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Genetic Diversity of the *Papillomaviridae* Family Using Reference Genomes

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Abstract

Papillomaviruses have the ability to induce infected squamous epithelial cells to form tumors, some of which can progress to malignancies. They are circular double-stranded DNA viruses with approximately 8kbp. The papillomavirus genome consists of a long control region (LCR), early coding regions (E1, E2, E4, E5, E6, and E7), and late coding regions (L1 and L2). We used 112 genomic DNA, all of papillomavirus sequences from the NCBI (RefSeq) and listed in the PaVE, comprising 47 human-infecting reference sequences and 65 animal-infecting reference sequences. The main papillomaviruses that infect humans, showed differences in the size of the proteins encoded by the viral genome. For human-infecting papillomaviruses, there was no significant difference between the phylogeny constructed with the E and L regions, compared to the tree constructed with the entire genome. For all genera of the *Papillomaviridae* family, *Betapapillomavirus* genera that infect humans were placed between *Chipapillomavirus* and *Taupapillomavirus,* in the phylogenetic tree using the entire genome, and showed similarity with *Betapapillomaviruses* infecting *Colobus guereza*, which is a species of primate. Human-infecting *Alphapapillomaviruses* was the most distinct specie among *Alphapapillomaviruses,* while *Gammapapillomaviruses* were more closely related to *Pipapillomaviruses* infecting *Mastomys coucha*, *Micromys minutus*, and *Mus musculus*, which are small rodents.

Keywords

Papilomavirus, Tumors, Neoplasia, Carcinoma, Oncology

1. Introduction

1.1. Genome and Life Cycle

Human Papillomaviruses (HPV) are circular double-stranded DNA viruses, with approximately 8kbp and about 55 nm in diameter, lacking an envelope. Their capsid is composed of 360 molecules of the L1 protein, the main components of the capsid, along with up to 72 copies of the L2 protein, in smaller proportion [1]. They infect the basal layer of the stratified epithelium of the skin and mucous membranes through microlesions, replicating as the cells differentiate [2].

The genomes of *Papillomaviridae* are conserved, and their eight genes are expressed in a controlled manner within the squamous epithelium. There are six early genes (E1, E2, E4, E5, E6 and E7) and two late genes (L1 and L2), in addition to a long control region (LCR), which acts as a replication origin and controls transcription [3]. The L1 and L2 proteins are produced in the final stage of the virus's life cycle, and encapsulate the viral DNA [4]. High-risk papillomaviruses have the ability to induce infected squamous epithelial cells to form tumors, some of which may progress to malignancies [5]. Cancer arises due to persistent infections by high-risk HPV that have not been cleared by the host's immune system. These infections are characterized by dysregulated expression of HPV genes, especially by the high constitutive expression of the virus's oncogenes E6 and E7 and by the absence of the viral capsid proteins L1 and L2, which are highly immunogenic. HPVs extensively utilize alternative splicing to express their genes, becoming highly dependent on cellular RNA-binding proteins for proper gene expression. The levels of these RNA-binding proteins are altered in precancerous cervical lesions containing HPVs, and in cervical cancer [6]. The E6 and E7 genes of the papillomavirus encode proteins responsible for establishing, and maintaining a cellular environment conducive to the synthesis of the viral genome, and the production of viral progeny in keratinocytes that are in the process of terminal differentiation, and present growth arrest. These E6 and E7 proteins accomplish this role by binding to and functionally reprogramming key cellular regulatory proteins [7]. The viral E6 and E7 genes are consistently expressed in cancers and play a crucial role in tumor initiation, progression and maintenance. E6 and E7 encode small proteins that lack intrinsic enzymatic activities. Instead, they function by binding to cellular regulatory molecules, disrupting normal cellular homeostasis [8]. The viral E6 and E7 proteins drive carcinogenesis by interacting with tumor suppressors and interfering with diverse cellular pathways [9]. Several proteins related to DNA damage response, and interferon modulation, such as BRCA1, H2AX, SIRT1 and LAMP3, are clearly upregulated in primary keratinocytes that express themselves as HPV16 E6 and E7 oncoproteins [10]. Data suggest that the E6 and E7 proteins of $\beta 3$ HPV49, and $\alpha 9$ HR-HPV16 influence crucial factors in cell cycle control through indirect mechanisms by altering the expression of microRNAs [11]. Regarding the oncogenic proteins expressed during the initial replication cycle of high-risk HPVs, the regulation mechanism of pre-mRNA splicing of E6 and E7 has a significant impact throughout the viral repli-

cation cycle. Furthermore, differentiation, control and transformation in HPV-infected immortalized cells are closely linked to the expression levels of E6 and E7 [12]. Innate immune genes (IIGs) are suppressed by HPV16, and this suppression persists until the cancerous stage, indicating that the HPV16 E6 and E7 proteins act synergistically to suppress IIG expression throughout the viral genome [13]. The E6 protein of high-risk HPVs directs several cellular pathways to promote viral DNA replication and is a crucial oncogene in HPV-associated neoplasms, inhibiting p53, suppressing apoptosis, activating telomerase, blocking cell adhesion, polarity, and epithelial differentiation, modifying protein G transcription and signaling, and reducing the immunological recognition of HPV-infected cells [14]. The degradation of p53 is a distinctive feature of human papillomaviruses (HPVs). The E6 oncoprotein forms a ternary complex with the E6 ubiquitin ligase-associated protein E3 (E6AP) and the tumor suppressor protein p53, targeting it for ubiquitination [15].

1.2. Genome Organization and Biological Properties

The E6 *and* E7 *proteins*

The viral oncoproteins E6 and E7 play an active role in increasing the intrinsic sensitivity to radiation (radiosensitivity) of infected cells [16]. The enhanced competitive ability of HPV16-infected cells to reach the basal cell surface is primarily attributed to the expression of the E6 oncoprotein, with E7 or E5 oncoproteins not having a significant influence [17]. E6 and E7 induce alterations in the cell cycle, proliferation, invasion, metastasis, and other biological behaviors, influencing tumor-related signaling pathways, which drive the malignant transformation of cells and consequently promote tumorigenesis and cancer progression. E6 and E7 proteins drive tumor formation and development by influencing the activation of various cancer-related signaling pathways, such as the Wnt/β-catenin, PI3K/Akt, and NF-κB pathways [18]. During the viral life cycle of HPV, E7 interferes with the tight linkage between cellular differentiation and proliferation in normal epithelium, allowing viral replication in cells that would normally no longer be in the division phase. This function is directly related to the transformative activities of E7, including tumorigenic initiation and induction of genomic instability [19]. E7 proteins play a fundamental role in the human Papillomavirus life cycle, modifying the cellular environment to favor viral replication. E7 proteins associated with cancer-linked alpha human papillomaviruses, have significant transformative activities, which, along with E6, are crucial, though not sufficient, to induce tumorigenesis in host squamous epithelial cells [20].

