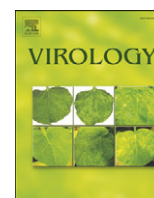


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Classification of papillomaviruses (PVs) based on 189 PV types and proposal of taxonomic amendments

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ABSTRACT

We present an expansion of the classification of the family *Papillomaviridae*, which now contains 29 genera formed by 189 papillomavirus (PV) types isolated from humans (120 types), non-human mammals, birds and reptiles (64, 3 and 2 types, respectively). To accommodate the number of PV genera exceeding the Greek alphabet, the prefix “dyo” is used, continuing after the Omega-PVs with Dyodelta-PVs. The current set of human PVs is contained within five genera, whereas mammalian, avian and reptile PVs are contained within 20, 3 and 1 genera, respectively. We propose standardizations to the names of a number of animal PVs. As prerequisite for a coherent nomenclature of animal PVs, we propose founding a reference center for animal PVs. We discuss that based on emerging species concepts derived from genome sequences, PV types could be promoted to the taxonomic level of species, but we do not recommend implementing this change at the current time.

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Introduction

Papillomaviruses (PVs) infect the epithelia of vertebrates, where they can cause neoplasias or persist asymptotically. PVs have circular double-stranded DNA genomes approximately 8 kb in size and typically contain eight genes. One of these genes, the L1, encodes the principal capsid protein and is necessary and sufficient to produce the virus-like particles used for the current vaccines. PVs have traditionally been referred to as “types”, a type being a cloned full-length PV genome, whose L1 nucleotide sequence is at least 10% dissimilar from that of any other PV type. The L1 gene is useful for classification and construction of phylogenetic trees, as it is reasonably well conserved and can be aligned for all known PVs. This allows a genome-based approach to PV nomenclature, since PVs are not amenable to classical culture techniques. This technical problem was also a reason the term “strain” was not initially employed, however, it is a taxonomic term

used in the publications of the International Committee on Taxonomy of Viruses (ICTV) (Fauquet et al., 2005). Furthermore, PVs do not elicit robust antibody responses, which impeded a classification based on “serotype” designations. As a consequence, classification of PV types based predominantly on nucleotide sequence similarities with some biological and medical properties (Chan et al., 1992; van Ranst et al., 1992b; de Villiers, 1994; Myers et al., 1994; Chan et al., 1995) served as the foundation for a formal nomenclature (de Villiers et al., 2004; Fauquet et al., 2005).

Papillomaviruses were designated as a distinct family, *Papillomaviridae*, in the 7th Report of the ICTV (van Regenmortel et al., 2002). Within the *Papillomaviridae*, the publication by de Villiers et al. (2004), whose authors constituted the Study Group of Papillomaviruses of the ICTV was proposed a classification of 92 human papillomavirus (HPV) and 24 animal PV types that consolidated guidelines established by the ICTV and the PV research community. This classification became formalized in the 8th Report of the International Committee on Taxonomy of Viruses (Fauquet et al., 2005). In these two publications, PVs were assigned to genera designated by Greek letters and to species within these genera according to set rules not familiar at that time to

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the majority of PV researchers. The concept of what constitutes a PV species has been discussed over the years (Van Ranst et al., 1993; Chan et al., 1995), and it was a decision of the ICTV to allocate its placement in the taxonomic hierarchy of PVs (de Villiers et al., 2004; Fauquet et al., 2005), since the “type” concept is not recognized by the ICTV. The adaptation of an official nomenclature that can be utilized by PV researchers, healthcare workers, scientists and the general public requires compromise and it is the purpose of the current manuscript to expand an effective nomenclature that will serve the broad community for the near future and that is reconciled with the fixed official ICTV taxonomic structure. Table 1 compares commonly used terms referring to PV taxa with the terms defined by the ICTV. The table reflects an inconsistency regarding designation of species, that will be discussed later in this paper: while de Villiers et al. (2004) had given phylogenetic groups of HPVs at the level of species a name consisting of a Greek letter combined with a number, e.g. alpha-9 PV in the case HPV16 and several related HPV types, the ICTV named the “species” after one HPV type (e.g. HPV16) and considered all HPV types within that “species” as “strains”, including HPV16 (Fauquet et al., 2005).

This manuscript addresses the following objectives: (1) to update the nomenclature of genera in order to incorporate 28 novel HPV and 45 novel animal PV types that were described since 2004; (2) to refine the rules to maintain coherence of animal PV nomenclature based on the scientific name of the host species and to describe the foundation of a reference center for animal PVs; (3) to reconcile differences between some commonly used taxonomic names with terms used by the ICTV; (4) to discuss—but not to implement—a phylogenetic species concept for PVs that may lead to raising the taxonomic level of the “type” to the level of a “species”. In order to improve readability of this paper, we use the abbreviation “PV” in isolation or in the context of Greek letters, and it should be pointed out that hyphenated abbreviations like Alpha-PVs identify, strictly speaking, genera like *Alphapapillomaviruses*.

Results and discussion

The family Papillomaviridae

The split of the *Papovaviridae* into two families, *Papillomaviridae* and *Polyomaviridae* was accepted by the ICTV nearly a decade ago (van Regenmortel et al., 2002). The genomes of papilloma- and polyomaviruses share only a homologous segment within the papillomavirus E1 genes and the polyomavirus T-antigens that correspond to a helix-case, suggesting an ancient common origin of the replication proteins of these viruses (Clertant and Seif, 1984; Rebrikov et al., 2002). This finding has so far no taxonomic ramifications.

Recently, two viruses of marsupials were published to contain a surprising genome organization, early genes resembling the polyomaviruses, and late genes resembling the papillomaviruses (Woolford et al., 2007; Bennett et al., 2008). These polyoma-papilloma “hybrid” viruses are not evaluated in this paper, as it seems more likely that they represent a recombination event rather than share a common ancestor and are not classified within the *Papillomaviridae* family.

Table 1

Comparison of commonly used and ICTV Papillomavirus nomenclature.

Commonly used names	ICTV term
Taxonomic level	
Family: Papillomavirus	Family: <i>Papillomaviridae</i>
Genus: alpha papillomavirus	Genus: <i>Alphapapillomavirus</i>
Species: alpha papillomavirus-9	Species: Human papillomavirus 16
Types: Human papillomavirus 16, 31, 33, etc.	Strains: Human papillomavirus 16, 31, 33, etc.
Type-species: n/a	Type-species: a term that identifies a papillomavirus typical of a genus (Fauquet et al., 2005) or of a species (de Villiers et al., 2004).

Empiric evidence of PV taxon groupings: pairwise comparisons of PV types

PV taxa are defined based on L1 nucleotide sequence identities and their topological position within PV phylogenetic trees. To evaluate the natural distribution of PV L1 identities, the L1 genes from the entire set of 189 currently characterized PVs were aligned by global multiple sequence alignment and a matrix of pairwise comparisons calculated and plotted (Fig. 1). As previously demonstrated, the distribution of L1 identities shows a bimodal pattern consistent with the genus and species nomenclature. Based on this classification, three histograms created by separate matrix analyses are displayed (Fig. 2) to evaluate the specific distribution of intraspecies, interspecies (within a genus) and intergeneric identities. (Examples: intraspecies comparison: HPV16 vs. HPV31 in the species alpha papillomavirus 9; interspecies comparison: HPV16 vs. 18, members of the species alpha papillomavirus 9 and 7, respectively; intergeneric comparison HPV16 vs. HPV41, members of the genera alpha and nu papillomavirus, respectively). Most types within a PV genus show less than 60% sequence identity to types of other genera based on global multiple sequence or pairwise alignments of the L1 genes. Nevertheless, the suggested percentage identities that define PV genera have to be taken as general, but not absolute criteria for a number of reasons. For instance, there is overlap between the intergeneric and interspecies PV identities seen at the tails of each histogram. Thus, assignment of PV types to species and genera cannot be relegated to a computer algorithm, but requires curation (i.e. interpretation based on phylogeny, genome organization, biology and pathogenicity).

Taxonomy of PVs on the level of genera

De Villiers et al. (2004) described the topology of phylogenetic trees, quantitative thresholds in nucleotide sequence comparisons and biologically distinguishing features (host species, target tissues, pathogenicity, and genome organization) that determine the classification of PVs on the level of genera. A nomenclature of these genera based on the Greek alphabet was introduced and has rapidly become accepted and widely used by the ICTV and community of PV researchers.

In 2004, sixteen groups of PVs or individual PVs fulfilled the criterion of genera, and the Greek alphabet from the letters alpha to pi was employed to create their nomenclature. Human PVs were members of five genera (Alpha-, Beta-, Gamma-, Mu- and Nu-PVs) and two genera (Eta- and Theta-PVs) were each comprised of a single bird PV. The remaining nine genera contained one or several PVs isolated from various mammals. Research over the ensuing 5 years has confirmed the notion that phylogenetic congruence of virus lineages with those of the host species is an important, although not the only mechanism of PV evolution. Consequently, search for PVs in previously understudied and remotely related hosts led to the identification of PVs, whose distant relationship with one another and with all previously published PVs fulfilled the criterion to establish 13 additional genera. These include the first two PVs found in reptiles (marine turtles). All established animal PVs are listed in alphabetical order of their abbreviated name in Table 2.

