgcatgt
      241 accatttgtc ttgaaaactg tttagctact gaaagaagac tttggcaagg tgttccagta
      301 acagGTgagg aagctgaatt attgcatggc aaaacacttg ataggctttg cataagatgc
       5' sj /\
      361 tgctactgtg ggggcaaact aacaaaaaat gaaaaacatc ggcatgtgct ttttaatgag
      421 cctttctgca aaaccagagc taacaTAAtt agaggacgct gctacgactg ctgcagacAT
                           E7 orf start ->                       E7 cds ->
      481 Ggttcaaggt ccaaataccc aTAGaaactt ggatgattca cctgcAGgac cgttgctgat
                                <- E6 end                /\ 3' sj
      541 tttaAGtcca tgtgcAGgca cacctaccag gtctcctgca gcacctgatg cacctgattt
                /\ 3' sj    /\ 3' sj
      601 cagacttccg tgccatttcg gccgtcctac taggaagcga ggtcccacta cGcctccgct
                                          ‘c’ replaced by ‘g’ ^
      661 ttcctctccc ggaaaactgt gtgcaacagg gccacgtcga gtgtattctg tgactgtctg
      721 ctgtggaaac tgcggaaaag agctgacttt tgctgtgaag accagctcga cgtccctgct
      781 tggatttgaa caccttttaa actcagattT AGacctcttg tgtccacgtt gtgaatctcg
                               E1 orf start ->
      841 cgagcgtcAT GgcaAACGAT AAAGGTagca attgggattc gggcttggga tgctcatatc
           E1 cds ->           <- E7 end                |-> P(890)
                            5' sj /\                    mRNA start |-> P(890)
                  E2 bind ->                                       mRNA start
      901 tgctgactga ggcagaatgt gaaagtgaca aagagaatga ggaacccggg gcaggtgtag
      961 aactgtctgt ggaatctgat cggtatgata gccaggatga ggattttgtt gacaatgcat
     1021 cAGtctttcA Gggaaatcac ctggaggtct tccaggcatt agagaaaaag gcgggtgagg
            /\ 3' sj /\ 3' sj
     1081 agcagatttt aaattTGAaa agaaaagtat tggggagttc gcaaAACAGC AGCGGTtccg
                E8 orf start ->                  E2 bind ->
     1141 aagcatctga aactccagtt aaaagacgga aatcaggagc aaagcgaaga ttatttgctg
     1201 aaaATGaagc taaccgtgtt cttacgcccc tccagGTaca gggggagggg gaggggaggc
      E8 cds ->                        5' sj /\
     1261 aagaacttaa tgaggagcag gcaattagtc atctacatct gcagcttgtt aaatctaaaa
     1321 atgctacagt ttttaagctg gggctcttta aatctttgtt cctttgtagc ttccatgata
     1381 ttacgaggtt gtttaagaat gataagacca ctaatcagca atgggtgctg gctgtgtttg
     1441 gccttgcaga ggtgtttttt gaggcgagtt tcgaactccT AAagaagcag tgtagttttc
                                                  <- E8 end
     1501 tgcagatgca aaaaagatct catgaaggag gaacttgtgc agtttactta atctgcttta
     1561 acacagctaa aagcagagaa acagtccgga atctgatggc aaacacgcta aatGTaagag
                                                         5' sj /\
     1621 aagagtgttt gatgctgcag ccagctaaaa ttcgaggact cagcgcagct ctattctggt
     1681 ttaaaagtag tttgtcaccc gctacactta aacatggtgc tttacctgag tggatacggg
```

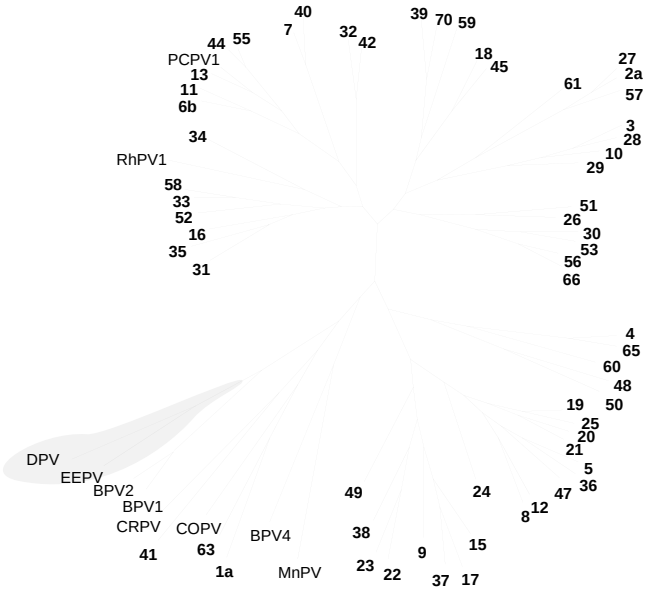
```
  1741 cgcaaactac tctgaacgag agcttgcaga ccgagaaatt cgacttcgga actatggtgc
  1801 aatgggccta tgatcacaaa tatgctgagg agtctaaaat agcctatgaa tatgctttgg
  1861 ctgcAGgatc tgatagcaat gcacgggctt ttttagcaac taacagccaa gctaagcatg
           /\ 3' sj
  1921 tgaaggactg tgcaactatg GTaagacact atctaagagc tgaaacacaa gcattaagca
                     5' sj /\
  1981 tgcctgcata tattaaagct aggtgcaagc tggcaactgg ggaaggaagc tggaagtcta
  2041 tcctaacttt ttttaactat cagaatattg aattaattac ctttattaat gctttaaagc
  2101 tctggctaaa aggaattcca aaaaaaaact gtttagcatt tattggccct ccaaacacag
  2161 gcaagtctat gctctgcaac tcattaattc atttttggg tggtagtgtt ttatcttttg
  2221 ccaaccataa aagtcacttt tggcttgctt ccctagcaga tactagagct gctttagtag
  2281 atgatgctac tcatgcttgc tggaggtact ttgacacata cctcagaaat gcattggatg
  2341 gctaccctgt cagtattgat agaaaacaca aagcagcggt tcaaattaaa gctccACCCC
                                                            E2 bind ->
  2401 TCCTGGTaac cagTAATATT gatgtgcagg cagaggacag atatttgtac ttgcatagtc
             signal ->                      |-> P(2443) mRNA start
               |-> P(2443) mRNA start       (various sites, 2436-2447)
  2461 gggtgcaaac ctttcgcttt gagcagccat gcacagatga atcggGTgag caacctttta
                                                 5' sj /\
  2521 atattactga tgcagattgg aaatcttttt ttgtaAGgtt atgggggcgt ttagaccTGA
                                                  /\ 3' sj
  2581 ttgacgagga ggaggatagt gaagaggATG gagacagcat gcgaacgttt acatgtagcg
E2 orf ->                      E2 cds ->
  2641 caagaaacac aaatgcagtt gatTGAgaaa agtagtgata agttgcaaga tcatatactg
                                 <- E1 end
  2701 tactggactg ctgttagaac tgagaacaca ctgctttatg ctgcaaggaa aaaaggggtg
  2761 actgtcctag gacactgcag agtaccacac tctgtagttt gtcaagagag agccaagcag
  2821 gccattgaaa tgcagttgtc tttgcaggag ttaagcaaaa ctgagtttgg ggatgaacca
  2881 tggtctttgc ttgacacaag ctgggaccga tatatgtcag AACCTAAACG GTgctttaag
                                            E2 bind ->
  2941 aaaggcgcca gggtggtaga ggtggagttt gatggaaatg caagcaatac aaactggtac
  3001 actgtctaca gcaatttgta catgcgcaca gaggacggct ggcagcttgc Gaaggctggg
               |-> P(3080) mRNA start    'c' replaced by 'g' ^
  3061 gctgacggaa ctgggctcta ctactgcACC ATGGCCGGTg ctggacgcat ttactattct
                                     -> E2 bind
               |-> P(3080) mRNA start (various sites, 3070-3080)
  3121 cgctttggtg acgaggcagc cagatttagt acaacagggc attactctgT AAgagatcag
                                                  E4 orf start ->
  3181 gacagagtgt ATGctggtgt ctcatccacc tcttctgatt ttAGagatcg cccagacgga
         E4 cds ->                                   /\ 3' sj
  3241 gtctgggtcg catccgaagg accTGAagga gaccctgcag gaaaagaagc cgagccagcc
                     E3 orf start ->
                     NH2 terminus unknown
  3301 cagcctgtct cttctttgct cggctccccc gcctgcggtc ccatcagagc aggcctcggt
  3361 tgggtacggg acggtcctcg ctcgcacccc tacaattttc ctgcaggctc ggggggctct
  3421 attctccgct cttcctccac cccgGtgcag ggcacggtac cggtggactt ggcatcaagg
                                  âdditional 'g'
  3481 caggaagaag aggagcagtc gcccgactcc acagaggaag aaccagTGAc tctcccaagg
                                                          <- E4 end
  3541 cgcaccacca aTGAtggatt ccacctgtta aaggcaggag ggtcatgctt tgctctaatt
                    <- E3 end
  3601 tcAGgaactg ctaaccaggt aaagtgctat cgctttcggg tgaaaaagaa ccatagacat
          /\ 3' sj
  3661 cgctacgaga actgcaccac cacctggttc acagttgctg acaacggtgc TGAaagacaa
                                                   E5 orf start ->
  3721 ggacaagcac aaatactgat caccttgga tcgccaagtc aaagGcaaga ctttctgaaa
                                     5' sj (atypical) /\
  3781 catgtaccac tacctcctgg aatgaacatt tccggcttta cagccagctt ggacttcTGA
                                                                  <- E2 end
```