The E1 *and* E2 *proteins*

The first set of viral proteins, HPV E1 and E2, triggers a DNA damage response and recruits repair proteins to viral replication sites. These proteins are likely co-opted to replicate the viral genome. However, since activation of the DNA damage response (DDR) pathways typically leads to cell cycle arrest, which can disrupt the viral life cycle, the second set of HPV proteins, HPV E6 and E7, prevents the DDR

response from halting cell cycle progression or inducing apoptosis [21]. Human Papillomaviruses adjust their replication levels, according to the differentiation status of infected keratinocytes. HPV genomes replicate at low levels in undifferentiated cells but at high levels in differentiated cells. For replication to occur, the viral helicase E1 and the viral transcription/replication activator E2 are required [22]. HPV genome replication is strongly controlled, depending on two viral proteins, E1 and E2. While E1 acts as a DNA helicase, essential for the formation of the genome replication complex, E2 initiates DNA replication and regulates the transcription of viral genes, especially the oncogenes E6 and E7 [6]. E1 encodes the sole HPV enzyme, which is an ATP-dependent DNA helicase that interacts with the cellular DNA replication machinery to replicate the viral genome [23]. It is crucial for the replication and amplification of the viral episome in the nucleus of infected cells. To perform this function, E1 forms a double hexamer at the viral origin, unwinds the DNA at the origin and ahead of the replication fork, and interacts with cellular DNA replication factors [24]. Previous studies have demonstrated that its function is not limited to helicase activity, also involving the recruitment and interaction with other host proteins, potentially driving cell proliferation. Recent research has highlighted the emerging role of HPV E1 protein in cervical carcinogenesis [2]. The E2 proteins of papillomaviruses are crucial for the HPV life cycle, performing well-defined functions in transcriptional regulation, DNA replication initiation, and viral genome partitioning. They are also involved in vegetative DNA replication, post-transcriptional processes, and possibly DNA packaging [25]. In addition to regulating viral gene expression, the HPV E2 protein is essential for the viral replication process [26]. To replicate the viral genome, two viral proteins are essential: E2, which binds to 12-base pair palindromic sequences around the A/T-rich replication origin, and recruits the viral helicase E1 through protein-protein interaction; and E1, which forms a di-hexameric complex that replicates the viral genome in association with host factors [27]. The viral E2 protein plays a fundamental role in episome replication throughout the virus's life cycle, and its activity is regulated through processes such as phosphorylation, acetylation, SUMOylation, and ubiquitination [28]. The substitution of serine 23 of the E2 protein with alanine disrupts the life cycle of HPV16, impairing its immortalization capability and halting the viral cycle, highlighting the critical importance of this residue in the protein's function [29]. The viral E1 and E2 proteins of HPV8 play a crucial role in the immune evasion of β-HPV, preventing innate recognition of viral nucleic acids. This mechanism may be essential for establishing persistent β-HPV infections [30]. Variants of E1, E2, and E4 are primarily involved in integration, replication, and viral transcription, while E6 and E7 act as oncoproteins, driving cancer progression. The E5 protein, in turn, regulates cell proliferation and apoptosis, as well as facilitating the activity of E6 and E7 [31].

The E4 *and* E5 *proteins*

The E5 proteins are small transmembrane proteins encoded by many papillomaviruses in animals and humans. These proteins have been shown to possess

transforming activity in cultured animal cells and presumably also play a role in the viral life cycle. It is believed that E5 proteins modify the activity of cellular proteins [32]. Although E5 is found in high-risk alpha-HPVs that infect mucosal tissues, it is absent in the genomes of high-risk beta-HPVs that affect cutaneous tissues, and are related to skin cancers. This observation raises questions about the role of E5 in papillomavirus-associated pathogenesis. The presence of E5 in some papillomaviruses (high-risk alpha-HPVs affecting mucosal tissues), and its absence in others (high-risk beta-HPVs affecting the skin; such as MmuPV1) has led to doubts about its role in papillomavirus-induced pathogenesis. These findings provide evidence that E5 acts as a co-carcinogen in papillomavirus-induced development [33]. Several studies have indicated that the HPV oncoprotein E5 has the ability to disrupt the normal cell cycle of HPV-infected cells by targeting certain crucial cellular signaling pathways, such as the epidermal growth factor receptor (EGFR) signaling pathway [34]. Over time, the oncoprotein E5 is becoming increasingly recognized, as the third transforming protein of Human Papillomavirus (HPV). Extensive cell proliferation is a distinctive feature of cancer development, and E5 is capable of promoting the proliferation of keratinocytes by positively regulating the epidermal growth factor receptor (EGFR) signaling pathway. Therefore, E5 is believed to indirectly contribute to the completion of the viral life cycle by creating the appropriate cellular environment. By increasing EGFR signaling, E5 delays differentiation and allows for the hyperproliferation of keratinocytes, which would otherwise follow a normal differentiation pathway [35]. Other studies have indicated the importance of HPV16 E5 protein in the late stages of the differentiation-dependent life cycle. It has been observed that organotypic cultures containing HPV16 genomes without E5 showed reduced markers of terminal differentiation compared to cultures containing wild-type HPV16. Additionally, levels and activation of the epidermal growth factor receptor (EGFR) were increased in an E5-dependent manner in these tissues, and EGFR promoted terminal differentiation and expression of the HPV16 L1 gene. These results suggest that E5 plays a role in preserving the differentiation capacity of keratinocytes containing HPV16, thereby facilitating the production of new virus progeny [36]. When E5 is lost during viral integration, its absence indicates a transition from benign lesions to malignant establishment [37]. E5 acts as a potent negative regulator of type I antiviral IFN response pathways and immunoproteasome expression and function, resulting in a reduction in the repertoire of presented peptides. Additionally, it has been observed that E5 directly binds to and blocks the mitochondrial antiviral signaling protein (MAVS) and stimulator of interferon genes (STING), leading to compromised antitumor immunity and decreased immunotherapeutic activity. This allows infected cancer cells to evade host immune surveillance, and resist the effectiveness of immunotherapies [38]. Furthermore, HPV16 genomes without E5 have been observed to have a higher tendency to integrate into the culture over time compared to the wild type, suggesting that E5-mediated suppression of IFN-κ may be crucial for the long-term maintenance of viral ge-

nomes, thus revealing a new function of E5 in the viral life cycle [39]. After infection, HPV viral DNA can remain latent and infectious in affected basal epithelial cells, potentially progressing to productive neoplastic infection. This process can lead to transformation over several years, culminating in invasive cancer [40]. The ability of E4 to induce disorders in keratin structure indicates its possible influence on viral release. Although the precise role of E4 in the viral replication cycle remains uncertain, there are suggestions that it may play a significant role in cell cycle disruption. Studies have demonstrated a correlation between E4 expression and levels of HPV DNA incorporation by the host [41]. The expression of HPV16 E4 and E5 proteins, has been shown to cause significant changes in the composition of the cell membrane and the extracellular environment. These alterations are linked to modifications in cell adhesion and differentiation [42]. In HPV infection, the E4 protein is initially produced as an E1^E4 fusion from spliced E1^E4 transcripts, resulting in the first amino acids of the E4 protein being derived from the N-terminal end of E1 [43]. The E4 protein, a phosphoprotein with low molecular weight (10 to 20 kDa), is expressed from a processed E1ΛE4 mRNA, whose transcription is initiated from the differentiation-dependent promoter. Expression of the papillomavirus E4 protein is associated with the onset of viral DNA amplification [44]. E4 proteins from various papillomaviruses interact with the serine-arginine-specific protein kinase SRPK1, an important kinase in the replication cycles of various DNA and RNA viruses. E4 inhibits the phosphorylation of SRPK1, not only of cellular SR proteins involved in the regulation of alternative RNA splicing, but also of the viral transcription/replication regulator E2, by regulating late viral gene expression through the inhibition of a host cell kinase [43].

