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# Animal papillomaviruses

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ABSTRACT

We provide an overview of the host range, taxonomic classification and genomic diversity of animal papillomaviruses. The complete genomes of 112 non-human papillomavirus types, recovered from 54 different host species, are currently available in GenBank. The recent characterizations of reptilian papillomaviruses extend the host range of the Papillomaviridae to include all amniotes. Although the genetically diverse papillomaviruses have a highly conserved genomic lay-out, deviations from this prototypic genome organization are observed in several animal papillomaviruses, and only the core ORFs E1, E2, L2 and L1 are present in all characterized papillomavirus genomes. The discovery of papilloma–polyoma hybrids BPCV1 and BPCV2, containing a papillomaviral late region but an early region encoding typical polyomaviral nonstructural proteins, and the detection of recombination breakpoints between the early and late coding regions of cetacean papillomaviruses, could indicate that early and late gene cassettes of papillomaviruses are relatively independent entities that can be interchanged by recombination.



## Host range of papillomaviruses

The majority of the established papillomavirus types are human isolates, with 148 HPV types currently listed as Reference Genomes for human papillomaviruses in the Papillomavirus Episteme (http://pave.niaid.nih.gov). This is not surprising, since humans are by far the most intensively studied species with regards to papillomaviral infection. Although a comparable genotype diversity has not yet been discovered within single non-human animal species, the introduction of the multiply primed rolling-circle amplification method for sequence-independent amplification of papillomaviral genomic DNA has led to an exponential increase in the number of completely characterized animal papillomavirus genomes over the last decade (Rector et al., 2004b; Stevens et al., 2010). Many of these new papillomavirus types are only distantly related to previously known types and were classified in novel, close-to-root genera. To date, 112 distinct non-human papillomavirus types have been genomically characterized and are available on GenBank (Table 1). These are distributed over 32 different genera, leaving only the genus Gammapapillomavirus, Mupapillomavirus and Nupapillomavirus to contain exclusively HPV types (Fig. 1). Within some well-studied vertebrate species, such as cynomolgus macaques, domestic cows and dogs, a multitude of different papillomavirus types have already been discovered (MfPV1 to MfPV11, BPV1 to BPV13 and CPV1 to CPV15, respectively; Table 1), indicating that also non-human vertebrate species could carry their own sets of species-specific papillomavirus types. Whether humans, with their extensive diversity of HPVs, will continue to occupy a unique position among the papillomavirus host species, and if so which factors contribute to this, remains an intriguing question that can only be resolved by intensive investigation of individual non-human species.

The non-human papillomavirus types known to date were recovered from 54 different host species, belonging to 16 taxonomic orders, and these include mostly mammals but also 3 bird species (a parrot, a chaffinch and a frankolin) and 3 reptiles (a python and two turtle species) (Table 1). Since papillomaviruses have (so far) not been found in amphibians it is tempting to speculate that the host range of papillomaviruses is restricted to amniotes, a clade of tetrapods that have diverged from anamniotic amphibians during the Carboniferous period of the late Paleozoic Era (estimated at 330 million years ago) (Benton and Donoghue, 2007).

Transmission of papillomaviruses requires close cutaneous or mucosal contact. Together with the species-specific nature of the virus and the genomic stability of their double-stranded DNA, this requirement for close physical contact makes it unlikely that recent interspecies transmissions can account for the global presence of a spectrum of papillomaviruses in many amniotes. It rather indicates that early ancestors of the Papillomaviridae were already infecting the earliest amniotes, and progeny virus could have been passed on to more than 20,000 extant species of the amniote clade, inhabiting virtually every habitat of the planet. This would imply that papillomaviruses are one of the oldest and largest viral families.

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**Table 1**
Overview of genomically characterized non-human papillomaviruses.