```
3841 tcactgccat tgccttttct tcatctgact ggtgtactAT Gccaaatcta tggtttctat
                                      E5 cds ->
3901 tgttcttggg actagttgct gcaatgcaac tgctgctatt actgttctta ctcttgtttt
3961 ttcttgtata ctgggatcat tttgagtgct cctgtacagg tctgcccttt TAAtgccttt
                                                          <- E5 end
4021 acatcactgg ctattggctg tgtttttact gttgtgtgga tttgatttgt tttatatact
4081 gtatgaagtt ttttcatttg tgcttgtatt gctgtttgta agtttttac tagagtttgt
4141 attccccctg ctcagatttt atatggttTA AgctgcagcA ATAAAaATGa gtgcacGaaa
                         L2 orf start ->       L2 cds ->
                                        signal ->    early poly-A |
4201 aaGagtaaaa cgtgccagtg cctatgacct gtacaggaca tgcaagcaag cgggcacatg
 early |
 poly-A
4261 tccaccagat gtgatacCaa aggtagaagg agatactata gcagataaaa ttttgaaatt
                      ^ 'g' replaced by 'c'
4321 tgggggtctt gcaatctact taggagggct aggaatagga acatggtcta ctggaagggt
4381 tgctgcaggt ggatcaccaa ggtacacacc actccgaaca gcagggtcca catcatcgct
4441 tgcatcaata ggatccagag ctgtaacagc agggacccgc cccagtatag gtgcgggcat
4501 tcctttagac acccttgaaa ctcttggggc cttgcgtcca ggggtgtatg aggacactgt
4561 gctaccagag gcccctgcaa tagtcactcc tgatgctgtt cctgcagatt cagggcttga
4621 tgccctgtcc ataggtacag actcgtccac ggagaccctc attactctgc tagagcctga
4681 gggtcccgag gacatagcgg ttcttgagct gcaacccctg gaccgtccaa cttggcaagt
4741 aagcaatgct gttcatcagt cctctgcata ccacgcccct ctgcagctgc aatcgtccat
4801 tgcagaaaca tctggtttag aaaatatttt tgtaggaggc tcgggtttag gggatacagg
4861 aggagaaaac attgaactga catacttcgg gtccccacga acaagcacgc cccgcagtat
4921 tgcctctaaa tcacgtggca ttttaaactg gttcagtaaa cggtactaca cacaggtgcc
4981 cacggaagat cctgaagtgt tttcatccca aacatttgca aacccactgt atgaagcaga
5041 accagctgtg cttaagggac ctagtggacg tgttggactc agtcaggttt ataaacctga
5101 tacacttaca acacgtagcg ggacagaggt gggaccacag ctacatgtca ggtactcatt
5161 gagtactata catgaagatg tagaagcaat cccctacaca gttgatgaaa atacacaggg
5221 acttgcattc gtacccttgc atgaagagca agcaggtttt gaggagatag aattagatga
5281 ttttagtgag acacatagac tgctacctca gaacacctct tctacacctg ttggtagtgg
5341 tgtacgaaga agcctcattc caactcagga atttagtgca acacggccta caggtgttgt
5401 aacctatggc tcacctgaca cttactctgc tagcccagtt actgaccctg attctacctc
5461 tcctagtcta gttatcgatg acactactac tacaccaatc attataattg atgggcacac
5521 agttgatttg tacagcagta actacacctt gcatccctcc ttgttgagga aacgaaaaaa
5581 acggaaacat gccTAAtttt ttttgcAGAT Ggcgttgtgg caacaaggcc agaagctgta
        L1 orf start ->          /\ 3' sj
                              L1 cds ->
                     <- L2 end
5641 tctccctcca acccctgtaa gcaaggtgct ttgcagtgaa acctatgtgc aaagaaaaag
5701 catttttat catgcagaaa cggagcgcct gctaactata ggacatccat attacccagt
5761 gtctatcggg gccaaaactg ttcctaaggt ctctgcaaat cagtataggg tatttaaaat
5821 acaactacct gatcccaatc aatttgcact acctgacagg actgttcaca acccaagtaa
5881 agagcggctg gtgtgGgcag tcataggtgt gcaggtgtcc agagggcagc ctcttggagg
                      ^ 'c' replaced by 'g'
5941 tactgtaact gggcacccca cttttaatgc tttgcttgat gcagaaaatg tgaatagaaa
6001 agtcaccacc caaacaacag atgacaggaa acaaacaggc ctagatgcta agcaacaaca
6061 gattctgttg ctaggctgta cccctgctga aggggaatat tggacaacag cccgtccatg
6121 tgttactgat cgtctagaaa atggcgcctg ccctcctctt gaattaaaaa acaagcacat
6181 agaagatggg gatatgatgg aaattgggtt tggtgcagcc aacttcaaag aaattaatgc
6241 aagtaaatca gatctacctc ttgacattca aaatgagatc tgcttgtacc cagactacct
6301 caaaatggct gaggacgctg ctggtaatag catgttcttt tttgcaagga aagaacaggt
6361 gtatgttaga cacatctgga ccagaggggg ctcggagaaa gaagccccta ccacagattt
6421 ttatttaaag aataataaag gggatgccac ccttaaaata cccagtgtgc attttggtag
6481 tcccagtggc tcactagtct caactgataa tcaaattttt aatcggccct actggctatt
6541 ccgtgcccag ggcatgaaca atggaattgc atggaataat ttattgtttt taacagtggg
6601 ggacaataca cgtggtacta atcttaccat aagtgtagcc tcagatggaa ccccactaac
6661 agagtatgat agctcaaaat tcaatgtata ccatagacat atggaagaat ataagctagc
```