Capsid proteins (L1 *and* L2)

L1 is the major capsid protein, with molecular weight of approximately 55 kDa, which has the ability to spontaneously self-assemble into virus-like particles (VLPs) after binding to cells. Upon binding, L1 must become flexible enough again to allow the release of the viral genome into a new target cell [45]. Its recombinant expression in various systems leads to self-assembly into empty capsids (VLPs). L1 and L2 are expressed in the granular layer of the epithelium but are not detectable in the basal epithelium that harbors infection [3]. L1 can activate the immune system to generate neutralizing antibodies, which help prevent HPV infections [46]. It has been used as the basis for human papillomavirus (HPV) vaccines [45]. The L2 protein, approximately 500 amino acids in length with an estimated molecular mass of 55 kDa, plays multiple roles in viral genome assembly, encapsidation, and the infectious process. While the L1 protein constitutes the majority of the capsid and can form VLPs, L2 is a smaller component and cannot form VLPs on its own [47]. L2 is tasked with ensuring nuclear delivery of the viral DNA during HPV infection, displacing viral DNA from degradative endolysosomal compartments and directing it to the trans-Golgi network. L2 accomplishes this through the characteristics of an "inducible transmembrane" protein, allowing it

to enter into and traverse local vesicular membranes via a transmembrane-like domain [48].

2. Materials and Methods

Genetic Diversity

The Papilloma Virus Episteme (PaVE) has been established to provide highly organized and curated papillomavirus genomic information and tools to the scientific community (https://pave.niaid.nih.gov/). PaVE is an important database that provides access to uniformly curated reference genomes [49]. For the analysis, 112 genomic DNA sequences were used, all of which are reference Papillomavirus sequences in the NCBI RefSeq listed on PaVE, accessed in May 2024. There were 47 curated reference sequences of human papillomaviruses (**Table 1**) and 65 curated reference sequences of papillomaviruses that infect animals (**Table 2**), as listed in the curated PaVE database. The NCBI Reference Sequence (RefSeq) is a collection of taxonomically diverse, non-redundant, and richly annotated sequences, the RefSeq collection provides redundancy-free genome data, is used internationally as a standard for genomic annotation, and represents significant taxonomic diversity [50]. Therefore, only the reference genome was chosen. For alignment and phylogeny construction, MEGA allows from DNA sequences, to infer evolutionary trees, estimate distances, genetic diversity, and infer ancestral sequences, MEGA 11 was used [51]. Constructing a multiple alignment corresponds to developing a hypothesis of how a series of sequences have changed over time. The multiple alignment of a series of homologous DNA sequences is the first step toward a phylogeny and was performed using MEGA 11 (by ClustalW). Phylogenetic trees aim to establish similarity among organisms based on their DNA sequence, assisting in forming closely related groups with common characteristics. This was done using MEGA 11 (Neighbor Joining (NJ) Tree, the NJ method is a simplified version of the minimum evolution (ME) method, which uses distance measures to correct for multiple hits at the same sites, and chooses a topology showing the smallest value of the sum of all branches as an estimate of the correct tree).

Table 1. Papillomaviruses that infect humans, listed in the PAVE as reference genomes in the NCBI database.

ID	Species Name	NCBI Refseq	PUBMED Reference
A-4	*Alphapapillomavirus* 4	NC_001352	1964523 [56]
G-1	*Gammapapillomavirus* 1	NC_001457	8389082 [57]
A-8	*Alphapapillomavirus* 8	NC_001595	8205838 [58]
B-2	*Betapapillomavirus* 2	NC_001596	8205838 [58]
A-2	*Alphapapillomavirus* 2	NC_001576	8205838 [58]
A-5	*Alphapapillomavirus* 5	NC_001583	8205838 [58]
A-1	*Alphapapillomavirus* 1	NC_001586	8205838 [58]
A-11	*Alphapapillomavirus* 11	NC_001587	8205838 [58]

Continued

N-1	*Nupapillomavirus* 1	NC_001354	1645904 [59]
G-2	*Gammapapillomavirus* 2	NC_001690	1645904 [60]
B-3	*Betapapillomavirus* 3	NC_001591	8205838 [58]
G-3	*Gammapapillomavirus* 3	NC_001691	[61]
A-6	*Alphapapillomavirus* 6	NC_001593	8205838 [58]
A-13	*Alphapapillomavirus* 13	NC_001676	Delius, Unpublished
G-4	*Gammapapillomavirus* 4	NC_001693	1326820 [62]
A-3	*Alphapapillomavirus* 3	NC_001694	Delius, Unpublished
M-2	*Mupapillomavirus* 2	NC_001458	8389082 [57]
G-5	*Gammapapillomavirus* 5	NC_010329	17935140 [63]
A-14	*Alphapapillomavirus* 14	NC_004104	12085327 [64]
B-4	*Betapapillomavirus* 4	NC_004500	12919731 [65]
B-5	*Betapapillomavirus* 5	NC_005134	17412976 [66]
G-6	*Gammapapillomavirus* 6	NC_008189	17125811 [67]
G-6	*Gammapapillomavirus* 6	NC_008188	17125811 [67]
G-6	*Gammapapillomavirus* 6	NC_012213	19153227 [68]
G-7	*Gammapapillomavirus* 7	NC_012485	19969321 [69]
G-8	*Gammapapillomavirus* 8	NC_012486	19969321 [69]
G-9	*Gammapapillomavirus* 9	NC_013035	19570953 [70]
G-10	*Gammapapillomavirus* 10	NC_014185	20206957 [52]
G-11	*Gammapapillomavirus* 11	NC_016157	22056388 [71]
G-12	*Gammapapillomavirus* 12	NC_014469	20542254 [72]
G-13	*Gammapapillomavirus* 13	NC_014952	21471318 [73]
G-9	*Gammapapillomavirus* 9	NC_014953	21471318 [73]
G-14	*Gammapapillomavirus* 14	NC_014954	21471318 [73]
G-12	*Gammapapillomavirus* 12	NC_014955	21471318 [73]
G-7	*Gammapapillomavirus* 7	NC_014956	21471318 [73]
G-15	*Gammapapillomavirus* 15	NC_017993	21844305 [74]
G-11	*Gammapapillomavirus* 11	NC_017994	21844305 [74]
G-16	*Gammapapillomavirus* 16	NC_017995	21844305 [74]
G-11	*Gammapapillomavirus* 11	NC_017996	21844305 [74]
G-17	*Gammapapillomavirus* 17	NC_017997	21844305 [74]
G-11	*Gammapapillomavirus* 11	NC_021483	24551244 [75]
G-19	*Gammapapillomavirus* 19	NC_019023	23043169 [76]
G-21	*Gammapapillomavirus* 21	NC_022892	24155922 [77]
G-24	*Gammapapillomavirus* 24	NC_023891	24855297 [78]
G-15	*Gammapapillomavirus* 15	NC_022095	Kocjan *et al*., Unpublished
G-27	*Gammapapillomavirus* 27	NC_027528	26318260 [79]
G-?	*Gammapapillomavirus*	NC_027779	Arroyo *et al*., Unpublished