The last official classification of PV genera ended with the genus *Pi-PVs*. The description of 13 new PV genera however, exhausts the Greek alphabet. In order to create a system that continues with the Greek alphabet, we propose to use the Greek alphabet a second time, employing the prefix “dyo”, (i.e., Greek “a second time”). In addition, we propose to omit the designations Dyoalpha, Dyobeta and Dyogamma, since the *Alpha-*, *Beta-* and *Gamma-PV* genera include the most common and medically important HPVs. To designate specific genera, we have followed the temporal order of publication and/or GenBank submissions of all PV nucleotide sequences and named the new genera *Rho-* to *Omega-PV*, and continued with the terms e.g., “Dyodelta-PVs”, “Dyoepsilon-PVs”. Table 3 contains a list of all PV genera and species, particularly the name of those PVs that led to the establishment of the new genera. A phylogenetic tree using the L1 nucleotide sequences of 189 PVs was generated using a Bayesian algorithm (Fig. 3) and visualizes the

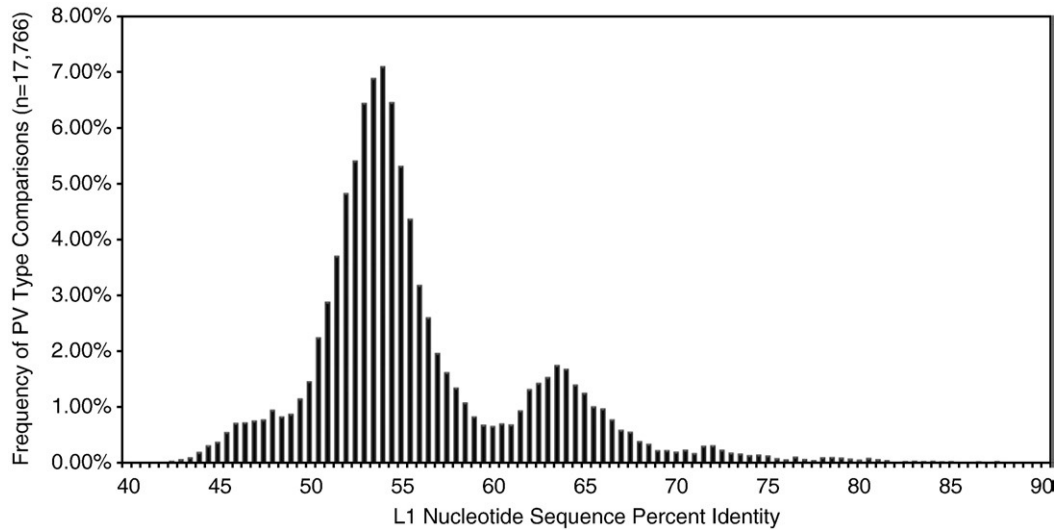


Fig. 1. Distribution of pairwise L1 nucleotide sequence comparisons of 189 Papillomaviruses. L1 nucleotide global multiple sequence alignments were guided by amino acid alignment using MUSCLE v3.7 (Edgar, 2004) and Seaview v4.1 (Galtier et al., 1996) software. A matrix of 189 L1 regions compared to each other, resulted in a total of 17,766 identity values. Gaps were included and counted as one position. The Y-axis represents the percent of the total number of comparisons. The X-axis shows the L1 nucleotide sequence percent identity. The figure has a predominantly bimodal distribution with overlap at around 60% nucleotide sequence identity.

relationship between all previously and newly described genera highlighting the three major genera containing the majority of HPV types.

Nomenclature of animal PV types

Table 2 lists the abbreviated scientific name of all animal PV types, the previously used names, the proposed phylogenetic genus, database accession numbers and references. The abbreviations have been edited to assure a coherent nomenclature of all animal PVs. Consensus within the community of papillomavirus researchers established that the name of an animal PV should be based on the scientific name of the host, using the host genus and species designation, for example FdPV1 for *Felis domesticus* PV type 1. We have applied this rule systematically, since an uncurated nomenclature of animal PVs resulted in confusion and

multiple use of the same or similar abbreviations for a single type of PV. For example, a PV isolated from the European elk had been named EEPV (Ahola et al., 1986), and subsequently a different PV isolated from *Erinaceus europaeus* (hedgehog) received a similar designation, EePV (Schulz et al., 2009). Moreover, ChPV1 has been used to describe *Capra hircus* PV type 1 (van Doorslaer et al., 2006) and chimpanzee PV type 1 (van Ranst et al., 1992a). To facilitate the isolation, characterisation and publication of novel animal PVs based on a standardized evaluation and nomenclature, an Animal Papillomavirus Reference Center is proposed (see below). While this paper was compiled using publication data and database acceptance dates, deposit of the cloned viral genome will be a future requirement to recognize new animal PV names and inclusion in the official PV taxonomy, just as it has been practiced for many years in the case of human PVs.

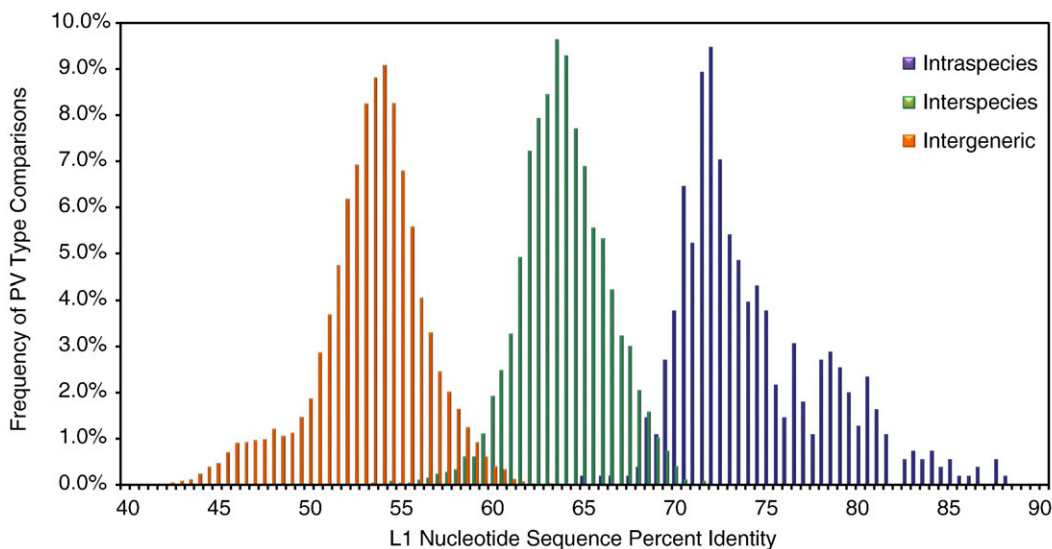


Fig. 2. Specific intergeneric, interspecies and intraspecies L1 nucleotide sequence comparisons based on the multiple sequence alignment matrix. L1 nucleotide global multiple sequence alignment was created as described in the legend to Fig. 1. The same matrix was used to evaluate the distribution of intraspecies: comparisons of PV types within the same species (161 PV types within 49 species, 558 comparisons); interspecies: comparisons of PV types within the same genus (161 PV types within 10 genera, 3207 comparisons); intergeneric: comparisons of all PV types within different genera (189 PVs in 30 genera, 14,001 comparison). The Y-axis represents the percent of the total number of comparisons. The X-axis shows the L1 nucleotide sequence percent identity.

Table 2

Alphabetical listing of the 69 known animal papillomaviruses. Designation of columns: Scient. abbrev., scientific abbreviation; prev. used abbreviation, previously used abbreviation. For details, see text in article.