```
     6721 ctttatatta gagctatgct ctgtggaaat cacagctcaa actgtgtcac atctgcaagg
     6781 acttatgccc tctgtgcttg aaaattggga aataggtgtg cagcctccta cctcatcgat
     6841 attagaggac acctatcgct atatagagtc tcctgcaact aaatgtgcaa gcaatgtaat
     6901 tcctgcaaaa gaagaccctt atgcagggtt taagttttgg aacatagatc ttaaagaaaa
     6961 gctttctttg gacttagatc aatttccctt gggaagaaga tttttagcac agcaaggggc
     7021 aggatgttca actgtgagaa aacgaagaat tagccaaaaa acttccagta agcctgcaaa
     7081 aaaaaaaaaa aaaTAAaagc taagtttcta taaatgttct gtaaatgtaa aacagaaggt
                       <- L1 end                                    /-> 3' UTR
                                                                       element
     7141 aagtcaactg cacctAATAA Aaatcactta atagCaatgt gctgtgtcag ttgtttattg
                  signal ->  late poly-A site |          ||-> mRNA start site
                                                          from P(7185)
                                                          promoter
     7201 gaACCACACC CGGTacacat cctgtccagc atttgcagtg cgtgcattga attattgtgc
            -> E2 bind  |-> PL mRNA start (various sites, 7214-7256)
     7261 tggctagact tcatggcgcc tggcaccgaa tcctgccttc tcagcCaaaa tgaataattg
                                    'g' replaced by 'c' ^
     7321 ctttgttggc aagaaactaa gcatcaatgg gacgcgtgca aagcACCGGC GGCGGTagat
                                                        -> E2 bind
     7381 gcgggGTaag tactgaattt taattcgACC TATCCCGGTa aagcgaaagc gacacgcttt
        5' sj /\                        -> E2 bind
     7441 tttttcacac atagcgggAC CGAACACGTT ataagtatcg attaggtcta tttttgtctc
                             -> E2 bind
     7501 tctgtcggaA CCAGAACTGG Taaaagtttc cattgcgtct gggcttgtct atcattgcgt
                   -> E2 bind
     7561 ctctatggtt tttggaggat tagacgggcc ACCAGTAATG GTgcatagcg gatgtctgtA
                                    /\ 'g' deleted                    ->
                                        -> E2 bind                E2 bind
     7621 CCGCCATCGG TgcACCGATA TAGGTttggg gctccccaag ggactgctgg gatgacagct
          E2 bind       -> E2 bind
     7681 tcatattata ttgaatgggc gcataatcag cttaattggt gaggacaagc tacaagttgt
     7741 aacctgatct ccacaaagtA CCGTTGCCGG TcggggtcAA ACCGTCTTCG GTgctcgAAA
                  additional 'c' ^                    -> E2 bind
                               -> E2 bind           ->    repeat region
     7801 CCGCCTTaaa ctacagacag gtcccagcca agtaggcgga tcaaaacctc aaaaaggcgg
     7861 gagccaatca aaatgcagca ttatatttta agctcACCGA AACCGGTaag taaagactat
                               /-> ori          -> E2 bind
                                                    5' sj /\
     7921 gtatttttc ccaGtgaata attgtt
     P(7940) mRNA start |->    /-> E1 binding
     (various sites, 7934-7940)
//
```

# Group C2 Sequences

**DPV EEPV**
**OvPV RPV**




## INTRODUCTION

Papillomaviruses infect a wide range of hosts including ungulates, birds, rodents, dogs, marsupials, and primates. However, only a subset of these animal papillomavirus types have been cloned and characterized, while an even smaller number have been sequenced over the entire genome. Group I of last year's compendium included those animal types whose complete genomes have been sequenced: COPV, CRPV, EEPV, DPV, BPV-1, BPV-2, BPV-4, PCPV-1, MnPV, and RhPV. This year, we have divided the animal papillomaviruses into Groups C1, C2, D1, and E.

Distinctive clinical pathologies have been associated with the various categories of animal papillomaviruses. DPV, EEPV, OvPV, and RPV, which comprise Group C2, cause ungulate fibropapillomas.

Full genomic sequences were published last year for EEPV and DPV. OvPV has been sequenced only over a portion of L1, and RPV is represented by four sequences which include the E5, E9, E1, and L1 genes.

RPV was cloned from a cutanteous fibropapilloma on a Swedish reindeer (*Rangifer tarandus*) [1]. EEPV, isolated from a Swedish wild elk, (*Alces a. alces*) causes fibromas and fibropapillomas [2]. DPV infection is unique compared to the clinical profiles of the other Subgroup A viruses; infection results in fibrobproliferation without epithelial proliferation [3]. Previously called deer fibromavirus, DPV was first isolated from the American white tailed deer (*Odocoileus virginianus*) [3].

Many clinical and sequence similarites are prevalent in the ungulate supergroup C. EEPV, BPV-1, BPV-2, RPV, and DPV all induce tumors in young hamsters [1,2,3]. These same viruses transform the mouse cell line NIH 3T3 in vitro, whereas all but DPV transform C127 [3]. The E5 regions of BPV-1, DPV, RPV and EEPV are very hydrophobic and both the BPV-1 and EEPV genomes exist in an episomal form in the transformed cell in high copy number [2].

## What's new?

Partial genomes of OvPV and RPV are given on the following pages. The sequences of other members of this group were published in *Human Papillomaviruses 1995* pp. I-I-13, and I-I-18.

### References


[1] Moreno-Lopez, J., Ahola, H., Eriksson, A., Bergman, P., and Pettersson, U. Reindeer papillomavirus transforming properties correlate with a highly conserved E5 region. *J Virol* **61**: 3394–3400 (1987)

[2] Ahola, H., Bergman, P., Strom, A.C., Moreno-Lopez, J., and Pettersson, U. Organization and expression of the transforming region from the European elk papillomavirus (EEPV). *Gene* **50**:195–205 (1986)

[3] Groff, D.E., and Lancaster, W.D. Molecular cloning and nucleotide sequence of deer papillomavirus. *J Virol* **56**: 85–91 (1985)

```
LOCUS       OPU21861      285 bp    DNA             VRL       13-JUL-1995
DEFINITION  Ovine papillomavirus L1 protein gene, partial cds.
ACCESSION   U21861
KEYWORDS    .
SOURCE      Ovine papillomavirus.
REFERENCE   1  (bases 1 to 285)
  AUTHORS   Chan,S.-Y., Delius,H., Halpern,A.L. and Bernard,H.U.
  TITLE     Analysis of genomic sequences of 95 papillomavirus types - uniting
            typing, phylogeny and taxonomy
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 285)
  AUTHORS   Chan,S.-Y.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-FEB-1995) Shih-Yen Chan, Institute of Molecular and
            Cell Biology, National University of Singapore, Lower Kent Ridge
            Road, Singapore, 0511, Republic of Singapore
COMMENT     NCBI gi: 896401
BASE COUNT       86 a     59 c     58 g     82 t
ORIGIN
        1 tatcatagac acgtggaaga atataaacta gcattcatct ttcaactgtg ctctgtgcag
  L1 cds ->
       61 ttaacccctg aaacagtgag tagtctgcag gggttaatgc ccagcatttt gcaaaactgg
      121 gaagtaaatg tacaacctcc tgcctcttca attctggaag atacctaccg ttatctagaa
      181 tcgccagcca ctaagtgtgc agataatgtg tctcctacta agccagatcc ctatgatggg
      241 ttaaaattct ggaagattga tctaaaagag aagttttctt tggat
                                                    L1 cds ->
//
```

**RPVE1L1**

```
LOCUS       RPVE1_L1        723 bp ds-DNA             VRL       15-MAR-1989
DEFINITION  Concatenated reindeer papillomavirus genomic E1 and L1 regions,
            partial cds.
ACCESSION   M18175
SOURCE      Reindeer papillomavirus (from epithelial layer of a single
            fibropapilloma) DNA.
REFERENCE   1  (bases 1 to 723)
  AUTHORS   Moreno-Lopez,J., Ahola,H., Eriksson,A., Bergman,P. and
            Pettersson,U.
  TITLE     Reindeer papillomavirus transforming properties correlate with a
            highly conserved E5 region
  JOURNAL   J. Virol. 61, 3394-3400 (1987)
COMMENT     The Reindeer Papillomavirus was isolated from a reindeer, specifically
            from the epithelial layer of a fibropapilloma.  The isolate was cloned
            and a restriction map was determined.  The isolated genome was
            unintegrated and circular, as indicated by restriction fragment
            patterns; total length was approximately 8.1 kb.  Segments of E1, E5
            and L1 were sequenced.  The RPV sequences were most similar to the
            homologous segments of DPV and EEPV genomes, and more distantly
            related to BPV1.  Syrian hamsters were inoculated with purified RPV
            and subsequently developed fibrosarcomas.  Mouse C127 cells were
            transformed by RPV, although more slowly (2 to 4 weeks) than by BPV1
            or EEPV (10 to 14 days).  Transformed mouse cells produced several
            mRNA species in a pattern similar to that of EEPV- transformed cells.
            No antibody crossreactivity was detected between anti-EEPV nor
            anti-BPV1 serum, although there was reactivity with anti-RPV serum.  A
            highly hydrophobic E5 protein of 44 amino acids is predicted; both the
            length and the sequence of the protein are highly conserved among
            those PVs which induce both fibromas and fibropapillomas, namely the
            group of PVs related to BPV1, including BPV2, BPV5, EEPV and DPV.
            There may be a distant relationship between the E5 of these viruses
            and an E5 ORF of HPV6b which has a predicted hydrophobic protein,
            although it has not been shown that this HPV6B ORF encodes a
            functional protein.
            NCBI gi: 333299
BASE COUNT      201 a    152 c    155 g    215 t
ORIGIN      406 bp upstream of NciI site.
        1 tggcttagca tcatgaactt gctcaaattt catgggattg aacctattca ttttgttaat
L1 orf ->
L1 cds ->
       61 gccttaaacc cttggttaaa aggcactcca aaacataact gtattgctat agtgggaccc
      121 ccaaatagtg gcaaatcact gctttgtaat agcctgatta ctttcctggg gggaaaagtt
      181 ctgacttttg caaatcactc tagtcatttc tggcttgccc caacagatga cgcgacacat
      241 gcatgttgga ggtattttga cacatacctc agaaatgtgc ttgacggtta tccagtttgt
      301 attgatcgaa agcacaaatc cgctgtgcag atgaaagcac ctccccttt actaaccagt
      361 aatattgatg tgcatgcaga tgaaaagtat ttctatctgc aaagccgggt gaaaagcttc
      421 tatttcacgg agccatgctg tgcatcagat aacggtgaGC CAAgtgtctt tttcccagta
                                          NF-1 bind ->
      481 cccagtggga gccttgtttc tacggatggt cagcttttca atagacctta ttggctattt
      541 agagctcagg gcatgaataa tggtatatgt tggacagttg gggacaacac tcgtggtacc
      601 acactgacca ttactgtacc aagtggtgga aagaagtccc ccctcactga atatgacaca
      661 agcaagttta atgtttatca gagacacgta gaagagtata agcttgcttt tgtatttcag
      721 ctt
      L1 orf ->
      L1 cds ->
//
```