Table 2. Papillomaviruses that infect animals, listed in the PAVE as reference genomes in the NCBI database.

Species Name	Host	NCBI Refseq	PUBMED Reference
Deltapapillomavirus 1	*Alces alces*	NC_001524	3034730 [80]
Xipapillomavirus 1	*Bos taurus*	NC_004197	12208979 [81]
Epsilonpapillomavirus 1	*Bos taurus*	NC_004195	12208979 [81]
Dyoxipapillomavirus 1	*Bos taurus*	NC_007612	17554025 [82]
Dyolambdapapillomavirus 1	*Bettongia penicillata*	NC_014143	20200246 [83]
Lambdapapillomavirus 2	*Canis familiaris*	NC_001619	21552821 [84]
Taupapillomavirus 1	*Canis familiaris*	NC_006564	17034826 [85]
Chipapillomavirus 1	*Canis familiaris*	NC_008297	17098970 [86]
Chipapillomavirus 2	*Canis familiaris*	NC_010226	Tobler *et al*., Unpublished
Lambdapapillomavirus 3	*Canis familiaris*	NC_013237	19656968 [87]
Chipapillomavirus 3	*Canis familiaris*	NC_016014	21883544 [88]
Chipapillomavirus 1	*Canis familiaris*	NC_016074	22532532 [89]
Chipapillomavirus 3	*Canis familiaris*	NC_016075	Yuan *et al*., Unpublished
Chipapillomavirus 3	*Canis familiaris*	NC_019852	23123172 [90]
Chipapillomavirus 2	*Canis familiaris*	NC_026640	Luff *et al*., Unpublished
Deltapapillomavirus 5	*Capreolus capreolus*	NC_011051	[91]
Dyosigmapapillomavirus 1	*Castor canadensis*	NC_023178	24309404 [92]
Lambdapapillomavirus 5	*Crocuta crocuta*	NC_018575	23405364 [93]
Deltapapillomavirus 6	*Camelus dromedarius*	NC_015267	21471319 [94]
Deltapapillomavirus 6	*Camelus dromedarius*	NC_015268	21471319 [94]
Betapapillomavirus 1	*Colobus guereza*	NC_015692	20921322 [95]
Phipapillomavirus 1	*Capra hircus*	NC_008032	16430985 [96]
Dyochipapillomavirus 1	*Equus asinus*	NC_023882	24636161 [97]
Zetapapillomavirus 1	*Equus ferus caballus*	NC_003748	15485669 [98]
Dyoiotapapillomavirus 1	*Equus ferus caballus*	NC_012123	Scase, Unpublished
Sigmapapillomavirus 1	*Erethizon dorsatum*	NC_006951	15629787 [99]
Dyoetapapillomavirus 1	*Erinaceus europaeus*	NC_011765	19218207 [100]
Lambdapapillomavirus 4	*Enhydra lutris*	NC_023873	Ng *et al*., Unpublished
Etapapillomavirus 1	*Fringilla coelebs*	NC_004068	12208979 [81]
Lambdapapillomavirus 1	*Felis domesticus*	NC_004765	Tachezy *et al*., Unpublished
Taupapillomavirus 3	*Felis domesticus*	NC_021472	23639476 [101]
Taupapillomavirus 3	*Felis domesticus*	NC_022373	Dunowska *et al*., Unpublished
Treiszetapapillomavirus	*Fulmarus glacialis*	NC_024300	Gaynor *et al*., Unpublished
Dyoepsilonpapillomavirus 1	*Francolinus leucoscepus*	NC_013117	19553340 [102]
Pipapillomavirus 2	*Mastomys coucha*	NC_008519	Nafz *et al*., Unpublished
Alphapapillomavirus 12	*Macaca fascicularis*	NC_012652	19716580 [103]

Continued

Alphapapillomavirus 12	*Macacca mulata*	NC_001678	8396814 [104]
Pipapillomavirus 2	*Micromys minutus*	NC_008582	17412977 [105]
Pipapillomavirus 2	*Mus musculus*	NC_014326	21084500 [106]
Iotapapillomavirus 1	*Mastomys natalensis*	NC_001605	8291235 [107]
Taupapillomavirus	*Mustela putorius*	NC_022253	23977082 [108]
Dyomupapillomavirus 1	*Morelia spilota*	NC_016013	21910860 [109]
Deltapapillomavirus 3	*Ovis aries*	NC_001789	Karlis *et al*., Unpublished
Kappapapillomavirus 1	*Oryctolagus cuniculus*	NC_002232	10753723 [110]
Deltapapillomavirus 2	*Odocoileus virginianus*	NC_001523	2993669 [111]
Treisepsilonpapillomavirus 1	*Pygoscelis adeliae*	NC_023894	24686913 [112]
Thetapapillomavirus 1	*Psittacus erithacus*	NC_003973	12110158 [113]
Alphapapillomavirus 12	*Papio hamadryas*	NC_017716	22446324 [114]
Lambdapapillomavirus 4	*Procyon lotor*	NC_007150	15958682 [115]
Omikronpapillomavirus 1	*Phocoena spinipinnis*	NC_003348	17554024 [116]
Psipapillomavirus 1	*Rousettus aegyptiacus*	NC_008298	16854536 [117]
Dyokappapapillomavirus 2	*Rupicapra rupicapra*	NC_023895	24910075 [118]
Xipapillomavirus 3	*Rangifer tarandus*	NC_021930	23874987 [119]
Kappapapillomavirus 2	*Sylvilagus floridanus*	NC_001541	2984661 [120]
Dyodeltapapillomavirus 1	*Sus scrofa*	NC_011280	18796716 [121]
Dyoomikronpapillomavirus 1	*Saimiri sciureus*	NC_023496	Chen *et al*., Unpublished
Rhopapillomavirus 1	*Trichechus manatus*	NC_006563	15507660 [122]
Rhopapillomavirus 1	*Trichechus manatus*	NC_016898	Wellehan, Unpublished
Upsilonpapillomavirus 1	*Tursiops truncatus*	NC_011109	18579177 [123]
Upsilonpapillomavirus 2	*Tursiops truncatus*	NC_008184	17098971 [124]
Omegapapillomavirus 1	*Ursus maritimus*	NC_010739	18215475 [125]
Dyonupapillomavirus 1	*Zalophus californianus*	NC_015325	Hoffman *et al*., Unpublished