Scient. abbrev.	Prev. used abbreviation	Papillomavirus name	Host scientific name	Host common name	Phylogeny	NCBI #	Reference (* direct submission)
AaPV1	EPPV	<i>Alces alces Papillomavirus 1</i>	<i>Alces Alces</i>	European elk	Delta-1	M15953	Ahola et al. (1986)
BPV1	BPV1	<i>Bos taurus Papillomavirus 1</i>	<i>Bos taurus</i>	Domestic cow	Delta-4	X02346	Chen et al. (1982)
BPV2	BPV2	<i>Bos taurus Papillomavirus 2</i>	<i>Bos taurus</i>	Domestic cow	Delta-4	M20219	Groff and Lancaster (1986)*
BPV3	BPV3	<i>Bos taurus Papillomavirus 3</i>	<i>Bos taurus</i>	Domestic cow	Xi	AF486184	Terai et al. (2002)
BPV4	BPV4	<i>Bos taurus Papillomavirus 4</i>	<i>Bos taurus</i>	Domestic cow	Xi	X05817	Patel et al. (1987)
BPV5	BPV5	<i>Bos taurus Papillomavirus 5</i>	<i>Bos taurus</i>	Domestic cow	Epsilon	AF457465	Terai, DeSalle, and Burk (2002)
BPV6	BPV6	<i>Bos taurus Papillomavirus 6</i>	<i>Bos taurus</i>	Domestic cow	Xi	AJ620208	Jarrett et al. (1984)
BPV8	BPV8	<i>Bos taurus Papillomavirus 8</i>	<i>Bos taurus</i>	Domestic cow	Epsilon	DQ098913	Tomita et al. (2007)
BPV9	BPV9	<i>Bos taurus Papillomavirus 9</i>	<i>Bos taurus</i>	Domestic cow	Xi	AB331650	Hatama et al. (2008)
BPV10	BPV10, AA5	<i>Bos taurus Papillomavirus 10</i>	<i>Bos taurus</i>	Domestic cow	Xi	AB331651	Hatama et al. (2008)
CcaPV1	RdPV1, CcPV1	<i>Capreolus capreolus Papillomavirus 1</i>	<i>Capreolus capreolus</i>	Western roe deer	Delta-5	EF680235	Erdelyi et al. (2008)
CcPV1	CcPV1	<i>Caretta caretta Papillomavirus 1</i>	<i>Caretta caretta</i>	Loggerhead turtle	Dyozeta	EU493092	Herbst et al. (2009)
CgPV1	CgPV1	<i>Colobus guereza Papillomavirus 1</i>	<i>Colobus guereza</i>	Colobus monkey	Alpha-14	GU014532	(Kloster et al., 1988; Reszka, Sundberg, and Reichmann, 1991)*
CgPV2	CgPV2	<i>Colobus guereza Papillomavirus 2</i>	<i>Colobus guereza</i>	Colobus monkey	Beta-1	GU014533	Kloster et al. (1988)*
ChPV1	ChPV1	<i>Capra hircus Papillomavirus 1</i>	<i>Capra hircus</i>	Domestic goat	Phi	DQ091200	Van Doorslaer et al. (2006)
CmPV1	CmPV1	<i>Chelonia mydas Papillomavirus 1</i>	<i>Chelonia mydas</i>	Green seaturtle	Dyozeta	EU493091	Herbst et al. (2009)
CPV1	CoPV, CPV1	<i>Canis familiaris oral Papillomavirus</i>	<i>Canis familiaris</i>	Domestic dog	Lambda-2	D55633	Isegawa et al. (1994)
CPV2	CPV2, CfPV2	<i>Canis familiaris Papillomavirus 2</i>	<i>Canis familiaris</i>	Domestic dog	Tau	AY722648	Yuan et al. (2007)
CPV3	CPV3	<i>Canis familiaris Papillomavirus 3</i>	<i>Canis familiaris</i>	Domestic dog	Chi-1	DQ295066	Tobler et al. (2006)
CPV4	CPV4	<i>Canis familiaris Papillomavirus 4</i>	<i>Canis familiaris</i>	Domestic dog	Chi-2	EF584537	Tobler et al. (2008)*
CPV5	CPV5	<i>Canis familiaris Papillomavirus 5</i>	<i>Canis familiaris</i>	Domestic dog	Chi-1	FJ492742	Lange et al. (2009a)
CPV6	CPV6	<i>Canis familiaris Papillomavirus 6</i>	<i>Canis familiaris</i>	Domestic dog	Lambda-3	FJ492743	Lange et al. (2009a)
CPV7	CPV7	<i>Canis familiaris Papillomavirus 7</i>	<i>Canis familiaris</i>	Domestic dog	Tau	FJ492744	Lange et al. (2009a)
EcPV1	EcPV1	<i>Equus caballus Papillomavirus 1</i>	<i>Equus ferus caballus</i>	Domestic horse	Zeta	AF498323	Ghim et al. (2004)
EcPV2	EqPV2	<i>Equus caballus Papillomavirus 2</i>	<i>Equus ferus caballus</i>	Domestic horse	Dyoiota	EU503122	Scase et al. (2009) *
EdPV1	EdPV1	<i>Erethizon dorsatum Papillomavirus 1</i>	<i>Erethizon dorsatum</i>	North American porcupine	Sigma	AY684126	Rector et al. (2005a)
EePV1	EhPV, HhPV1, EEPV1	<i>Erinaceus europaeus Papillomavirus 1</i>	<i>Erinaceus europaeus</i>	European hedgehog	Dyoeta	FJ379293	Schulz et al. (2009)
FcPV1	FcPV	<i>Fringilla coelebs Papillomavirus</i>	<i>Fringilla coelebs</i>	Chaffinch (bird)	Eta	AY057109	Terai et al. (2002)
FdPV1	FdPV1	<i>Felis domesticus Papillomavirus 1</i>	<i>Felis domesticus</i>	Domestic cat	Lambda-1	AF480454	Tachezy et al. (2002a)
FdPV2	FdPV2	<i>Felis domesticus Papillomavirus 2</i>	<i>Felis domesticus</i>	Domestic cat	Dyotheta	EU796884	Lange et al. (2009b)
FIPV1	FLPV	<i>Francolinus leucoscepus Papillomavirus 1</i>	<i>Francolinus leucoscepus</i>	Yellownecked Francolin (bird)	Dyoepsilon	EU188799	Van Doorslaer et al. (2009)
LrPV1	LrPV1	<i>Lynx rufus Papillomavirus 1</i>	<i>Lynx rufus</i>	Bobcat	Lambda-1	AY904722	Rector et al. (2007)
MaPV1	HaOPV	<i>Mesocricetus auratus Papillomavirus 1</i>	<i>Mesocricetus auratus</i>	Syrian golden hamster	Pi-2	E15111	Iwasaki et al. (1997) (patent)
McPV2	McPV2	<i>Mastomys coucha Papillomavirus 2</i>	<i>Mastomys coucha</i>	Multimammate mouse	Pi-1	DQ664501	Nafz et al. (2008)
MfPV1	MfPV1	<i>Macaca fascicularis Papillomavirus 1</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Beta-1	EF028290	Joh et al. (2009)
MfPV2	MfPV2	<i>Macaca fascicularis Papillomavirus 2</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Beta-6	GU014531	Chen et al. (2009)
MfPV3	MfPV3, RhPV-d	<i>Macaca fascicularis Papillomavirus 3</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Alpha-12	EF558839	Chen et al. (2009)
MfPV4	MfPV4	<i>Macaca fascicularis Papillomavirus 4</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Alpha-12	EF558841	Chen et al. (2009)
MfPV5	MfPV5, MfPV-a	<i>Macaca fascicularis Papillomavirus 5</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Alpha-12	EF558843	Chen et al. (2009)
MfPV6	MfPV6	<i>Macaca fascicularis Papillomavirus 6</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Alpha-12	EF558840	Chen et al. (2009)
MfPV7	MfPV7	<i>Macaca fascicularis Papillomavirus 7</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Alpha-12	EF558838	Chen et al. (2009)
MfPV8	MfPV8, RhPV-a	<i>Macaca fascicularis Papillomavirus 8</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Alpha-12	EF558842	Chen et al. (2009)
MfPV9	MfPV9	<i>Macaca fascicularis Papillomavirus 9</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Alpha-12	EU490516	Chen et al. (2009)
MfPV10	MfPV10	<i>Macaca fascicularis Papillomavirus 10</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Alpha-12	EU490515	Chen et al. (2009)
MfPV11	MfPV11, RhPV-b	<i>Macaca fascicularis Papillomavirus 11</i>	<i>Macaca fascicularis</i>	Cynomolgus macaque	Alpha-12	GQ227670	Chen et al. (2009)
MmiPV1	MmPV1	<i>Micromys minutus Papillomavirus 1</i>	<i>Micromys minutus</i>	Old World harvest mouse	Pi-1	DQ269468	Van Doorslaer et al. (2007)
MmPV1	RhPV-1	<i>Macaca mulata Papillomavirus 1</i>	<i>Macaca mulata</i>	Rhesus macaque	Alpha-12	M60184	Ostrow et al. (1991)
MnPV1	MnPV1, MrPV, MmPV	<i>Mastomys natalensis Papillomavirus 1</i>	<i>Mastomys natalensis</i>	Multimammate mouse	lota	U01834	Tan et al. (1994)
OaPV1	OvPV1	<i>Ovis aries Papillomavirus 1</i>	<i>Ovis aries</i>	Domestic sheep	Delta-3	U83594	Karlis et al. (2000) *
OaPV2	OvPV2	<i>Ovis aries Papillomavirus 2</i>	<i>Ovis aries</i>	Domestic sheep	Delta-3	U83595	Karlis et al. (2000) *
OcPV1	ROPV	<i>Oryctolagus cuniculus Papillomavirus 2</i>	<i>Oryctolagus cuniculus</i>	New Zealand white rabbit	Kappa-1	AF227240	Christensen et al. (2000)
OvPV1	DPV	<i>Odocoileus virginianus Papillomavirus 1</i>	<i>Odocoileus virginianus</i>	American White-tailed deer	Delta-2	M11910	Groff and Lancaster (1985)
PcPV1	PcPV1	<i>Puma concolor Papillomavirus 1</i>	<i>Puma concolor</i>	Puma	Lambda-1	AY904723	Rector et al. (2007)
PePV1	PePV	<i>Psittacus erithacus Papillomavirus</i>	<i>Psittacus erithacus</i>	Gray parrot (bird)	Theta	AF420235	Tachezy et al. (2002b)

(continued on next page)

Table 2 (continued)