| Host species taxonomic order | Host species | | Papillomavirus name | Abbreviation (previous) | Classification | # bp | Accession no. | Isolated from | Reference |
|---|---|---|---|---|---|---|---|---|---|
| **Artiodactyla** | European elk | *Alces alces* | Alces alces papillomavirus 1 | AaPV1 (EEPV) | Deltapapillomavirus 1 | 8095 | M15953 | Cutaneous fibroma | Ahola et al. (1986) |
| | Yak | *Bos grunniens* | Bos grunniens papillomavirus 1 | BgPV1 | Deltapapillomavirus 4* | 7946 | JX174437 | Cutaneous fibropapilloma | Zhu et al. (2013) |
| | Domestic cow | *Bos taurus* | Bos taurus papillomavirus 1 | BPV1 | Deltapapillomavirus 4 | 7945 | X02346** | Cutaneous fibropapilloma | Chen et al. (1982) |
| | | | Bos taurus papillomavirus 2 | BPV2 | Deltapapillomavirus 4 | 7937 | M20219 | Cutaneous fibropapilloma | Groff and Lancaster (unpublished) |
| | | | Bos taurus papillomavirus 3 | BPV3 | Xipapillomavirus 1 | 7276 | AF486184 | Cutaneous papilloma | Terai et al. (2002) |
| | | | Bos taurus papillomavirus 4 | BPV4 | Xipapillomavirus 1 | 7265 | X05817 | Oral/esophageal papilloma | Patel et al. (1987) |
| | | | Bos taurus papillomavirus 5 | BPV5 | Epsilonpapillomavirus 1 | 7841 | AF457465 | Udder fibropapilloma | Terai et al. (2002) |
| | | | Bos taurus papillomavirus 6 | BPV6 | Xipapillomavirus 1 | 7296 | AJ620208 | Udder papilloma | Jarrett et al. (1984) |
| | | | Bos taurus papillomavirus 7 | BPV7 | Dyoxipapillomavirus 1* | 7412 | DQ217793 | Teat papilloma and healthy skin | Ogawa et al. (2007) |
| | | | Bos taurus papillomavirus 8 | BPV8 | Epsilonpapillomavirus 1 | 7791 | DQ098913 | Cutaneous papilloma | Tomita et al. (2007) |
| | | | Bos taurus papillomavirus 9 | BPV9 | Xipapillomavirus 1 | 7303 | AB331650 | Teat papilloma | Hatama et al. (2008) |
| | | | Bos taurus papillomavirus 10 | BPV10 | Xipapillomavirus 1 | 7399 | AB331651 | Teat papilloma | Hatama et al. (2008) |
| | | | Bos taurus papillomavirus 11 | BPV11 | Xipapillomavirus 1 | 7251 | AB543507 | Cutaneous papilloma | Hatama et al. (2011) |
| | | | Bos taurus papillomavirus 12 | BPV12 | Xipapillomavirus 2* | 7197 | JF834523 | Tongue epithelial papilloma | Zhu et al. (2012) |
| | | | Bos taurus papillomavirus 13 | BPV13 | Deltapapillomavirus 4* | 7961 | JQ798171 | Ear cutaneous papilloma | Lunardi et al. (2013) |
| | Arabian camel | *Camelus dromedarius* | Camelus dromedarius papillomavirus 1 | CdPV1 | Deltapapillomavirus 6* | 7679 | HQ912790 | Cutaneous fibropapilloma | Ure et al. (2011) |
| | | | Camelus dromedarius papillomavirus 2 | CdPV2 | Deltapapillomavirus 6* | 7906 | HQ912791 | Cutaneous fibropapilloma | Ure et al. (2011) |
| | Domestic goat | *Capra hircus* | Capra hircus papillomavirus 1 | ChPV1 | Phipapillomavirus 1 | 7542 | DQ091200 | Healthy skin | Van Doorslaer et al. (2006) |
| | Western roe deer | *Capreolus capreolus* | Capreolus capreolus papillomavirus 1 | CcaPV1 (RdPV1, CcPV1) | Deltapapillomavirus 5 | 8032 | EF680235 | Cutaneous fibropapilloma | Erdelyi et al. (2008) |
| | White-tailed deer | *Odocoileus virginianus* | Odocoileus virginianus papillomavirus 1 | OvPV1 (DPV) | Deltapapillomavirus 2 | 8374 | M11910*** | Cutaneous fibroma | Groff and Lancaster (1985) |
| | Domestic sheep | *Ovis aries* | Ovis aries papillomavirus 1 | OaPV1 (OvPV1) | Deltapapillomavirus 3 | 7761 | U83594 | Cutaneous fibropapilloma | Karlis et al. (unpublished) |
| | | | Ovis aries papillomavirus 2 | OaPV2 (OvPV2) | Deltapapillomavirus 3 | 7758 | U83595 | Cutaneous fibropapilloma | Karlis et al. (unpublished) |
| | | | Ovies aries papillomavirus 3 | OaPV3 | Dyolambdapapillomavirus 1 | 7334 | FJ796965 | Squamous carcinoma | Alberti et al. (2010) |
| | Reindeer | *Rangifer tarandus* | Rangifer tarandus papillomavirus 1 | RtPV1 (RPV) | Deltapapillomavirus 1 | 8090 | AF443292 | Cutaneous fibropapilloma | Terai et al. (2002) |
| | Domestic pig | *Sus scrofa domesticus* | Sus scrofa domesticus papillomavirus 1 | SsPV1 | Dyodeltapapillomavirus 1 | 7260 | EF395818 | Healthy skin | Stevens et al. (2008b) |
| **Carnivora** | Domestic dog (Shar Pei) | *Canis lupus familiaris* | Canis familiaris oral papillomavirus | CPV1 (COPV) | Lambdapapillomavirus 2 | 8607 | D55633 | Oral/cutaneous papilloma | Delius et al. (1994) |
| | Domestic dog (Golden retriever) | | Canis familiaris papillomavirus 2 | CPV2 (CfPV2) | Taupapillomavirus 1 | 8101 | AY722648 | Cutaneous papilloma on footpad | Yuan et al. (2007) |
| | Domestic dog (Rhodesian ridgeback ) | | Canis familiaris papillomavirus 3 | CPV3 | Chipapillomavirus 1 | 7801 | DQ295066 | Malignant EV lesion | Tobler et al. (2006) |
| | Domestic dog (European pug) | | Canis familiaris papillomavirus 4 | CPV4 | Chipapillomavirus 2 | 7742 | EF584537 | Pigmented lesion | Tobler et al. (unpublished) |
| | Domestic dog | | Canis familiaris papillomavirus 5 | CPV5 | Chipapillomavirus 1 | 7810 | FJ492743 | Pigmented plaque | Lange et al. (2009a) |
| | Domestic dog | | Canis familiaris papillomavirus 6 | CPV6 | Lambdapapillomavirus 3 | 8242 | FJ492744 | Inverted papilloma | (Lange et al., 2009a) |
| | Domestic dog | | Canis familiaris papillomavirus 7 | CPV7 | Taupapillomavirus 1 | 7955 | FJ492742 | In situ quamous cell carcinoma | Lange et al. (2009a) |