3. Results and Discussion

In the *Papillomaviridae* family, there are currently 29 genera, named according to the Greek alphabet from alpha to omega. The term "Dyo" was added for extra genera. After the exhaustion of the Greek alphabet, the classification of papillomavirus types is based on the DNA sequence of the L1 gene. Papillomavirus types within a species share between 71% and 89% nucleotide identity within the complete L1 ORF, and members of the same genus share > 60% nucleotide sequence identity in the L1 ORF [52]. The main papillomaviruses that infect humans (alpha, beta, and gamma) present differences in the size of the proteins encoded by the viral genome: E6 142aa, E7 104aa, E1 642aa, E2 394 aa, E5 42aa, L2 476aa and L1 503aa for *Alphapapillomavirus* (NC_001586); E6 148aa, E7 93aa, E1 605aa, E2 461aa, L2 533aa and L1 507aa for *Betapapillomavirus* (NC_001596); and E6 140aa,

E7 100aa, E1 599aa, E2 402aa, L2 521aa and L1 516aa for *Gammapapillomavirus* (NC_001457), as shown in **Figure 1**. The structure prediction of the proteins shown in **Figure 1** was performed for *Alphapapillomavirus* (NC_001586), using Galaxy (Galaxy TBM) [53]. Human papillomaviruses are the most studied and are distributed in give genera (Alpha, Beta, Gamma, Mu, and Nu) [54]. According to the phylogenetic trees, there was no significant difference between the phylogeny formed with the E region (**Figure 2(B)**) and L region (**Figure 2(C)**) in comparison to the tree formed with the entire genome (**Figure 2(A)**). *Gamma-papillomavirus* is more related to *Betapapillomavirus* than to *Alphapapillomavirus* in all three phylogenetic trees (**Figure 2**). The two papillomaviruses *Mupapillomavirus* and *Nupapillomavirus* are grouped together in the tree based on the genome (**Figure 2(A)**) and for the L region (**Figure 2(C)**), whereas for the E region, *Nupapillomavirus* appeared to be the most distinctive virus (**Figure 2(B)**). The papillomavirus with the highest number of species and reference genomes is *Gammapapillomavirus*. Species 2, 3, 12, and 14, as well as 9, 11 and 16, remain grouped in all three trees. Species 6 and 7 remain grouped in the E and L regions, but when the entire genome is used, they are not closely related. The same occurs for 5, 8 and G, which is an unclassified papillomavirus. Within the genus *Alphapapillomavirus*, species 2, 3, 4, and 14 showed almost the same phylogenetic associations obtained with E, L, and the genome. In *Betapapillomavirus*, the grouping of L was different (5, 4, 2, and 3), while in using the E region and the genome, the same arrangement was maintained in the phylogenetic trees (5, 4, 3, and 2). Comparative analysis of the trees generated by the genome revealed almost the same phylogenetic associations as obtained by the E and L regions. For all genera of the *Papillomaviridae* family, the human-infecting *Betapapillomavirus* was positioned between *Chipapillomavirus* and *Taupapillomavirus* in the phylogenetic tree using the entire genome (**Figure 3**), and showed similarity to the *Betapapillomavirus* infecting *Colobus guereza*, which is a species of primate. The human-infecting *Alphapapillomavirus* was the most distinctive species among the *Alphapapillomavirus*. The genus *Alphapapillomavirus* is the most extensively studied of all genera. According to the PAVE database, there are currently 82 types of Alpha-PVs, classified into 14 species [54]. Phylogenetic analysis revealed that *Dyonupapillomavirus*, which infects *Zalophus californianus* (California sea lion), is more closely related to the genus *Alphapapillomavirus*. According to the phylogenetic tree (**Figure 3**), *Gammapapillomavirus* is close to *Pipapillomavirus*, which infects *Mastomys coucha*, *Micromys minutus*, and *Mus musculus* (small rodents). The phylogenetic tree inferred from genomic DNA sequences (**Figure 3**) showed that *Epsilonpapillomavirus*, which infects *Bos taurus*, falls within the clade of *Deltapapillomavirus*, which exhibits high diversity and infects various domestic animals such as *Ovis aries*, *Bos taurus*, and *Camelus dromedarius*. The two main domestic animals, dogs (*Canis familiaris*) and cats (*Felis catus*), are infected by several genera that have been classified into two groups. Group I contains *Chipapillomavirus*, which has been identified only in dogs so far. Group II comprises genera that infect large domestic

animals such as *Bos taurus*, *Camelus dromedarius*, and *Equus ferus*, with the main genus being *Deltapapillomavirus*. Cattle and dogs can be infected by three different genera. *Bos taurus* can be infected by *Xipapillomavirus*, *Epsilonpapillomavirus*, and *Dyoxipapillomavirus*, while *Canis familiaris* can be infected by *Lambdapapillomavirus*, *Taupapillomavirus*, and *Chipapillomavirus*. Papillomaviruses have been discovered in a wide variety of vertebrates, comprising a diverse group of viruses that infect humans and animals. The L1 gene was chosen from the beginning as the standard for classification, since for some types of papillomaviruses, there is little sequence information outside of this region. To be classified as distinct types, individual papillomaviruses must be at least 10% divergent from each other in their L1 nucleotide sequences. Overall, sequence-based phylogeny provides some useful insights into disease associations, although closely related types may, in some cases, present distinct pathologies. It is evident that viral pathogenicity depends on multiple factors, including viral genotype, the nature of the infected cell (tropism), and the host's immune status [55].