Scient. abbrev.	Prev. used abbreviation	Papillomavirus name	Host scientific name	Host common name	Phylogeny	NCBI #	Reference (* direct submission)
PlpPV1	PlpPV1	<i>Panthera leo persica</i> Papillomavirus 1	<i>Panthera leo persica</i>	Asiatic lion	Lambda-1	AY904724	Rector et al. (2007)
PIPV1	PIPV1	<i>Procyon lotor</i> Papillomavirus 1	<i>Procyon lotor</i>	Raccoon	Lambda-4	AY763115	Rector et al. (2005b)
PpPV1	PpPV1, PCPV	<i>Pan paniscus</i> Papillomavirus 1	<i>Pan paniscus</i>	Pygmy chimpanzee	Alpha-10	X62844	Van Ranst et al. (1991)
PsPV1	PsPV	<i>Phocoena spinipinnis</i> Papillomavirus	<i>Phocoena spinipinnis</i>	Burmeister's porpoise	Omikron	AJ238373	Cassonnet et al. (2007)*
RaPV1	RaPV1	<i>Rousettus aegyptiacus</i> Papillomavirus 1	<i>Rousettus aegyptiacus</i>	Egyptian roussette (fruitbat)	Psi	DQ366842	Rector et al. (2006)
RnPV1	RnPV1	<i>Rattus norvegicus</i> Papillomavirus 1	<i>Rattus norvegicus</i>	Norwegian rat	Pi-1	GQ180114	Schulz et al. (2009)
RtPV1	RtPV, RPV	<i>Rangifer tarandus</i> Papillomavirus 1	<i>Rangifer tarandus</i>	Reindeer	Delta-1	AF443292	Moreno-Lopez et al. (1987)
SfPV1	CRPV, SPV	<i>Sylvilagus floridanus</i> Papillomavirus 1	<i>Sylvilagus floridanus</i>	Cottontail rabbit	Kappa-2	K02708	(Giri, Danos, and Yaniv (1985); Giri et al., 1985)
SsPV1	SsPV1	<i>Sus scrofa</i> Papillomavirus 1	<i>Sus scrofa</i>	Domestic pig	Dyodelta	EF395818	Stevens et al. (2008b)
TmPV1	TmPV1	<i>Trichechus manatus latirostris</i> Papillomavirus 1	<i>Trichechus manatus latirostris</i>	Caribbean manatee	Rho	AY609301	Rector et al. (2004)
TtPV1	TtPV1	<i>Tursiops truncatus</i> Papillomavirus 1	<i>Tursiops truncatus</i>	Bottlenosed dolphin	Upsilon-1	EU240894	Rector et al. (2008)
TtPV2	TtPV2	<i>Tursiops truncatus</i> Papillomavirus 2	<i>Tursiops truncatus</i>	Bottlenosed dolphin	Upsilon-2	AY956402	Rehtanz et al. (2006)
TtPV3	TtPV3	<i>Tursiops truncatus</i> Papillomavirus 3	<i>Tursiops truncatus</i>	Bottlenosed dolphin	Upsilon-1	EU240895	Rector et al. (2008)
UmPV1	UmPV1	<i>Ursus maritimus</i> Papillomavirus 1	<i>Ursus maritimus</i>	Polar bear	Omega	EF536349	Stevens et al. (2008a)
UuPV1	UuPV1	<i>Uncia uncia</i> Papillomavirus 1	<i>Uncia uncia</i>	Snow leopard	Lambda-1	DQ180494	Rector et al. (2007)

See Supplemental table for ICTV animal papillomavirus nomenclature.

To enhance a robust and workable nomenclature, we have sustained the historical use of the abbreviation “HPV” (with H standing for human or Homo, but avoiding the species designation “sapiens”) as well as “BPV” (with B standing for bovine or Bos, but avoiding the species designation “taurus”). However, the name of the cottontail rabbit PV was modified from CRPV1 to SfPV1 (for *Sylvilagus floridanus*), as it had been originally named SPV by one group at the time it was cloned (Wettstein and Stevens, 1980). This nomenclature affects the taxonomic designation, but not necessarily the working terminology as listed under “previously used abbreviations” in Table 2. With the revised nomenclature set forth here, all PV names are unique. Where renaming was necessary, we kept the name of the PV type with publication priority or, as in the example above (EePV1) the one that adapted the name adherent to these rules. In case of overlaps, a third letter was and will be added (e.g., the *Caretta caretta* PV became CcPV1, while the *Capreolus capreolus* PV became CcaPV1). All prototype PVs for a genus were consistently given the number “1”, even when there was no second PV yet known from the same host. Subsequent types were and will be numbered sequentially following the publication date of the virus and/or the submission of the sequence to a public database and deposit of the cloned viral genome. The numbers are added without hyphens to facilitate electronic searches.

The taxonomic status of new HPV types

De Villiers et al. (2004) described the taxonomy of human papillomaviruses HPV1 to HPV96. Since HPV46, 55, 64 and 79 did not meet the criteria as a unique HPV type, they were omitted and their numbers left vacant (de Villiers, 2004). In addition, PV types cloned from PCR products are now accepted for full classification and the term “candidate” has been eliminated. Table 4 lists 28 HPV types (ICTV strains, see Table 1) described since 2004 and their placement within genera. Five PVs (HPV97, 102, 106, 114, and 117) belong to the Alpha-PVs, fourteen PVs (HPV98, 99, 100, 104, 105, 107, 110, 111, 113, 115, 118, 120, 122, and 124) to the Beta-PVs, and nine PVs (HPV101, 103, 108, 109, 112, 116, 119, 121, and 123) to the Gamma-PVs. Among these nine PVs, HPV101, 103, and 108 diverge convincingly from all other HPV types in that they lack an E6 ORF (Chen et al., 2007a; Nobre et al., 2009). In spite of this distinction, these three types are included in the genus *Gamma-PV* based on the present rules of sequence similarities in the L1 ORF and the resulting topology of the phylogenetic tree.

Subtypes and variants of PV types

The definition and properties of PV subtypes and variants as DNA isolates with less than 10% sequence diversity in the L1 gene have been discussed (de Villiers et al., 2004; Calleja-Macias et al., 2005; Bernard et al., 2006). These issues are not further addressed here, as the ICTV does not implement taxonomic systems below the species level. A nomenclature of variants of Alpha-PV types associated with cervix cancer, which will be based on complete genome sequences and extending beyond the historic classification of HPV16 and 18 variant lineages that were based on geographic association (Bernard et al., 2006), is being developed by some of us (Burk et al., in prep.).

Reference centers for human and animal papillomaviruses

The Reference Center for Human Papillomaviruses at the German Cancer Research Center in Heidelberg under the leadership of E.M. de Villiers has for the past 25 years been instrumental in confirming the nucleotide sequence of novel HPV types, assigning the appropriate HPV numbers, depositing and maintaining reference samples, and, if permitted by proprietary rules, distributing DNA samples. This process has been essential to assure an orderly expansion of HPV types and avoid misinterpretation of incomplete or heterologous DNA clones and isolates not meeting the established criteria. The continued maintenance of this reference center and service to the community is of great importance.

In order to avoid misclassifications and maintain a unique nomenclature, we have made efforts to support the establishment of a Repository for Animal Papillomaviruses since no similar reference center for animal PVs has yet been established. One of us (R.D.B.) in collaboration with Dr. Rob DeSalle of the Sackler Institute for Comparative Genomics at the American Museum for Natural History will facilitate the creation of this service. The function of such a center for animal PVs will be to (i) streamline the curation of non-human PVs, (ii) establish a repository for all characterized non-human PVs, and (iii) establish a reference center for all non-human PVs by obtaining the cloned genomes and re-sequencing the provided clones to confirm the existence of each novel non-human PV. As curation of novel HPVs has been necessary for an orderly HPV nomenclature, this repository will implement a similar system for animal PVs, where, prior to publication of a novel animal PV, an “official name” has been designated and the cloned genome been publicly deposited.

Table 3
Papillomavirus genera and species.