```
LOCUS       RPVE5         207 bp ds-DNA             VRL       15-MAR-1989
DEFINITION  Reindeer papillomavirus E5 ORF region.
ACCESSION   M18176
SOURCE      Reindeer papillomavirus (from epithelial layer of a single
            fibropapilloma) DNA.
REFERENCE   1  (bases 1 to 207)
  AUTHORS   Moreno-Lopez,J., Ahola,H., Eriksson,A., Bergman,P. and
            Pettersson,U.
  TITLE     Reindeer papillomavirus transforming properties correlate with a
            highly conserved E5 region
  JOURNAL   J. Virol. 61, 3394-3400 (1987)
COMMENT     The Reindeer Papillomavirus was isolated from a reindeer, specifically
            from the epithelial layer of a fibropapilloma.  The isolate was cloned
            and a restriction map was determined.  The isolated genome was
            unintegrated and circular, as indicated by restriction fragment
            patterns; total length was approximately 8.1 kb.  Segments of E1, E5
            and L1 were sequenced.  The RPV sequences were most similar to the
            homologous segments of DPV and EEPV genomes, and more distantly
            related to BPV1.  Syrian hamsters were inoculated with purified RPV
            and subsequently developed fibrosarcomas.  Mouse C127 cells were
            transformed by RPV, although more slowly (2 to 4 weeks) than by BPV1
            or EEPV (10 to 14 days).  Transformed mouse cells produced several
            mRNA species in a pattern similar to that of EEPV- transformed cells.
            No antibody crossreactivity was detected between anti-EEPV nor
            anti-BPV1 serum, although there was reactivity with anti-RPV serum.  A
            highly hydrophobic E5 protein of 44 amino acids is predicted; both the
            length and the sequence of the protein are highly conserved among
            those PVs which induce both fibromas and fibropapillomas, namely the
            group of PVs related to BPV1, including BPV2, BPV5, EEPV and DPV.
            There may be a distant relationship between the E5 of these viruses
            and an E5 ORF of HPV6b which has a predicted hydrophobic protein,
            although it has not been shown that this HPV6B ORF encodes a
            functional protein.
            NCBI gi: 333298
BASE COUNT       42 a     32 c     47 g     86 t
ORIGIN      406 bp upstream of NciI site.
        1 ttgctcctgc agtgaaggac atctttgtgc agaaaaactg tgATGaacca tccgggtctt
E5 orf ->                                          E5 cds ->
       61 ttcctgtttc tgggactcac ctttgcagta caactgttat tacttgtatt tttattgttt
      121 ttttttcttg tgtggtggga tcagtttggg tgtcggtgtg atggttttat actgtaatTA
      181 Gtcatactca aggtgtaaat attcatt
            <- E5 end
//
```

**RPVE5E9**

```
LOCUS       RPVE5E9       740 bp    DNA             UNA       16-MAR-1995
DEFINITION  Reindeer papillomavirus (RPV) sequence containing complete
            E5 cds and E9 cds.
ACCESSION   S74218
SOURCE      reindeer papillomavirus RPV.
REFERENCE   1  (bases 1 to 740)
  AUTHORS   Eriksson,A., Stewart,A.C., Moreno-Lopez,J. and Pettersson,U.
  TITLE     The genomes of the animal papillomaviruses European Elk
            papillomavirus, deer papillomavirus, and reindeer papillomavirus
            contain a novel transforming gene (E9) near the early
            polyadenylation site
  JOURNAL   J. Virol. 68 (12), 8365-8373 (1994)
  MEDLINE   95056068
COMMENT     This sequence, which begins at the start of the E5 gene and ends
            at the 5' end of L2, contains a hitherto unrecognized ORF, E9, that
            encodes a putative, extremely hydrophobic protein. The E9 ORF is also
            present in the European elk papillomavirus (EEPV) and the deer
            papillomavirus (DPV), but is apparently absent in bovine papillomavirus
            (BPV). The E9 gene, unlike the E5 gene, is not required for cell
            transformation, but may have an accessory role.
            NCBI gi: 712784
BASE COUNT      177 a    153 c    133 g    277 t
ORIGIN
        1 ATGaaccatc cgggtctttt cctgtttctg ggactcacct ttgcagtaca actgttatta
   E5 cds ->
       61 cttgtatttt tattgttttt ttttcttgtg tggtgggatc agtttgggtg tcggtgtgat
      121 ggttttatac tgTAAttagt catactcaag gtgtaaatat tcatttgatc tttgtacagt
                        <- E5 cds
      181 ttttatacca tatttacatt attataggtt actggttgct acatcctggt catagtcaca
      241 tcatcatcat aggtctaggt cacaattagg tttgtcagat actcaagacg acgtggaatc
      301 tctcttgtca cctgaatcct atcctttact gtcctatcct atcctatctg cctttgtttt
      361 gttatccaaa gtcagcaagt gccatctttc tccaagtgca atgtcatctg cctgtaatcc
      421 aaaagctggt gtcatccttg tcagtagaac agtcaaacta agcctttgaa aagaaagcct
      481 cacacggaaa ccttgtatgt atacctcgtg aaaaagcttt gaactgccac gacattgacg
      541 cctgcATGaa gttttgttta ctcatatttt tgctgctatt attcggccaa ttgaatttta
        E9 cds ->
      601 tgtgggttat cattttattt gtatggtttg cattttgca ttctttgaac tatacatgat
      661 TGAaatgtac atgtgaaggc tgtttccacc tgccttctgt ctcgcgtaca cgtgcacAAT
           <- E9 end                                            signal ->
      721 AAAcccacca tgtcatccca
//
```

# Isolated "*C*" Sequences

### BPV-5

Bovine papillomavirus type 5 appears to be a member of supergroup C, but does not cluster with either group C1 or C2, and is probably an isolated taxon of "group" rank. BPV-5 was isolated from a fibropapilloma ("rice grain") of the bovine teat [1]. It has repeatedly been observed in teat warts [2], and is not known to have been isolated from any other anatomical regions. The only available sequence, a fragment of L1, was released this year and is presented on the following page [3].

**References**


[1] Campo,M.S., Moar,M.H., Laird,H.M., and Jarrett,W.F. Molecular heterogeneity and lesion site specificity of cutaneous bovine papillomaviruses. *Virology* **113**: 323-35 (1981)

[2] Lindholm,I., Murphy,J., O'Neil,B.W., Campo,M.S., and Jarrett,W.F. Papillomas of the teats and udder of cattle and their causal viruses. *Veterinary Record* **115**: 574-7 (1984)

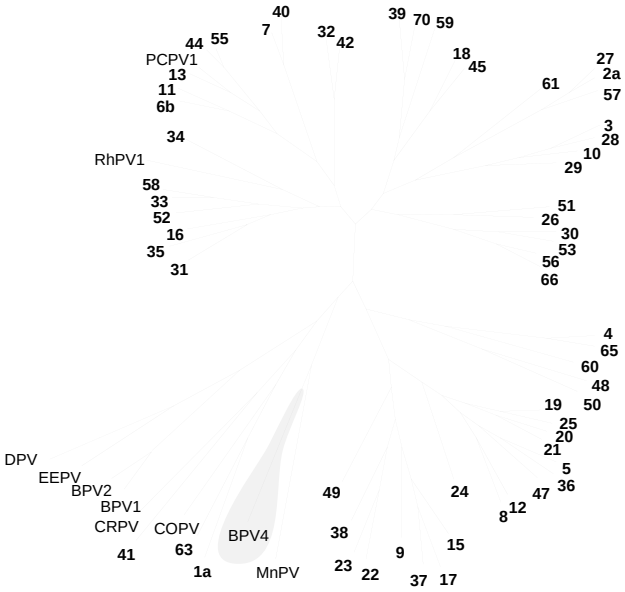
[3] Chan,S.Y., Delius,H., Halpern,A.L., and Bernard, H.U. Analysis of genomic sequences of 95 papillomavirus types: uniting typing, phylogeny, and taxonomy. *Journal of Virology* **69**: 3074-83 (1995)

**BPV5L1**