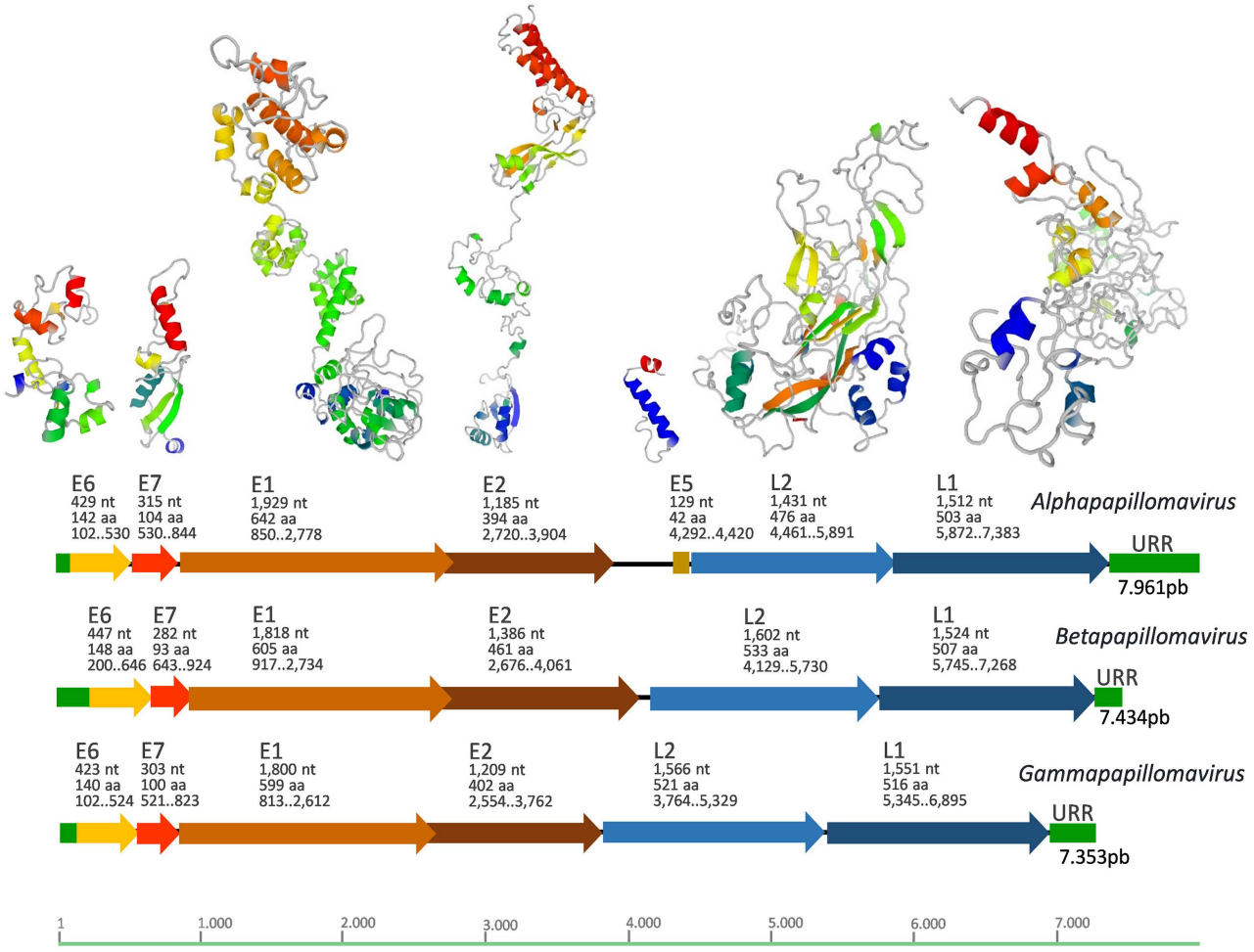

Figure 1. Proteins encoded by genes of *Alphapapillomavirus* 1 (NC_001586). Genome map of *Alphapapillomavirus* 1 (NC_001586), *Betapapillomavirus* 2 (NC_001596), and *Gammapapillomavirus* 1 (NC_001457). Showing the differences (number of amino acids—aa) in the size of the main structures of the three genera.

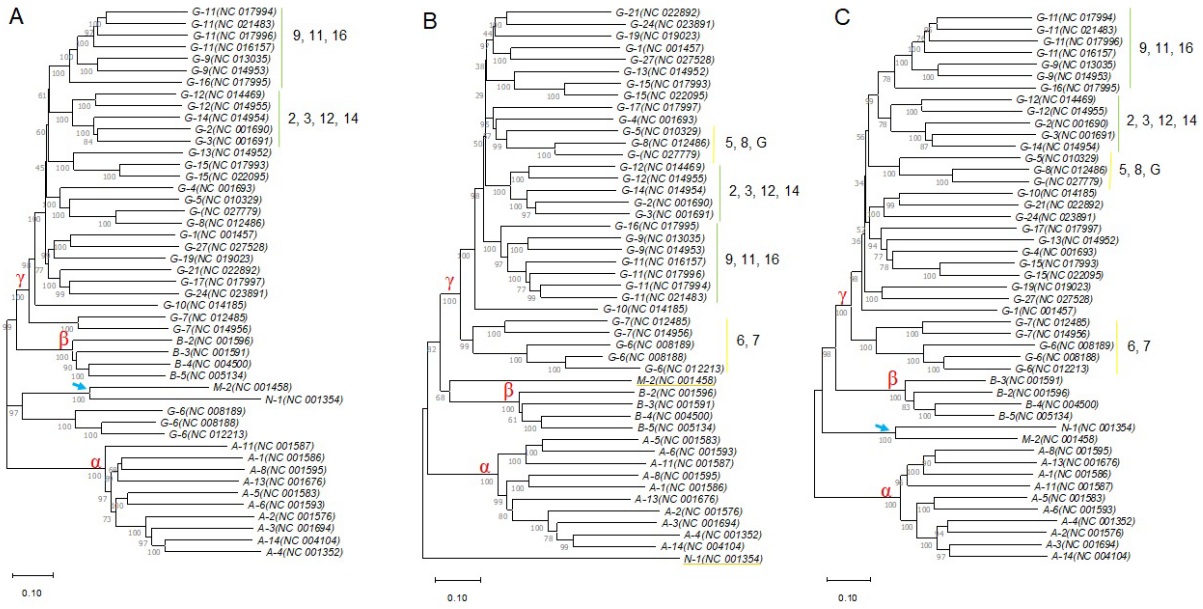

Figure 2. Phylogenetic tree of human papillomavirus: A) whole genome, B) E region (E6 to E2), and C) L region (L1 and L2). Showing the relationship between the *Alphapapillomavirus* (*α*), *Betapapillomavirus* (*β*), and *Gammapapillomavirus* (*γ*). Several species tend to maintain the same topology within the trees, regardless of whether they use the entire genome, or use only the L region and the E region, as in the example of species 2, 3, 12 and 14 of the *Gammapapillomavirus*. Numbers at the nodes indicate bootstrap support (percentage of 500 bootstrap replications). Scale bars represent 10% nucleotide substitution.