Genus	Species (common use)	Species (ICTV)
Alphapapillomavirus	Alpha-1	<i>Human Papillomavirus 32</i>
	Alpha-2	<i>Human Papillomavirus 10</i>
	Alpha-3	<i>Human Papillomavirus 61</i>
	Alpha-4	<i>Human Papillomavirus 2</i>
	Alpha-5	<i>Human Papillomavirus 26</i>
	Alpha-6	<i>Human Papillomavirus 53</i>
	Alpha-7	<i>Human Papillomavirus 18</i>
	Alpha-8	<i>Human Papillomavirus 7</i>
	Alpha-9	<i>Human Papillomavirus 16</i>
	Alpha-10	<i>Human Papillomavirus 6</i>
	Alpha-11	<i>Human Papillomavirus 34</i>
	Alpha-12	<i>Macaca mulata Papillomavirus 1</i>
	Alpha-13	<i>Human Papillomavirus 54</i>
	Alpha-14	<i>Human Papillomavirus 90</i>
Betapapillomavirus	Beta-1	<i>Human Papillomavirus 5</i>
	Beta-2	<i>Human Papillomavirus 9</i>
	Beta-3	<i>Human Papillomavirus 49</i>
	Beta-4	<i>Human Papillomavirus 92</i>
	Beta-5	<i>Human Papillomavirus 96</i>
	Beta-6	<i>Macaca fascicularis Papillomavirus 2</i>
Gammapapillomavirus	Gamma-1	<i>Human Papillomavirus 4</i>
	Gamma-2	<i>Human Papillomavirus 48</i>
	Gamma-3	<i>Human Papillomavirus 50</i>
	Gamma-4	<i>Human Papillomavirus 60</i>
	Gamma-5	<i>Human Papillomavirus 88</i>
	Gamma-6	<i>Human Papillomavirus 101</i>
	Gamma-7	<i>Human Papillomavirus 109</i>
	Gamma-8	<i>Human Papillomavirus 112</i>
	Gamma-9	<i>Human Papillomavirus 116</i>
	Gamma-10	<i>Human Papillomavirus 121</i>
Deltapapillomavirus	Delta-1	<i>Alces alces Papillomavirus 1</i>
	Delta-2	<i>Odocoileus virginianus Papillomavirus 1</i>
	Delta-3	<i>Ovis aries Papillomavirus 1</i>
	Delta-4	<i>Bos taurus Papillomavirus 1</i>
	Delta-5	<i>Capreolus capreolus Papillomavirus 1</i>
Epsilonpapillomavirus	Epsilon-1	<i>Bos taurus Papillomavirus 5</i>
Zetapapillomavirus	Zeta-1	<i>Equus caballus Papillomavirus 1</i>
Etapapillomavirus	Eta-1	<i>Fringilla coelebs Papillomavirus</i>
Thetapapillomavirus	Theta-1	<i>Psittacus erithacus Papillomavirus 1</i>
Iotapapillomavirus	Iota-1	<i>Mastomys natalensis Papillomavirus 1</i>
Kappapapillomavirus	Kappa-1	<i>Oryctolagus cuniculus Papillomavirus 1</i>
	Kappa-2	<i>Sylvilagus floridanus Papillomavirus 1</i>
	Kappa-3	<i>Sylvilagus floridanus Papillomavirus 1</i>
Lambdapapillomavirus	Lambda-1	<i>Felis domesticus Papillomavirus 1</i>
	Lambda-2	<i>Canis familiaris Papillomavirus 1</i>
	Lambda-3	<i>Canis familiaris Papillomavirus 6</i>
	Lambda-4	<i>Procyon lotor Papillomavirus 1</i>
Mupapillomavirus	Mu-1	<i>Human Papillomavirus 1</i>
	Mu-2	<i>Human papillomavirus 63</i>
Nupapillomavirus	Nu-1	<i>Human papillomavirus 41</i>
Xipapillomavirus	Xi-1	<i>Bos taurus Papillomavirus 3</i>
Pipapillomavirus	Pi-1	<i>Mesocricetus auratus Papillomavirus 1</i>
	Pi-2	<i>Micromys minutus Papillomavirus 1</i>
Rhopapillomavirus	Rho-1	<i>Trichechus manatus latirostris Papillomavirus 1</i>
Sigmapapillomavirus	Sigma-1	<i>Erethizon dorsatum Papillomavirus 1</i>
Taupapillomavirus	Tau-1	<i>Canis familiaris Papillomavirus 2</i>
Upsilonpapillomavirus	Upsilon-1	<i>Tursiops truncatus Papillomavirus 1</i>
	Upsilon-2	<i>Tursiops truncatus Papillomavirus 2</i>
Phipapillomavirus	Phi-1	<i>Capra hircus Papillomavirus 1</i>
Chipapillomavirus	Chi-1	<i>Canis familiaris Papillomavirus 3</i>
	Chi-2	<i>Canis familiaris Papillomavirus 4</i>
Psipapillomavirus	Psi-1	<i>Rousettus aegyptiacus Papillomavirus 1</i>
Omegapapillomavirus	Omega-1	<i>Ursus maritimus Papillomavirus 1</i>
Dyodeltapapillomavirus	Dyodelta-1	<i>Sus scrofa Papillomavirus 1</i>
Dyoepsilontapapillomavirus	Dyoepsilon-1	<i>Francolinus leucoscepus Papillomavirus 1</i>
Dyozetapapillomavirus	Dyozeta-1	<i>Caretta caretta Papillomavirus 1</i>
Dyoetapapillomavirus	Dyoeta-1	<i>Erinaceus europaeus Papillomavirus 1</i>
Dyothetapapillomavirus	Dyotheta-1	<i>Felis domesticus Papillomavirus 2</i>
Dyoiotapapillomavirus	Dyoiota-1	<i>Equus caballus Papillomavirus 2</i>

Phylogenetic and biological considerations regarding the nature of “PV species” and “PV types”

Defining PV taxa below the level of genera resulted in some inconsistencies between the official ICTV PV nomenclature (Fauquet et al., 2005) and that used by the scientific community (de Villiers et al., 2004). A goal of the current Study Group of Papillomaviruses is to harmonize the official ICTV designations with the known genetics and biology of PVs. The ICTV only names species after a specific virus, such as HPV16, and related types including the “type-species” are designated as strains within the species (see Table 1) (Fauquet et al., 2005). For example, the commonly used term “PV species Alpha-9” (de Villiers et al., 2004) is a synonym for what the ICTV called the “HPV16 species”, which contains the HPV types (strains) 16, 31, 35, 33, 52, 58 and 67. Although it can be argued (see below) that a PV “type” has many characteristics of a “species”, we recommend maintaining the current allocation of the taxonomic levels of genus and species. Nevertheless, since the species designations of de Villiers et al. (2004) have been widely accepted and useful to the scientific community, we support their continued use.

The ICTV proposed guidelines defining that a species should be “a polythetic class of viruses that constitute a replicating lineage and occupies a particular ecological niche” (van Regenmortel et al., 1991). The term “polythetic” means that several or all possible criteria or attributes be used to determine a viral species. This definition suggests that a single property, even genomic sequences, might be insufficient to define a viral species. This definition has been challenged (van Regenmortel et al., 2000; Drebot et al., 2002; Gibbs and Gibbs, 2006). Concepts of defining viral species have always been complicated and are not yet mature. Among several complimentary approaches, nucleotide sequence-based comparisons developed in the last few decades have impacted taxonomic research throughout biology, led to completely new insights into the species concept, and have become widely accepted as a solid taxonomic criterion. Papillomaviruses were the first viruses to be significantly classified by comparison of viral genomes, in part, because of the lack of a culture or serologic system.

The age of PV types is a major component of equating PV types with PV species (Rector et al., 2007). Even closely related PV types have evolved over time scales equivalent to those that gave rise to their host species, i.e. over millions of years. This is fundamentally different from the emergence of quasi-species of RNA viruses over very short periods of time, such as the human immunodeficiency viruses (Rambaut et al., 2004), or from human rhinoviruses that have rapidly evolved in the relatively short time span since the origin of humans (Palmenberg et al., 2009). In addition, the distribution of PV type identities within a species (intraspecific identity) as shown in Figs. 1 and 2 has a normal distribution suggestive of a natural taxonomic order. Moreover, reports of phenotypic idiosyncrasies of closely related PV types, classified within a single species, continue to accumulate. Some notable examples are found among the members of the Alpha-PV 10 species (species HPV6 and related “strains” in ICTV nomenclature). For example, HPV6 and 11 show significantly different tissue tropism, HPV6 being more common in genital warts, HPV11 more common in laryngeal papillomas. The closely related type, HPV13, causes focal epithelial hyperplasia of the oral cavity and has neither been found in genital warts nor in laryngeal papillomas (de Villiers, 1994, 2001). HPV16, 31 and 35 are grouped in the species Alpha-PV 9 (species HPV16 and related “strains” in ICTV nomenclature). The association between HPV16 and cancer is significantly stronger than that between either HPV31 or HPV35 (Munoz et al., 2003). HPV16 is uniquely associated with tumors of the oropharyngeal region.

In summary, we presented arguments on how a phylogenetic species concept could be applied to PV taxonomy. This concept has increasing impact throughout biology, but is presently not implemented in virology, and we therefore do not yet recommend implementation at this point. Once widely accepted, a phylogenetic PV species concept would



Table 4
Human papillomaviruses characterized since 2004.