```
LOCUS       BPV5L1        285 bp    DNA             VRL       13-JUL-1995
DEFINITION  Bovine papillomavirus type 5 L1 protein gene, partial cds.
ACCESSION   U21863
KEYWORDS    .
SOURCE      Bovine papillomavirus type 5.
REFERENCE   1  (bases 1 to 285)
  AUTHORS   Chan,S.-Y., Delius,H., Halpern,A.L. and Bernard,H.U.
  TITLE     Analysis of genomic sequences of 95 papillomavirus types - uniting
            typing, phylogeny and taxonomy
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 285)
  AUTHORS   Chan,S.-Y.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-FEB-1995) Shih-Yen Chan, Institute of Molecular and
            Cell Biology, National University of Singapore, Lower Kent Ridge
            Road, Singapore, 0511, Republic of Singapore
COMMENT
            NCBI gi: 896376
BASE COUNT       98 a     52 c     62 g     73 t
ORIGIN
        1 tattgcaggc atgtagagga atataagcta gccgttattc tggagctatg tagtgtggag
  L1 cds ->
       61 ctgacctacg aaaccgttgc atatttgcag accgttaacc cttctgtctt agaaaaatgg
      121 gaagtaggag tgaaccctcc cccagccact gtattagaag acacttatag atatcaggaa
      181 tccaaggcta taaaatgcat agatcagacg gcagcagcta aaaaagataa atatgaaaat
      241 cttagctttt ggaatattga tctcagagaa aaattatccg cagat
                                                        L1 cds ->
//
```

# Group D1 Sequences

**BPV3 BPV4**
**BPV6**




## INTRODUCTION

Papillomaviruses infect a wide range of hosts including ungulates, birds, rodents, dogs, marsupials and primates. However, only a subset of these animal papillomavirus types have been cloned and characterized, while an even smaller number have been sequenced over the entire genome. Group I of last year's compendium included those animal types whose complete genomes have been sequenced: COPV, CRPV, EEPV, DPV, BPV-1, BPV-2, BPV-4, PCPV-1, MnPV, and RhPV. This year, we have divided the animal papillomaviruses into Groups C1, C2, D1, and E. Furthermore three animal sequences, FPV, MmPV, and MnPV are isolated lineages which may represent taxa at the supergroup level. The bovine papillomaviruses can be classified into two groups, C1 composed of BPV-1 and BPV-2, and D1 which comprises BPV-3, BPV-4 and BPV-6, based on the tissues they infect [1], and on phylogenetics. Distinctive clinical pathologies have been associated with the various categories of animal papillomaviruses. BPV-3, BPV-4, and BPV-6 cause true papillomas.

The group D1 viruses are commonly associated with true epithelial papillomas [2]. BPV-3 was isolated from cutaneous epithelial papillomas [1]. Teat-frond epithelial papillomas are characteristic of BPV-6 [1]. BPV-4, cloned from alimentary epithelial papillomas, can progress to malignancy when infected cattle feed on bracken [1]. Because of its oncogenic potential, more research has focused on BPV-4 than any of the other group D1 viruses.

In addition to differences in host tissue restriction, several other characteristics distinguish the groups of the bovine papillomaviruses. First, group D1 viruses have smaller genomes (7.2 kB) than group C1 viruses (7.9 kB). Second, the analogous position of the group C1 E6 ORF is occupied by the group D1 E8 ORF [1]. This coding region encodes a protein which strongly resembles the E5 transforming protein of the group C1 viruses [1].

## What's new?

Partial sequences that include the L1, E8, E7, and E1 of BPV-3 and BPV-6 are also presented here. The complete genomic sequence of BPV-4 was treated in *Human Papillomaviruses 1994* page I-I-32.

### References


[1] Jackson, M.E., Pennie, W.D., McCaffery, R.E., Smith, K.T., Grindlay, G.J., and Campo, M.S. The B subgroup bovine papillomaviruses lack an identifiable E6 open reading frame. *Molecular Carcinogenesis* **4**: 382–387 (1991)

[2] Coggins, L.W., Ma, J.Q., Slater, A.A., and Campo, M.S. Sequence homologies between bovine papillomavirus genomes mapped by a novel low-stringency heteroduplex method. *Virology* **143**: 603–611 (1985)

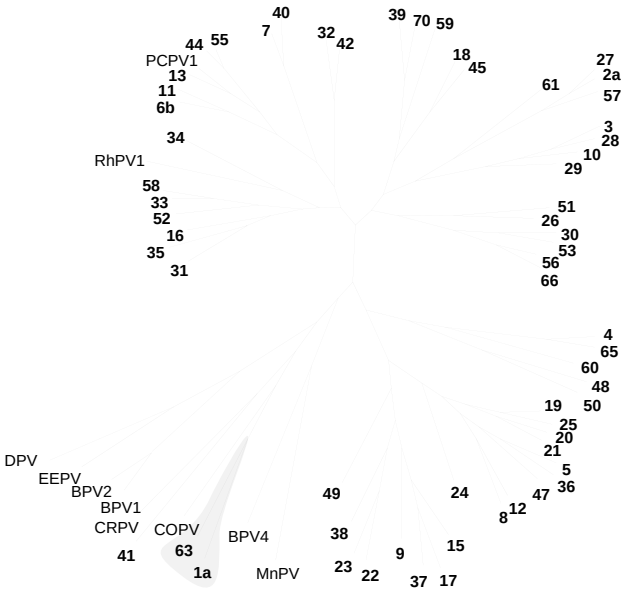
**BPV3L1**

```
LOCUS       BPV3L1        285 bp    DNA             VRL       13-JUL-1995
DEFINITION  Bovine papillomavirus type 3 L1 protein gene, partial cds.
ACCESSION   U21862
KEYWORDS    .
SOURCE      Bovine papillomavirus type 3.
REFERENCE   1  (bases 1 to 285)
  AUTHORS   Chan,S.-Y., Delius,H., Halpern,A.L. and Bernard,H.U.
  TITLE     Analysis of genomic sequences of 95 papillomavirus types - uniting
            typing, phylogeny and taxonomy
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 285)
  AUTHORS   Chan,S.-Y.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-FEB-1995) Shih-Yen Chan, Institute of Molecular and
            Cell Biology, National University of Singapore, Lower Kent Ridge
            Road, Singapore, 0511, Republic of Singapore
COMMENT
            NCBI gi: 896374
BASE COUNT       92 a     55 c     60 g     78 t
ORIGIN
        1 tatttaagac atgtagaaga atgggaagtg tccttagttc tgcaactgtg tatagtggac
  L1 cds ->
       61 ctaacaccag aggctttagc tcacattaat tgcatggatc ctcgaattat agagagctgg
      121 aacttaggct ttatacatgc accgaataat atagaggatc aatacagata cctacagtca
      181 attgcaacta gatgcccccc taaagaagat gctgctgcaa ctgaggaccc ttatgcaaag
      241 tacacatttt gggatgtgga ccttacagaa cgattttcta tgaat
                                                        L1 cds ->
//
```