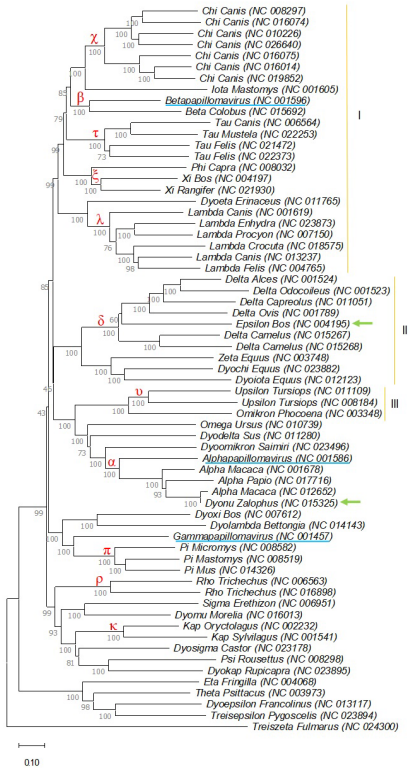

Figure 3. Phylogenetic tree of papillomaviruses that infect animals, together with *Alphapapillomavirus* 1, *Betapapillomavirus* 2 and *Gammapapillomavirus* 1 that infect humans (highlighted in blue). Showing the relationship of these three, with the other papillomaviruses. Numbers on nodes indicate the bootstrap support (500 bootstrap replication percentage). Scale bars represent 10% nucleotide substitution.

4. Conclusion

There is a difference in the number of amino acids in the main structures (E and L) between *Alphapapillomavirus, Betapapillomavirus* and *Gammapapillomavirus*. There was no difference between the phylogeny constructed with the E and L regions when compared with the tree constructed with the entire genome; both trees presented very similar topologies. The viruses that infect humans (*Alphapapillomavirus, Betapapillomavirus* and *Gammapapillomavirus*) were distributed along the phylogenetic tree, containing the viruses that infect animals, *Gammapapillomavirus* was close to *Pipapillomavirus*, *Betapapillomavirus* was between *Chipapillomavirus* and *Taupapillomavirus*.

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Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Xie, J., Zhang, P., Crite, M., Lindsay, C.V. and DiMaio, D. (2021) Retromer Stabilizes Transient Membrane Insertion of L2 Capsid Protein during Retrograde Entry of Human Papillomavirus. *Science Advances*, **7**, eabh4276. https://doi.org/10.1126/sciadv.abh4276

[2] Baedyananda, F., Sasivimolrattana, T., Chaiwongkot, A., Varadarajan, S. and Bhattarakosol, P. (2022) Role of HPV16 E1 in Cervical Carcinogenesis. *Frontiers in Cellular and Infection Microbiology*, **12**, Article ID: 955847. https://doi.org/10.3389/fcimb.2022.955847

[3] Olczak, P. and Roden, R.B.S. (2020) Progress in L2-Based Prophylactic Vaccine Development for Protection against Diverse Human Papillomavirus Genotypes and Associated Diseases. *Vaccines*, **8**, Article No. 568. https://doi.org/10.3390/vaccines8040568

[4] Chen, J., Wang, D., Wang, Z., Wu, K., Wei, S., Chi, X., *et al*. (2023) Critical Residues Involved in the Coassembly of L1 and L2 Capsid Proteins of Human Papillomavirus 16. *Journal of Virology*, **97**, e0181922. https://doi.org/10.1128/jvi.01819-22

[5] Chen, B., Zhao, L., Yang, R. and Xu, T. (2023) Advances in Molecular Mechanism of HPV16 E5 Oncoprotein Carcinogenesis. *Archives of Biochemistry and Biophysics*, **745**, Article ID: 109716. https://doi.org/10.1016/j.abb.2023.109716

[6] Evande, R., Rana, A., Biswas-Fiss, E.E. and Biswas, S.B. (2023) Protein-DNA Interactions Regulate Human Papillomavirus DNA Replication, Transcription, and Oncogenesis. *International Journal of Molecular Sciences*, **24**, Article No. 8493. https://doi.org/10.3390/ijms24108493

[7] Wei, T., Grace, M., Uberoi, A., Romero-Masters, J.C., Lee, D., Lambert, P.F., *et al*. (2021) The Mus Musculus Papillomavirus Type 1 E7 Protein Binds to the Retinoblastoma Tumor Suppressor: Implications for Viral Pathogenesis. *mBio*, **12**, e0227721. https://doi.org/10.1128/mbio.02277-21

[8] Sharma, S. and Munger, K. (2020) The Role of Long Noncoding RNAs in Human Papillomavirus-Associated Pathogenesis. *Pathogens*, **9**, Article No. 289. https://doi.org/10.3390/pathogens9040289

[9] Lim, J., Lilie, H., Kalbacher, H., Roos, N., Frecot, D.I., Feige, M., *et al*. (2023) Evidence for Direct Interaction between the Oncogenic Proteins E6 and E7 of High-Risk Human Papillomavirus (HPV). *Journal of Biological Chemistry*, **299**, Article ID: 104954. https://doi.org/10.1016/j.jbc.2023.104954

[10] Dust, K., Carpenter, M., Chen, J.C., Grant, C., McCorrister, S., Westmacott, G.R., *et al*. (2022) Human Papillomavirus 16 E6 and E7 Oncoproteins Alter the Abundance of Proteins Associated with DNA Damage Response, Immune Signaling and Epidermal Differentiation. *Viruses*, **14**, Article No. 1764. https://doi.org/10.3390/v14081764

[11] Chiantore, M.V., Iuliano, M., Mongiovì, R.M., Dutta, S., Tommasino, M., Di Bonito, P., *et al*. (2022) The E6 and E7 Proteins of Beta3 Human Papillomavirus 49 Can Deregulate Both Cellular and Extracellular Vesicles-Carried microRNAs. *Infectious Agents and Cancer*, **17**, Article No. 29. https://doi.org/10.1186/s13027-022-00445-z

[12] Zheng, Y., Li, X., Jiao, Y. and Wu, C. (2022) High-Risk Human Papillomavirus Oncogenic E6/E7 mRNAs Splicing Regulation. *Frontiers in Cellular and Infection Microbiology*, **12**, Article ID: 929666. https://doi.org/10.3389/fcimb.2022.929666

[13] James, C.D., Fontan, C.T., Otoa, R., Das, D., Prabhakar, A.T., Wang, X., *et al*. (2020) Human Papillomavirus 16 E6 and E7 Synergistically Repress Innate Immune Gene Transcription. *mSphere*, **5**, e00828-19. https://doi.org/10.1128/msphere.00828-19

[14] Howie, H.L., Katzenellenbogen, R.A. and Galloway, D.A. (2009) Papillomavirus E6 Proteins. *Virology*, **384**, 324-334. https://doi.org/10.1016/j.virol.2008.11.017

[15] Conrady, M.C., Suarez, I., Gogl, G., Frecot, D.I., Bonhoure, A., Kostmann, C., *et al*. (2020) Structure of High-Risk Papillomavirus 31 E6 Oncogenic Protein and Characterization of E6/E6AP/p53 Complex Formation. *Journal of Virology*, **95**, e00730-20. https://doi.org/10.1128/jvi.00730-20

[16] Bruyere, D., Roncarati, P., Lebeau, A., Lerho, T., Poulain, F., Hendrick, E., *et al*. (2023) Human Papillomavirus E6/E7 Oncoproteins Promote Radiotherapy-Mediated Tumor Suppression by Globally Hijacking Host DNA Damage Repair. *Theranostics*, **13**, 1130-1149. https://doi.org/10.7150/thno.78091