HPV type	PV genus	PV species (common use)	PV species (ICTV)	GenBank No.	Reference
HPV 97	<i>Alphapapillomavirus</i>	Alpha-7	<i>Human Papillomavirus 18</i>	DQ080080	Chen et al. (2007a)
HPV 98	<i>Betapapillomavirus</i>	Beta-1	<i>Human Papillomavirus 5</i>	FM955837	de Villiers and Gunst (2009)
HPV 99	<i>Betapapillomavirus</i>	Beta-1	<i>Human Papillomavirus 5</i>	FM955838	de Villiers and Gunst (2009)
HPV 100	<i>Betapapillomavirus</i>	Beta-2	<i>Human Papillomavirus 9</i>	FM955839	de Villiers and Gunst (2009)
HPV 101	<i>Gammmapapillomavirus</i>	Gamma-6	<i>Human Papillomavirus 101</i>	NC_008189	Chen et al. (2007c)
HPV 102	<i>Alphapapillomavirus</i>	Alpha-3	<i>Human Papillomavirus 61</i>	DQ080083	Chen et al. (2007b)
HPV 103	<i>Gammmapapillomavirus</i>	Gamma-6	<i>Human Papillomavirus 101</i>	NC_008188	Chen et al. (2007c)
HPV 104	<i>Betapapillomavirus</i>	Beta-2	<i>Human Papillomavirus 9</i>	FM955840	de Villiers and Gunst (2009)
HPV 105	<i>Betapapillomavirus</i>	Beta-1	<i>Human Papillomavirus 5</i>	FM955841	de Villiers and Gunst (2009)
HPV 106	<i>Alphapapillomavirus</i>	Alpha-14	<i>Human Papillomavirus 90</i>	DQ080082	Chen et al. (2007b)
HPV 107	<i>Betapapillomavirus</i>	Beta-2	<i>Human Papillomavirus 9</i>	EF422221	Vasiljevic et al. (2008)
HPV 108	<i>Gammmapapillomavirus</i>	Gamma-6	<i>Human Papillomavirus 101</i>	NC_012213	Nobre et al. (2009)
HPV 109	<i>Gammmapapillomavirus</i>	Gamma-7	<i>Human Papillomavirus 109</i>	NC_012485	Ekstrom et al. (in press)
HPV 110	<i>Betapapillomavirus</i>	Beta-2	<i>Human Papillomavirus 9</i>	EU410348	Vasiljevic et al. (2008)
HPV 111	<i>Betapapillomavirus</i>	Beta-2	<i>Human Papillomavirus 9</i>	EU410349	Vasiljevic et al. (2008)
HPV 112	<i>Gammmapapillomavirus</i>	Gamma-8	<i>Human Papillomavirus 112</i>	EU541442	Ekstrom et al. (in press)
HPV 113	<i>Betapapillomavirus</i>	Beta-2	<i>Human Papillomavirus 9</i>	FM955842	de Villiers and Gunst (2009)
HPV 114	<i>Alphapapillomavirus</i>	Alpha-3	<i>Human Papillomavirus 61</i>	GQ244463	Ekstrom et al. (in press)
HPV 115	<i>Betapapillomavirus</i>	Beta-3	<i>Human Papillomavirus 49</i>	FJ947080	Chouhy et al. (2010)
HPV 116	<i>Gammmapapillomavirus</i>	Gamma-9	<i>Human Papillomavirus 116</i>	FJ804072	Li et al. (2009)
HPV 117	<i>Alphapapillomavirus</i>	Alpha-2	<i>Human Papillomavirus 10</i>	GQ246950	Köhler et al. (in press)
HPV 118	<i>Betapapillomavirus</i>	Beta-1	<i>Human Papillomavirus 5</i>	GQ246951	Nindl et al., unpubl.
HPV 119	<i>Gammmapapillomavirus</i>	Gamma-8	<i>Human Papillomavirus 112</i>	GQ845441	Chen et al., unpubl.
HPV 120	<i>Betapapillomavirus</i>	Beta-2	<i>Human Papillomavirus 9</i>	GQ845442	Chen et al., unpubl.
HPV 121	<i>Gammmapapillomavirus</i>	Gamma-10	<i>Human Papillomavirus 121</i>	GQ845443	Chen et al., unpubl.
HPV 122	<i>Betapapillomavirus</i>	Beta-2	<i>Human Papillomavirus 9</i>	GQ845444	Chen et al., unpubl.
HPV 123	<i>Gammmapapillomavirus</i>	Gamma-7	<i>Human Papillomavirus 109</i>	GQ845445	Chen et al., unpubl.
HPV 124	<i>Betapapillomavirus</i>	Beta-1	<i>Human Papillomavirus 5</i>	GQ845446	Chen et al., unpubl.

lead to a promotion of PV types (strains) to species, and of the present species to sub-genera, while genera would remain unchanged.

Online papillomavirus database

PV nucleotide sequences are deposited in the GenBank and EMBL nucleotide sequence databases. A compilation of all sequences available in the mid-1990s, was compiled and reviewed in the “Papillomavirus Database” sponsored by NIAID and published online and as hardcopy by the Los Alamos National Laboratory (Myers et al., 1994). A new interactive database “Papillomavirus Episteme” (<http://pave.niaid.nih.gov/#home>) is currently under development.

Materials and methods

Origin of sequences

This paper is based on published PV sequences, which can be accessed either through the listed references, or the GenBank accession numbers in the Tables 2 and 4.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.virol.2010.02.002](https://doi.org/10.1016/j.virol.2010.02.002).

References

- Ahola, H., Bergman, P., Ström, A.C., Moreno-López, J., Pettersson, U., 1986. Organization and expression of the transforming region from the European elk papillomavirus (EPPV). *Gene* 50, 195–205.
- Bennett, M.D., Woolford, L., Stevens, H., Van Ranst, M., Oldfield, T., Slaven, M., O'Hara, A.J., Warren, K.S., Nicholls, P.K., 2008. Genomic characterization of a novel virus found in papillomatous lesions from a southern brown bandicoot (*Isodon obesulus*) in Western Australia. *Virology* 376, 173–182.
- Bernard, H.U., Calleja-Macias, I.E., Dunn, S.T., 2006. Genome variation of human papillomavirus types: phylogenetic and medical implications. *Internat. J. Cancer* 118, 1071–1076.
- Calleja-Macias, I.E., Kalantari, M., Allan, B., Williamson, A.L., Chung, L.P., Collins, R.J., Zuna, R.E., Dunn, S.T., Ortiz-Lopez, R., Barrera-Saldaña, H.A., Cubie, H.A., Villa, L.L., Bernard, H.U., 2005. Papillomavirus subtypes are natural and old taxa: phylogeny of the human papillomavirus (HPV) types 44/55 and 68a/b. *J. Virol.* 79, 6565–6569.
- Chan, S.Y., Bernard, H.U., Ong, C.K., Chan, S.P., Hofmann, B., Delius, H., 1992. Phylogenetic analysis of 48 papillomavirus types and 28 subtypes and variants: a showcase for the molecular evolution of DNA viruses. *J. Virol.* 66, 5714–5725.
- Chan, S.Y., Delius, H., Halpern, A.L., Bernard, H.U., 1995. Analysis of genomic sequences of 95 papillomavirus types: uniting typing, phylogeny, and taxonomy. *J. Virol.* 69, 3074–3083.
- Chen, E.Y., Howley, P.M., Levinson, A.D., Seeburg, P.H., 1982. The primary structure and genetic organization of the bovine papillomavirus type 1 genome. *Nature* 299, 529–534.
- Chen, Z., Fu, L., Herrero, R., Schiffman, M., Burk, R.D., 2007a. Identification of a novel human papillomavirus (HPV97) related to HPV18 and HPV45. *Int. J. Cancer* 121, 193–198.
- Chen, Z., Schiffman, M., Herrero, R., Burk, R.D., 2007b. Identification and characterization of two novel human papillomaviruses (HPVs) by overlapping PCR: HPV102 and HPV106. *J. Gen. Virol.* 88, 2952–2955.
- Chen, Z., Schiffman, M., Herrero, R., Desalle, R., Burk, R.D., 2007c. Human papillomavirus (HPV) types 101 and 103 isolated from cervicovaginal cells lack an E6 open reading frame (ORF) and are related to gamma-papillomaviruses. *Virology* 360, 447–453.

Fig. 3. Phylogenetic tree inferred from the L1 nucleotide sequences of 189 papillomaviruses. The phylogeny analysis is based on the multiple L1 nucleotide sequence alignment of 189 PV types that was used in Figs. 1 and 2. MrBayes v3.1.2 (Huelsenbeck and Ronquist, 2001; Ronquist and Huelsenbeck, 2003) with 10,000,000 cycles for the Markov chain Monte Carlo (MCMC) algorithm was used to generate a phylogenetic tree. For Bayesian tree construction, the computer program ModelTest v3.7 (Posada and Crandall, 1998) identified the best evolutionary model. The identified gamma model was set for among-site rate variation and allowed all substitution rates of aligned sequence to be different.