```
LOCUS       BPV6L1        285 bp    DNA             VRL       13-JUL-1995
DEFINITION  Bovine papillomavirus type 6 L1 protein gene, partial cds.
ACCESSION   U21864
KEYWORDS    .
SOURCE      Bovine papillomavirus type 6.
REFERENCE   1  (bases 1 to 285)
  AUTHORS   Chan,S.-Y., Delius,H., Halpern,A.L. and Bernard,H.U.
  TITLE     Analysis of genomic sequences of 95 papillomavirus types - uniting
            typing, phylogeny and taxonomy
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 285)
  AUTHORS   Chan,S.-Y.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-FEB-1995) Shih-Yen Chan, Institute of Molecular and
            Cell Biology, National University of Singapore, Lower Kent Ridge
            Road, Singapore, 0511, Republic of Singapore
COMMENT
            NCBI gi: 896378
BASE COUNT      102 a     52 c     53 g     78 t
ORIGIN
        1 tacttaagac atgttgagga gtgggaacta tcatgtataa tgcagctttg cattgtagat
  L1 cds ->
       61 ttaaaaccag aaaccttagc acatctgcac aacatggatc cacgtatatt agagacctgg
      121 aacttgggat tcattcagcc cccaactaat atagaagatc agtacaggtt tattaagtct
      181 ttagccacta aatgccctgg taaagaggaa actgcagaaa aagaagaccc atatgctaaa
      241 tataaattct gggatattaa cctaacagaa aggttttctt ctaat
                                                      L1 cds ->
//
```

# Group E1 Sequences

**HPV1 HPV63**




## INTRODUCTION

Group E1 consists of the human papillomaviruses HPV-1, and HPV-63, which are associated with benign cutaneous lesions, commonly seen in the general population. These two viruses were members of the old group G.

HPV-1, HPV-4 (group B2), and HPV-2 (group A4) are the major etiological agents of benign cutaneous papillomas in the general population. HPV-1 is primarily associated with deep palmo-plantar warts, while HPV-4 has been correlated with common warts and keratotic flat lesions on the hands and feet, and hand warts of meat handlers [1–3], and HPV-2 with common and filiform warts [4]. HPV-63 is associated with multiple punctate keratotic lesions of the foot [2]. While the primary target tissue of the group E1 viruses is the epithelium, rare mucosal infection has been reported for HPV-1, which has been identified in benign anogenital warts [5,6,7].

The viruses HPV-1 and HPV-63 produce intracytoplasmic inclusion bodies in most infected epidermal cells. The inclusion bodies primarily contain E4 proteins that can be used to histologically identify these viruses. HPV-63 is associated with a filamentous type of ICB (FI-ICB) and HPV-1 presents a granular type (Gr-ICB) [2].

The members of Group E1 appear to be closer phylogenetically to the nonprimate animal papillomaviruses COPV and CRPV than to other human papillomaviruses.

## What's new?

No new sequences in Group E1 were released during 1995. The sequences of members of this group were published in *Human Papillomaviruses 1994* pp. I-G-3, and I-G-16.

### References


[1] Danos,O., Katinka,M., and Yaniv,M. Human papillomavirus 1a complete DNA sequence: a novel type of genome organization among Papovaviridae. *EMBO* **1**: 231–236 (1982)

[2] Egawa, K., Delius,H., Matsukura,T., Kawashima,M., and de Villiers,E.M. Two novel types of human papillomavirus, HPV 63 and HPV 65: comparisons of their clinical and histological features and DNA sequences to other HPV types. *Virology* **194**: 789–99 (1993)

[3] Melchers,W., de Mare,S., Kuitert,E., Galama,J., Walboomers,J., van den Brule,A.J. Human papillomavirus and cutaneous warts in meat handlers. *J Clin Microbiol* **31**: 2547–9 (1993)

[4] Corley,E., Pueyo,S., Goc,B., Diaz,A., and Zorzopulos,J. Papillomaviruses in human skin warts and their incidence in an Argentine population. *Diagn Microbiol Infect Dis* **10**: 93–101 (1988)

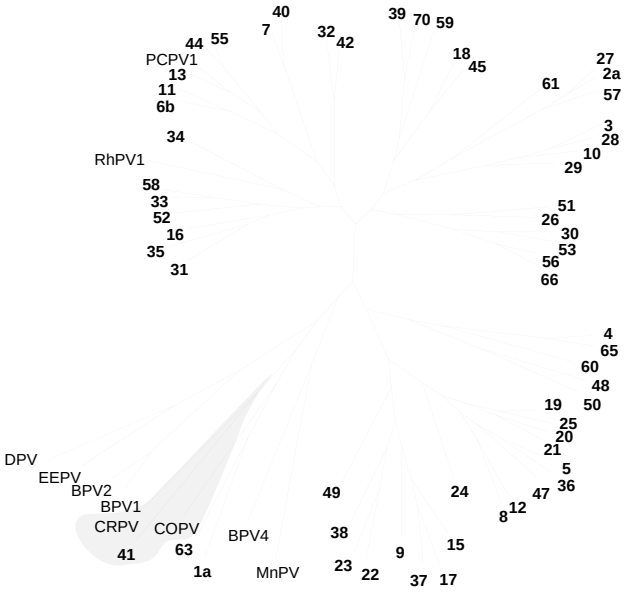
[5] Grimmel,M., de Villers, E.M., Neumann,C., Pawlita,M., and zur Hausen, H. Characterization of a new human papillomavirus (HPV 41) from disseminated warts and detection of its DNA in some skin carcinomas. *Int. J. Cancer* **41**: 5–9 (1988)

[6] Krzyzek,R.A., Watts,S.L., Anderson,D.L., Faras,A.J., and Pass,F. Anogenital warts contain several distinct species of human papillomavirus. *J Virol* **36**: 236–44 (1980)

[7] Gissmann,L., deVilliers,E.M., and zur Hausen,H. Analysis of human genital warts (condylomata acuminata) and other genital tumors for human papillomavirus type 6 DNA. *Int J Cancer* **29**: 143–6 (1982)

# Isolated “E” Sequences

**COPV CRPV**
**ROPV HPV41**




## INTRODUCTION

Most closely related to viruses in group E1, but probably representing clades of “group” status within the E supergroup, are the viruses COPV, CRPV, ROPV, and HPV-41. Like the viruses of group E1 they are cutaneous PVs.

The cottontail rabbit papillomavirus, CRPV was the first papillomavirus to be studied in depth. In 1933, Shope isolated CRPV DNA from large horny warts of cottontail rabbits, thus establishing the link between papillomavirus infection and cutaneous papillomas in this animal [1]. CRPV infects epithelial tissue exclusively in both wild and domestic rabbits [1]. The virus has been shown to induce cutaneous papillomas in domestic rabbits under experimental conditions [1]. Malignant progression occurs in up to 25% of infected cottontail rabbits and up to 75% of infected domestic rabbits [1]. Because of its oncogenic potential, CRPV is a potential model for viral-induced multistage transformation, a progression mediated by genetic susceptibility of the host and environmental factors. The most distinctive characteristic of the CRPV genome is the length of the E6 coding region. This coding region is roughly twice as long as any of the E6 proteins sequenced thus far [1]. CRPV, strictly infects cutaneous tissue.

The rabbit oral papillomavirus (ROPV), the second papillomavirus discovered that infects rabbits, is isolated from benign lesions on the tongues of domestic rabbits. It is represented here by two sequence fragments, one covering the end of E2 and beginning of L2, the other starting approximately 140 bp downstream of the first segment in L2.

Canine oral papillomavirus, COPV, mainly infects the oral cavity of dogs, although it has been observed in lesions of conjunctival epithelium, eyelid, and skin around the nose and mouth [2]. In addition, canine papillomavirus has been detected in cutaneous papillomas [2].

HPV-41 has been linked to flat warts, which are mainly found on the face and feet, and has been detected in cutaneous squamous cell carcinomas and their precursor lesions [3]. Unique to HPV-41 is the absence of typical E2 binding sites in the LCR; however, modified E2 sites, as reported for BPV-1, have been located near the E6 gene [4]. The patterns for these sites are $ACCN_6GTT$, $AACN_6GGT$, each appearing once, and two copies of the perfect palindrome AACGAATTCGTT. Rare mucosal infection has been reported for HPV-41; it has been identified in benign anogenital warts [3,5,6].

## What’s new?

The sequences of COPV, CRPV, and HPV-41 were published in *Human Papillomaviruses 1994* on pages I-I-5, I-I-9, and I-G-12. We present the two fragments of ROPV on the following pages.

### References


[1] Giri, I., Danos, O., and Yaniv, M. Genomic structure of the cottontail rabbit (Shope) papillomavirus. *P.N.A.S.* **82**: 1580–1584 (1985)

[2] Pfister, H., and Meszaros,J. Partial characterization of a canine oral papillomavirus. *Virology* **104**: 243–246 (1980)

[3] Grimmel,M., de Villers, E.M., Neumann,C., Pawlita,M., and zur Hausen, H. Characterization of a new human papillomavirus (HPV 41) from disseminated warts and detection of its DNA in some skin carcinomas. *Int. J. Cancer* **41**: 5–9 (1988)

[4] Hirt,L., Hirsch-Behnam,A., de Villiers,E.M. Nucleotide sequence of human papillomavirus (HPV) type 41: an unusual HPV type without a typical E2 binding site consensus sequence. *Virus Res* **18**: 179–89 (1991)

[5] Krzyzek,R.A., Watts,S.L., Anderson,D.L., Faras,A.J., and Pass,F. Anogenital warts contain several distinct species of human papillomavirus. *J Virol* **36**: 236–44 (1980)

[6] Gissmann,L., deVilliers,E.M., and zur Hausen,H. Analysis of human genital warts (condylomata acuminata) and other genital tumors for human papillomavirus type 6 DNA. *Int J Cancer* **29**: 143–6 (1982)