- Chen, Z., van Doorslaer, K., Desalle, R., Wood, C.E., Kaplan, J.R., Wagner, J.D., Burk, R.D., 2009. Genomic diversity and interspecies host infection of alpha12 *Macaca fascicularis* papillomaviruses (MPPVs). *Virology* 393 (2), 304–310.
- Christensen, N.D., Cladel, N.M., Reed, C.A., Han, R., 2000. Rabbit oral papillomavirus complete genome sequence and immunity following genital infection. *Virology* 269, 451–461.
- Chouhy, D., Gorosito, M., Sanchez, A., Serra, E.C., Bergero, A., Fernandez Bussy, R., Giri, A.A., 2010. New generic primer system targeting mucosal/genital and cutaneous human papillomaviruses leads to the characterization of HPV 115, a novel Beta-papillomavirus species 3. *Virology* 397 (1), 205–216.
- Clertant, P., Seif, I., 1984. A common function for polyoma virus large-T and papillomavirus E1 proteins? *Nature* 311, 276–279.
- de Villiers, E.M., 1994. Human pathogenic papillomavirus types, an update. *Curr. Top. Microbiol. Immunol.* 186, 1–12.
- de Villiers, E.M., 2001. Taxonomic classification of papillomaviruses. *Papillomavir. Report* 12, 57–63.
- de Villiers, E.M., Fauquet, C., Broker, T.R., Bernard, H.U., zur Hausen, H., 2004. Classification of papillomaviruses. *Virology* 324, 17–27.
- de Villiers, E.M., Gunst, K., 2009. Characterization of seven novel human papillomavirus types isolated from cutaneous tissue, but also present in mucosal lesions. *J. Gen. Virol.* 90, 1999–2004.
- Drebot, M.A., Henchal, E., Hjelle, B., LeDuc, J.W., Repik, P.M., Roehrig, J.T., Schmaljohn, C.S., Shope, R.E., Tesh, R.B., Weaver, S.C., Calisher, C.H., 2002. Improved clarity of meaning from the use of both formal species names and common (vernacular) virus names in virological literature. *Arch. Virol.* 147, 2464–2472.
- Edgar, R.C., 2004. MUSCLE: multiple sequence alignment with high accuracy and high throughput. *Nucleic Acids Res.* 32, 1792–1797.
- Erdelyi, K., Balint, A., Dencso, L., Dan, A., Ursu, K., 2008. Characterisation of the first complete genome sequence of the roe deer (*Capreolus capreolus*) papillomavirus. *Virus Res.* 135, 307–311.
- Fauquet, C.M., Mayo, M.A., Maniloff, J., Desselberger, U., Ball, L.A., 2005. Virus taxonomy. The Eighth Report of the International Committee on Taxonomy of Viruses. Family *Papillomaviridae*. Elsevier, pp. 239–255.
- Galtier, N., Gouy, M., Gautier, C., 1996. SEAVIEW and PHYLO_WIN: two graphic tools for sequence alignment and molecular phylogeny. *Comput. Appl. Biosci.* 12, 543–548.
- Gibbs, A.J., Gibbs, M.J., 2006. A broader definition of 'the virus species'. *Arch. Virol.* 151, 1419–1422.
- Ghim, S.J., Rector, A., Delius, H., Sundberg, J.P., Jenson, A.B., Van Ranst, M., 2004. Equine papillomavirus type 1: complete nucleotide sequence and characterization of recombinant virus-like particles composed of the E6/E7 major capsid protein. *Biochem. Biophys. Res. Commun.* 324, 1108–1115.
- Giri, I., Danos, O., Yaniv, M., 1985. Genomic structure of the cottontail rabbit (Shope) papillomavirus. *Proc. Natl. Acad. Sci. U.S.A.* 82, 1580–1584.
- Groff, D.E., Lancaster, W.D., 1985. Molecular cloning and nucleotide sequence of deer papillomavirus. *J. Virol.* 56, 85–91.
- Hatama, S., Nobumoto, K., Kanno, T., 2008. Genomic and phylogenetic analysis of two novel bovine papillomaviruses, BPV-9 and BPV-10. *J. Gen. Virol.* 89, 158–163.
- Herbst, L.H., Lenz, J., Van Doorslaer, K., Chen, Z., Stacy, B.A., Wellehan Jr., J.F., Manire, C.A., Burk, R.D., 2009. Genomic characterization of two novel reptilian papillomaviruses, *Chelonina mydas* papillomavirus 1 and *Caretta caretta* papillomavirus 1. *Virology* 383, 131–135.
- Huelsenbeck, J.P., Ronquist, F., 2001. MRBAYES: Bayesian inference of phylogenetic trees. *Bioinformatics* 17, 754–755.
- Isegawa, N., Nakano, K., Ohta, M., Shirasawa, H., Tokita, H., Simizu, B., 1994. Cloning and sequencing of the L1 gene of canine oral papillomavirus. *Gene* 146 (2), 261–265.
- Iwasaki, T., Maeda, H., Kameyama, M., Moriyama, M., Kanai, S., Kurata, T., 1997. Presence of a novel hamster oral papillomavirus in dysplastic lesions of hamster lingual mucosa induced by application of dimethylbenzanthracene and excisional wounding: molecular cloning and complete nucleotide sequence. *J. Gen. Virol.* 78 (Pt 5), 1087–1093.
- Jarrett, W.F., Campo, M.S., O'Neil, B.W., Laird, H.M., Coggins, L.W., 1984. A novel bovine papillomavirus (BPV-6) causing true epithelial papillomas of the mammary gland skin: a member of a proposed new BPV subgroup. *Virology* 136, 255–264.
- Joh, J., Hopper, K., Van Doorslaer, K., Sundberg, J.P., Jenson, A.B., Ghim, S.J., 2009. *Macaca fascicularis* papillomavirus type 1: a non-human primate betapapillomavirus causing rapidly progressive hand and foot papillomatosis. *J. Gen. Virol.* 90, 987–994.
- Kloster, B.E., Manias, D.A., Ostrow, R.S., Shaver, M.K., McPherson, S.W., Rangen, S.R., Uno, H., Faras, A.J., 1988. Molecular cloning and characterization of the DNA of two papillomaviruses from monkeys. *Virology* 166, 30–40.
- Köhler, A., Gottschling, M., Förster, J., Rówert-Huber, J., Stockfleth, E., Nindl, I., in press. Genomic characterization of a novel human papillomavirus (HPV-117) with a high viral load in a persisting wart. *Virology*.
- Lange, C.E., Tobler, K., Ackermann, M., Panakova, L., Thoday, K.L., Favrot, C., 2009a. Three novel canine papillomaviruses support taxonomic clade formation. *J. Gen. Virol.* 90 (Pt 11), 2615–2621.
- Lange, C.E., Tobler, K., Markau, T., Alhaidari, Z., Bornand, V., Stockli, R., Trussel, M., Ackermann, M., Favrot, C., 2009b. Sequence and classification of FdPV2, a papillomavirus isolated from feline Bowenoid in situ carcinomas. *Vet. Microbiol.* 137, 60–65.
- Li, L., Barry, P., Yeh, E., Glaser, C., Schnurr, D., Delwart, E., 2009. Identification of a novel human gammapapillomavirus species. *J. Gen. Virol.* 90, 2413–2417.
- Moreno-Lopez, J., Ahola, H., Eriksson, A., Bergman, P., Pettersson, U., 1987. Reindeer papillomavirus transforming properties correlate with a highly conserved E5 region. *J. Virol.* 61 (11), 3394–3400.
- Munoz, N., Bosch, F.X., de Sanjosé, S., Herrero, R., Castellsagué, X., Shah, K.V., Snijders, P.J.F., Meijer, C.J.L.M., 2003. Epidemiological classification of human papillomavirus types associated with cervical cancer. *New Engl. J. Med.* 348, 518–527.
- Human papillomaviruses 1994 Compendium. In: Myers, G., Bernard, H.U., Delius, H., Favre, M., Iconogole, J., van Ranst, M., Wheeler, C. (Eds.), Los Alamos National Laboratory, Los Alamos, New Mexico, USA. <http://hvp-web.lanl.gov/>.
- Nafz, J., Schafer, K., Chen, S.F., Bravo, I.G., Ibberson, M., Nindl, I., Stockfleth, E., Rosl, F., 2008. A novel rodent papillomavirus isolated from anogenital lesions in its natural host. *Virology* 374 (1), 186–197.
- Nobre, R.J., Herráez-Hernández, E., Fei, J.W., Langbein, L., Kaden, S., Gröne, H.J., de Villiers, E.M., 2009. E7 oncoprotein of novel human papillomavirus type 108 lacking the E6 gene induces dysplasia in organotypic keratinocyte cultures. *J. Virol.* 83, 2907–2916.
- Ostrow, R.S., LaBresh, K.V., Faras, A.J., 1991. Characterization of the complete RhPV 1 genomic sequence and an integration locus from a metastatic tumor. *Virology* 181, 424–429.
- Palmenberg, A.C., Spiro, D., Kuzmickas, R., Wang, S., Dijkeng, A., Rathe, J.A., Fraser-Liggett, C.M., Liggett, S.B., 2009. Sequencing and analyses of all known human rhinovirus genomes reveal structure and evolution. *Science* 324, 55–59.
- Patel, K.R., Smith, K.T., Campo, M.S., 1987. The nucleotide sequence and genome organization of bovine papillomavirus type 4. *J. Gen. Virol.* 68, 2117–2128.
- Posada, D., Crandall, K.A., 1998. MODELTEST: testing the model of DNA substitution. *Bioinformatics* 14, 817–818.
- Rambaut, A., Posada, D., Crandall, K.A., Holmes, E.C., 2004. The causes and consequences of HIV evolution. *Nat. Rev. Genet.* 5, 52–61.
- Rebrikov, D.V., Bogdanova, E.A., Bulina, M.E., Lukyanov, S.A., 2002. A new planarian extrachromosomal virus-like element revealed by subtractive hybridization. *Mol. Biol.* 36, 813–820.
- Rector, A., Bossart, G.D., Ghim, S.J., Sundberg, J.P., Jenson, A.B., Van Ranst, M., 2004. Characterization of a novel close-to-root papillomavirus from a Florida manatee by using multiply primed rolling-circle amplification: *Trichechus manatus latirostris* papillomavirus type 1. *J. Virol.* 78, 12698–12702.
- Rector, A., Lemey, P., Tachezy, R., Mostmans, S., Ghim, S.J., Van Doorslaer, K., Roelke, M., Bush, M., Montali, R.J., Joslin, J., Burk, R.D., Jenson, A.B., Sundberg, J.P., Shapiro, B., Van Ranst, M., 2007. Ancient papillomavirus-host co-speciation in Felidae. *Genome Biol.* 8, R57.
- Rector, A., Mostmans, S., Van Doorslaer, K., McKnight, C.A., Maes, R.K., Wise, A.G., Kiupel, M., Van Ranst, M., 2006. Genetic characterization of the first chiropteran papillomavirus, isolated from a basosquamous carcinoma in an Egyptian fruit bat: the *Rousettus aegyptiacus* papillomavirus type 1. *Vet. Microbiol.* 117, 267–275.
- Rector, A., Stevens, H., Lacave, G., Lemey, P., Mostmans, S., Salbany, A., Vos, M., Van Doorslaer, K., Ghim, S.J., Rehtanz, M., Bossart, G.D., Jenson, A.B., Van Ranst, M., 2008. Genomic characterization of novel dolphin papillomaviruses provides indications for recombination within the Papillomaviridae. *Virology* 378, 151–161.
- Rector, A., Tachezy, R., Van Doorslaer, K., MacNamara, T., Burk, R.D., Sundberg, J.P., Van Ranst, M., 2005a. Isolation and cloning of a papillomavirus from a North American porcupine by using multiply primed rolling-circle amplification: the *Erethizon dorsatum* papillomavirus type 1. *Virology* 331, 449–456.
- Rector, A., Van, D.K., Bertelsen, M., Barker, I.K., Olberg, R.A., Lemey, P., Sundberg, J.P., Van Ranst, M., 2005b. Isolation and cloning of the raccoon (*Procyon lotor*) papillomavirus type 1 by using degenerate papillomavirus-specific primers. *J. Gen. Virol.* 86, 2029–2033.
- Rehtanz, M., Ghim, S.J., Rector, A., Van Ranst, M., Fair, P.A., Bossart, G.D., Jenson, A.B., 2006. Isolation and characterization of the first American bottlenose dolphin papillomavirus: *Tursiops truncatus* papillomavirus type 2. *J. Gen. Virol.* 87, 3559–3565.
- Reszka, A.A., Sundberg, J.P., Reichmann, M.E., 1991. In vitro transformation and molecular characterization of *Colobus monkey* venereal papillomavirus DNA. *Virology* 181 (2), 787–792.
- Ronquist, F., Huelsenbeck, J.P., 2003. MrBayes 3: Bayesian phylogenetic inference under mixed models. *Bioinformatics* 19, 1572–1574.
- Schulz, E., Gottschling, M., Bravo, I.G., Wittstatt, U., Stockfleth, E., Nindl, I., 2009. Genomic characterization of the first insectivoran papillomavirus reveals an unusually long, second non-coding region and indicates a close relationship to betapapillomavirus. *J. Gen. Virol.* 90, 626–633.
- Stevens, H., Rector, A., Bertelsen, M.F., Leifsson, P.S., Van Ranst, M., 2008a. Novel papillomavirus isolated from the oral mucosa of a polar bear does not cluster with other papillomaviruses of carnivores. *Vet. Microbiol.* 129, 108–116.
- Stevens, H., Rector, A., Van Der Krogh, K., Van Ranst, M., 2008b. Isolation and cloning of two variant papillomaviruses from domestic pigs: *Sus scrofa* papillomaviruses type 1 variants a and b. *J. Gen. Virol.* 89, 2475–2481.
- Tachezy, R., Duson, G., Rector, A., Jenson, A.B., Sundberg, J.P., Van Ranst, M., 2002a. Cloning and genomic characterization of *Felis domesticus* papillomavirus type 1. *Virology* 301, 313–321.
- Tachezy, R., Rector, A., Havelkova, M., Wollants, E., Fiten, P., Opendakker, G., Jenson, B., Sundberg, J., Van Ranst, M., 2002b. Avian papillomaviruses: the parrot *Psittacus erithacus* papillomavirus (PePV) genome has a unique organization of the early protein region and is phylogenetically related to the chaffinch papillomavirus. *BMC Microbiol.* 2, 19–27.
- Tan, C.H., Tachezy, R., Van Ranst, M., Chan, S.Y., Bernard, H.U., Burk, R.D., 1994. The *Mastomys natalensis* papillomavirus: nucleotide sequence, genome organization, and phylogenetic relationship of a rodent papillomavirus involved in tumorigenesis of cutaneous epithelia. *Virology* 198, 534–541.
- Terai, M., DeSalle, R., Burk, R.D., 2002. Lack of canonical E6 and E7 open reading frames in bird papillomaviruses: *Fringilla coelebs* papillomavirus and *Psittacus erithacus* timneh papillomavirus. *J. Virol.* 76, 10020–10023.
- Tobler, K., Favrot, C., Nespeca, G., Ackermann, M., 2006. Detection of the prototype of a potential novel genus in the family Papillomaviridae in association with canine epidermodysplasia verruciformis. *J. Gen. Virol.* 87, 3551–3557.