```
LOCUS       ROPVE2L2        1519 bp    DNA             VRL       17-MAY-1995
DEFINITION  Rabbit oral papillomavirus DNA fragment with partial E2, E4 and
            L2 coding regions.
ACCESSION   M19497
SEGMENT     1 of 2
SOURCE      Rabbit papillomavirus (clone: ROPV B and ROPV C) DNA.
REFERENCE   1  (bases 1 to 1519)
  AUTHORS   O'Banion,M.K., Cialkowski,M.E., Reichmann,M.E. and Sundberg,J.P.
  TITLE     Cloning and molecular characterization of an oral papillomavirus of
            domestic rabbits
  JOURNAL   Virology 162 (1), 221-231 (1988)
COMMENT     The rabbit oral papillomavirus, the second papillomavirus discovered
            that infects rabbits, is isolated from benign lesions on the tongues
            of domestic rabbits. Draft entry and computer-readable sequence for [1]
            kindly provided by M.K.O'Banion, 14-MAR-1988.

            NCBI gi: 333532
BASE COUNT      438 a    365 c    367 g    349 t
ORIGIN      5 bp upstream of KpnI site.
        1 ggtacctagc actgttgatg agaagggggt gtattatagg gatacagaag gaaacaatat
          -> E2 orf
          -> E4 orf
       61 atattatgtg gactttgaga ctgatgctgc acgcttttca agcaaaggag agtatgaagt
      121 tgtatataaa agccaaaaac tttctgtgtc ctctgttacc agctcaaccc ccctacggcc
      181 catcgctctt ggcaacaccc ttgacaacgc caccgcgtcg cccgcccctg cagtatccgc
      241 aggccccgcg caccatccgc aaaccccggt caagtcgtta tcggggccgg tttctcgtta
      301 cggacggagg agatccagat ccccaggagt tggattcgac ccagcaagat ccagaagaca
      361 aggaaaacat cccaccgact tcaacgccaa caccatctcc gccgactcca ccgactccac
      421 cgacttctcg cccgccttta gaccacctac tccttcagag gttggaagaa gaaatacgac
      481 agctccaaga gagtctgcaa gaggacttgg aggaagagtt cggcaactta tatctgaggc
      541 tcgggatccg ccagTGAtct gtttaaaagg gggcaacaac cagcttaagt gcttaaggta
                  E4 end <-
      601 tcgcttaaaa gccaaacacc gcactttgtt tgactgtatt agtaccacat ggagttgggt
      661 agataatagc agcacatgta gagtaggtag tgggagagtg ctgataaaat tcaaagatga
      721 agcacaacgt gaaaaggttt tagaggaggt accgataccc agacatatgc aagtgtttgt
      781 tgggaacttc tttggcttgT AAatgcatta ctgTGAatta tctgtatctg tgaaatttgt
                          E2 end <-               -> L2 orf start
      841 acattgttta caATGgtgct acgcacgcgc aagcgcagag ctgctccaca agacatttat
                        -> L2 cds
      901 cctgcatgca aaatatctaa cacatgtccc ccagacatta ttAATAAAta tgaaAATAAA
                                                signal ->    signal ->
      961 acagtggctg acaagatttt acagtatgga agtcttggag tgtactttgg gggtttggga
     1021 ataggtactg gaactgggtc gggtggcaga ggtggttatg ttcccttggg aggctcatca
     1081 ggcggacggg tagtaggtgg ctctgctgta agaccaccta tccctacaga cactgtaggt
     1141 cctttagaag taatccctga agcggttgac cccgcaggtc tttcaatcgt tccccttgaa
     1201 gaatatcctg ctgaaatacc aacaacaagt ggcactaatg tcataggtga aggaggtgcc
     1261 cagcccccac ccagttcagg gggcggcagc gcaatcctgg acgtaatcag cgaggaaagt
     1321 ggagtcacaa gcagaacaca ctttaataac cccacctttg aagcccccaa tacaaataat
     1381 attagtgtcc ctgacattgt agacccccaa ccagaagaca tagttattag ctacacagat
     1441 gccccagaac ctggtgagct catagaattg gtaccttgca tcaggggaga gacattgaca
     1501 tacaagagaa cctatcata
                           -> L2 cds
```

**ROPVL2**

```
LOCUS       ROPVL2         433 bp    DNA             VRL       17-MAY-1995
DEFINITION  Rabbit oral papillomavirus DNA fragment with partial L2 cds.
ACCESSION   M19498
SEGMENT     2 of 2
SOURCE      Rabbit papillomavirus (clone: ROPV C) DNA.
REFERENCE   1  (bases 1 to 433)
  AUTHORS   O'Banion,M.K., Cialkowski,M.E., Reichmann,M.E. and Sundberg,J.P.
  TITLE     Cloning and molecular characterization of an oral papillomavirus of
            domestic rabbits
  JOURNAL   Virology 162 (1), 221-231 (1988)
  MEDLINE   88101370
COMMENT     The rabbit oral papillomavirus, the second papillomavirus discovered
            that infects rabbits, is isolated from benign lesions on the tongues
            of domestic rabbits. Draft entry and computer-readable sequence for [1]
            kindly provided by M.K.O'Banion, 14-MAR-1988.

            NCBI gi: 333533
BASE COUNT      116 a    113 c     98 g    106 t
ORIGIN      Approximately 140 bp after segment 1.
        1 aatcccgcct tcgtagatga tgatcagtca actcttttgt ttgatcagga ccttgataat
          -> L2 cds
       61 gtccttgctg caccagaccc ccaattcact gacgtggtca aactgtccag accctcttat
      121 acaagaacgg cctcaggtcg agtgagagtc agcagacttg gtactactgg cactatccgc
      181 acacgcagtg gtctgcaaat aggccccgc aagcactttt attatgatat ctcatcgata
      241 ccatctgaaa gtatagagct acaacccatt gcagaatctg caaatgaaga cacagttagt
      301 gggctgcctg acctagacat catcaatgca gatgaaactg catttactga ggctgacctt
      361 ttggatgagc cagaatctgt gggcgaaggc ctgcagctgg tgattagttc cactagacgg
      421 gcaccacgga tcc
                      -> L2 cds
```

# Isolated Supergroup Sequences

**FPV**
**MnPV**
**MmPV**

This set of viruses contains taxa that differ by such a degree from all other known PVs that they each probably represent unnamed supergroups. All sequences are fragments. The chaffinch papillomavirus, FPV, [1] is represented by sequences of the E1 and L1 regions; the *Micromys minutus* (mouse) papillomavirus, MmPV, [2] by an E6 sequence.

## What's new?

The sequences of FPV and MmPV appear on the following pages. The sequence for MnPV was published in *Human Papillomaviruses 1994* pp. I-I-42.

**References**


[1] Moreno-Lopez,J., Ahola,H., Stenlund,A., Osterhaus,A. and Pettersson,U. Genome of an avian papillomavirus. *J Virol* **51**:872–875 (1984)

[2] Van Ranst,M., Tachezy,R., Pruss,J. and Burk,R. Primary structure of the E6 protein of Micromys minutus papillomavirus and Mastomys natalensis papillomavirus. *Nucleic Acids Res* **20**:2889–2889 (1992)

**FPV1E1**