- Tobler, K., Lange, C., Carlotti, D.N., Ackermann, M., Favrot, C., 2008. Detection of a novel papillomavirus in pigmented plaques of four pugs. *Vet. Dermatol.* 19 (1), 21–25.
- Tomita, Y., Literak, I., Ogawa, T., Jin, Z., Shirasawa, H., 2007. Complete genomes and phylogenetic positions of bovine papillomavirus type 8 and a variant type from a European bison. *Virus Genes* 3, 243–249.
- Van Doorslaer, K., Rector, A., Jenson, A.B., Sundberg, J.P., Van Ranst, M., Ghim, S.J., 2007. Complete genomic characterization of a murine papillomavirus isolated from papillomatous lesions of a European harvest mouse (*Micromys minutus*). *J. Gen. Virol.* 88, 1484–1488.
- Van Doorslaer, K., Rector, A., Vos, P., Van Ranst, M., 2006. Genetic characterization of the *Capra hircus* papillomavirus: a novel close-to-root artiodactyl papillomavirus. *Virus Res.* 118, 164–169.
- Van Doorslaer, K., Sidi, A.O., Zanier, K., Rybin, V., Deryckere, F., Rector, A., Burk, R.D., Lienau, E.K., van Ranst, M., Trave, G., 2009. Identification of unusual E6 and E7 proteins within avian papillomaviruses: cellular localization, biophysical characterization, and phylogenetic analysis. *J. Virol.* 83, 8759–8770.
- Van Ranst, M., Fuse, A., Sobis, H., De Meurichy, W., Syrjanen, S.M., Billiau, A., Opdenakker, G., 1991. A papillomavirus related to HPV type 13 in oral focal epithelial hyperplasia in the pygmy chimpanzee. *J. Oral Pathol. Med.* 20 (7), 325–331.
- Van Ranst, M., Fuse, A., Fiten, P., Beuken, E., Pfister, H., Burk, R.D., Opdenakker, G., 1992a. Human papillomavirus type 13 and pygmy chimpanzee papillomavirus type 1: comparison of the genome organizations. *Virology* 190, 587–596.
- Van Ranst, M., Kaplan, J.B., Burk, R.D., 1992b. Phylogenetic classification of human papillomaviruses: correlation with clinical manifestations. *J. Gen. Virol.* 73, 2653–2660.
- Van Ranst, M., Tachezy, R., Delius, H., Burk, R.D., 1993. Taxonomy of the human papillomaviruses. *Papillomavir. Rep.* 4, 61–65.
- Van Regenmortel, M.H., Maniloff, J., Calisher, C.H., 1991. The concept of virus species. *Arch. Virol.* 120, 313–314.
- Van Regenmortel, M.H., Mayo, M.A., Fauquet, C.M., Maniloff, J., 2000. Virus nomenclature: consensus versus chaos. *Arch. Virol.* 145, 2227–2232.
- Van Regenmortel, M.H.V., Fauquet, C.M., Bishop, D.H.L., Calisher, C.H., Carsten, E.B., Estes, M.K., Lemon, S.M., Maniloff, J., Mayo, M.A., McGeoch, D.J., Pringle, C.R., Wickner, R.B., 2002. *Virus Taxonomy. Seventh Report of the International Committee for the Taxonomy of Viruses*. Academic Press, New-York, San Diego.
- Vasiljevic, N., Hazard, K., Dillner, J., Forslund, O., 2008. Four novel human betapapillomaviruses of species 2 preferentially found in actinic keratosis. *J. Gen. Virol.* 89, 2467–2474.
- Wettstein, F.O., Stevens, J.G., 1980. Distribution and state of viral nucleic acid in tumors induced by *Shope papilloma* virus. *Cold Spring Harbor Conf. Cell Proliferation* 7, 301–307.
- Woolford, L., Rector, A., Van Ranst, M., Ducki, A., Bennett, M.D., Nicholls, P.K., Warren, K.S., Swan, R.A., Wilcox, G.E., O'Hara, A.J., 2007. A novel virus detected in papillomas and carcinomas of the endangered western barred bandicoot (*Perameles bougainville*) exhibits genomic features of both the *Papillomaviridae* and *Polyomaviridae*. *J. Virol.* 81, 13280–13290.
- Yuan, H., Ghim, S., Newsome, J., Apolinario, T., Olcese, V., Martin, M., Delius, H., Felsburg, P., Jenson, B., Schlegel, R., 2007. An epidermotropic canine papillomavirus with malignant potential contains an E5 gene and establishes a unique genus. *Virology* 359, 28–36.