```
LOCUS       FPV1E1        456 bp ds-DNA             VRL       30-SEP-1988
DEFINITION  Avian papillomavirus FPV-1, E1 protein.
ACCESSION   K02019
SEGMENT     1 of 2
SOURCE      FPV-1 DNA from chaffinch epithelial warts.
REFERENCE   1  (bases 1 to 456)
  AUTHORS   Moreno-Lopez,J., Ahola,H., Stenlund,A., Osterhaus,A. and
            Pettersson,U.
  TITLE     Genome of an avian papillomavirus
  JOURNAL   J. Virol. 51, 872-875 (1984)
COMMENT     FPV1 and FPV1a were isolated from chaffinches in the Netherlands and
            Sweden, respectively; FPV1 was isolated from a skin papilloma on the
            leg, FPV1a from a wart on the foot.  The isolates give identical
            restriction fragment patterns for several restriction enzymes,
            although the patterns for ClaI are distinct.  The genomes have been
            cloned and their genomes partially characterized and sequenced; the
            genome is approximately 7.8 kb.  Low stringency hybridization to BPV1
            revealed some sequence homology.  The organization of the genome
            appears to be similar to that of mammalian PVs.  Partial sequencing of
            the E1 and L1 ORFs revealed greatest homology to BPV1 and related
            types within L1; within E1, high similarity to the same sequences is
            observed, although HPV65 is more similar in this region.  FPV DNA
            (crude and purified) failed to raise tumors in the chaffinch and
            canary foot or tarsus, and also did not demonstrably lead to
            transformation of C127 mouse cells.
            NCBI gi: 332991
BASE COUNT      130 a     87 c    105 g    134 t
ORIGIN      213 bp upstream of HindIII site.
        1 tatgatgtag agagcaccga tgaagatggt tggaaaaaga ttttggtgtt ccttacgttc
E1 cds ->
       61 caacatatta attttaaaga gtttatctct atcctttgta tgtggctaaa aggaaggcct
      121 aaaaaaagct gcataacaat tgccggcgtt ccagacagtg gcaagagtat gtttgcatat
      181 tctctgatca aattcctcaa tggttctgta ctaagctttg caaacagtaa gtcacacttc
      241 tggctgcaac cattaacgga atgcaaggct gctttgatag acgatgtaac cttaccttgt
      301 tgggattatg tggacacctt tttaagaaat gcacttgatg gtaatgccat atgtattgat
      361 tgtaagcacc gtgcacccgt ccaaactaaa tgtccgccat tgctgctaac cagtaactat
      421 gaccctcgat tgcatggggt agatagcggg gggggg
                                           E1 cds ->
//
```

```
LOCUS       FPV1L1        330 bp ds-DNA             VRL       30-SEP-1988
DEFINITION  Avian papillomavirus FPV-1, L1 region.
ACCESSION   K02020
SEGMENT     2 of 2
SOURCE      FPV-1 DNA from chaffinch epithelial warts.
REFERENCE   1  (bases 1 to 330)
  AUTHORS   Moreno-Lopez,J., Ahola,H., Stenlund,A., Osterhaus,A. and
            Pettersson,U.
  TITLE     Genome of an avian papillomavirus
  JOURNAL   J. Virol. 51, 872-875 (1984)
COMMENT     FPV1 and FPV1a were isolated from chaffinches in the Netherlands and
            Sweden, respectively; FPV1 was isolated from a skin papilloma on the
            leg, FPV1a from a wart on the foot.  The isolates give identical
            restriction fragment patterns for several restriction enzymes,
            although the patterns for ClaI are distinct.  The genomes have been
            cloned and their genomes partially characterized and sequenced; the
            genome is approximately 7.8 kb.  Low stringency hybridization to BPV1
            revealed some sequence homology.  The organization of the genome
            appears to be similar to that of mammalian PVs.  Partial sequencing of
            the E1 and L1 ORFs revealed greatest homology to BPV1 and related
            types within L1; within E1, high similarity to the same sequences is
            observed, although HPV65 is more similar in this region.  FPV DNA
            (crude and purified) failed to raise tumors in the chaffinch and
            canary foot or tarsus, and also did not demonstrably lead to
            transformation of C127 mouse cells.
            NCBI gi: 332992
BASE COUNT      104 a     61 c     82 g     83 t
ORIGIN      About 4.3 kb after <fpv11>.
        1 gaacctgtac cagagacagt tcccatcgct tctagggaac agattgaaaa gaacaatagt
L1 cds ->
       61 gcctacatgg cctgcccgtc tggctccgtt atcacgagtg atacgaatct ttttaacagg
      121 tcatactgga cgaacaatgg catattgtgg aacgaaaact tattcgtgac agtgctggat
      181 aatagcagga atgtcattat gaaaataagc agcttagctg aaggtgctca ggagaataat
      241 gccacagtct atgactggaa aaattactac gagtgtgtca ggcatgtaga ggagtatggc
      301 atatctgcaa tagtaaggct ttgcagagtt
                                  L1 cds ->
//
```

**MmPVE6**

```
LOCUS       MMPVE6        465 bp    DNA             VRL       30-MAY-1992
DEFINITION  Micromys minutus Papillomavirus E6 gene.
ACCESSION   X65200
SOURCE      Micromys minutus papillomavirus.
REFERENCE   1  (bases 1 to 465)
  AUTHORS   Van Ranst,M.A.
  TITLE     Direct Submission
  JOURNAL   Submitted (03-APR-1992) M.A. Van Ranst, Albert Einstein College of
            Medicine, Ullmann Bldg-Room 515, 1300 Morris Park Avenue, Bronx NY
            10461, USA
REFERENCE   2  (bases 1 to 465)
  AUTHORS   Van Ranst,M., Tachezy,R., Pruss,J. and Burk,R.
  TITLE     Primary structure of the E6 protein of Micromys minutus
            papillomavirus and Mastomys natalensis papillomavirus
  JOURNAL   Nucleic Acids Res. 20, 2889-2889 (1992)
COMMENT     MmPV was isolated from spontaneously occuring papillomas of the
            European harvest mouse (Micromys minutus).  DNA was extracted from a
            tail papilloma, and cloned into pUC18 plasmids which were transformed
            into TB-1 cells.  The 7.6 kb genome was physically mapped by
            restriction enzymes.  Partial sequencing and sequence comparison
            indicated colinearity with other PV genomes.  Low stringency
            hybridization to HPV1a and MnPV, but no other PV types, was observed.
            Neither NIH 3T3 and C127I cells were transformed within 15 and 28 days,
            respectively, of exposure to crude MmPV DNA, although transfection
            appears to have been achieved.  Virus was detected in normal tissues
            as well as papillomas and one tumor.  A pulmonary lesion positive for
            MmPV indicates that pulmonary epithelial cells may be infected by this
            virus.  Viral genomes appeared to be unintegrated and circular in
            all samples.

            The MmPV E6 gene contains four Cys-X-X-Cys motifs which are conserved
            in all known PVs; these zinc finger (zinc binding) motifs are
            furthermore separated from one another by similar numbers of aa
            residues in all types, indicating the importance of their biological
            function.  Within E6, the highest degree of similarity between MmPV
            and another PV type is to HPV4, another PV type mainly associated with
            cutaneous lesions.

            Additional short fragments of DNA sequence are presented in
            O'Banion et al. J. Virol. 62(1):226-33; these fragments are homologous
            to portions of the HPV1a E1 (3' end) ORF and two portions of the L1
            ORF.

            NCBI gi: 60571
BASE COUNT      119 a     87 c    113 g    146 t
ORIGIN
        1 aagATGccgc agcccaccag ACCGTATTCG TTcatggaac tttgcagaga gtacactttg
     E6 cds  ->                 -> E2 binding
       61 gagcagctac tgaaatttct aaatgttact ttggatactc ttatgctacc ttgccatttt
      121 tgcagtagtt ttatggatct taataataag gccagctacc ttgcttctca actaaaggtt
      181 attgttaaag attgttgctt taaggggct tgcattaaat gtcgccgtaa gcttgctttt
      241 gcagaaaggc agaaatatca agtatgtgtt ggggaggcag atttggtaga ggctatggtt
      301 ggttcacatg ttattaacct aaccgttcgc tgtagtgaat gccttgcttt gcttactgcg
      361 tcagagaaac ttgatGCCAA gtgtgagctg cagactttta ttttagtgcg gcacatgtgg
                NF-1 bind ->
      421 agaacttcct gcagagcgtg cagaactccg gcaatagaat gcTAG
                                                          <- E6 end
//
```