[17] Brimer, N. and Vande Pol, S. (2022) Human Papillomavirus Type 16 E6 Induces Cell Competition. *PLOS Pathogens*, **18**, e1010431. https://doi.org/10.1371/journal.ppat.1010431

[18] Peng, Q., Wang, L., Zuo, L., Gao, S., Jiang, X., Han, Y., *et al*. (2023) HPV E6/E7: Insights into Their Regulatory Role and Mechanism in Signaling Pathways in HPV-Associated Tumor. *Cancer Gene Therapy*, **31**, 9-17. https://doi.org/10.1038/s41417-023-00682-3

[19] McLaughlin-Drubin, M.E. and Münger, K. (2009) The Human Papillomavirus E7 Oncoprotein. *Virology*, **384**, 335-344. https://doi.org/10.1016/j.virol.2008.10.006

[20] Roman, A. and Munger, K. (2013) The Papillomavirus E7 Proteins. *Virology*, **445**, 138-168. https://doi.org/10.1016/j.virol.2013.04.013

[21] Wallace, N.A. and Galloway, D.A. (2014) Manipulation of Cellular DNA Damage Repair Machinery Facilitates Propagation of Human Papillomaviruses. *Seminars in Cancer Biology*, **26**, 30-42. https://doi.org/10.1016/j.semcancer.2013.12.003

[22] Dreer, M., van de Poel, S. and Stubenrauch, F. (2017) Control of Viral Replication and Transcription by the Papillomavirus E8^E2 Protein. *Virus Research*, **231**, 96-102. https://doi.org/10.1016/j.virusres.2016.11.005

[23] Archambault, J. and Melendy, T. (2013) Targeting Human Papillomavirus Genome Replication for Antiviral Drug Discovery. *Antiviral Therapy*, **18**, 271-283. https://doi.org/10.3851/imp2612

[24] Bergvall, M., Melendy, T. and Archambault, J. (2013) The E1 Proteins. *Virology*, **445**, 35-56. https://doi.org/10.1016/j.virol.2013.07.020

[25] McBride, A.A. (2013) The Papillomavirus E2 Proteins. *Virology*, **445**, 57-79. https://doi.org/10.1016/j.virol.2013.06.006

[26] Jamal, D.F., Rozaimee, Q.A., Osman, N.H., Mohd Sukor, A., Elias, M.H., Shamaan, N.A., *et al*. (2022) Human Papillomavirus 16 E2 as an Apoptosis-Inducing Protein for Cancer Treatment: A Systematic Review. *International Journal of Molecular Sciences*, **23**, Article No. 12554. https://doi.org/10.3390/ijms232012554

[27] Das, D., Bristol, M.L., Pichierri, P. and Morgan, I.M. (2020) Using a Human Papillomavirus Model to Study DNA Replication and Repair of Wild Type and Damaged DNA Templates in Mammalian Cells. *International Journal of Molecular Sciences*, **21**, Article No. 7564. https://doi.org/10.3390/ijms21207564

[28] Jose, L., Gilson, T., Androphy, E. and DeSmet, M. (2021) Regulation of the Human Papillomavirus Lifecyle through Post-Translational Modifications of the Viral E2 Protein. *Pathogens*, **10**, Article No. 793. https://doi.org/10.3390/pathogens10070793

[29] Prabhakar, A.T., James, C.D., Das, D., Otoa, R., Day, M., Burgner, J., *et al*. (2021) CK2 Phosphorylation of Human Papillomavirus 16 E2 on Serine 23 Promotes Interaction with TopBP1 and Is Critical for E2 Interaction with Mitotic Chromatin and the Viral Life Cycle. *mBio*, **12**, e0116321. https://doi.org/10.1128/mbio.01163-21

[30] Rattay, S., Hufbauer, M., Hagen, C., Putschli, B., Coch, C., Akgül, B., *et al*. (2022) Human Beta Papillomavirus Type 8 E1 and E2 Proteins Suppress the Activation of the RIG-I-Like Receptor MDA5. *Viruses*, **14**, Article No. 1361. https://doi.org/10.3390/v14071361

[31] Bhattacharjee, R., Das, S.S., Biswal, S.S., Nath, A., Das, D., Basu, A., *et al*. (2022) Mechanistic Role of HPV-Associated Early Proteins in Cervical Cancer: Molecular Pathways and Targeted Therapeutic Strategies. *Critical Reviews in Oncology/Hematology*, **174**, Article ID: 103675. https://doi.org/10.1016/j.critrevonc.2022.103675

[32] DiMaio, D. and Petti, L.M. (2013) The E5 Proteins. *Virology*, **445**, 99-114. https://doi.org/10.1016/j.virol.2013.05.006

[33] Torres, A.D., Spurgeon, M.E., Bilger, A., Blaine-Sauer, S., Uberoi, A., Buehler, D., *et al*. (2020) The Human Papillomavirus 16 E5 Gene Potentiates Mmupv1-Dependent Pathogenesis. *Virology*, **541**, 1-12. https://doi.org/10.1016/j.virol.2019.12.002

[34] Hemmat, N., Amin Doustvandi, M., Asadzadeh, Z., Mokhtarzadeh, A., Baradaran, B. and Bannazadeh Baghi, H. (2021) Suppression of Human Papillomavirus Type 16 E5 Oncoprotein: A Promising Step in Fostering the Treatment of Cervical Cancer. *Oncology Research*, **29**, 141-148. https://doi.org/10.32604/or.2022.023346

[35] Ilahi, N.E. and Bhatti, A. (2020) Impact of HPV E5 on Viral Life Cycle via EGFR Signaling. *Microbial Pathogenesis*, **139**, Article ID: 103923. https://doi.org/10.1016/j.micpath.2019.103923

[36] Trammel, J., Amusan, O., Hultgren, A., Raikhy, G. and Bodily, J.M. (2024) Epidermal Growth Factor Receptor-Dependent Stimulation of Differentiation by Human Papillomavirus Type 16 E5. *Virology*, **590**, Article ID: 109952. https://doi.org/10.1016/j.virol.2023.109952

[37] Ganguly, N. (2012) Human Papillomavirus-16 E5 Protein: Oncogenic Role and Therapeutic Value. *Cellular Oncology*, **35**, 67-76.

https://doi.org/10.1007/s13402-011-0069-x

[38] Miyauchi, S., Kim, S.S., Jones, R.N., Zhang, L., Guram, K., Sharma, S., *et al*. (2023) Human Papillomavirus E5 Suppresses Immunity via Inhibition of the Immunoproteasome and STING Pathway. *Cell Reports*, **42**, Article ID: 112508. https://doi.org/10.1016/j.celrep.2023.112508

[39] Scott, M.L., Woodby, B.L., Ulicny, J., Raikhy, G., Orr, A.W., Songock, W.K., *et al*. (2020) Human Papillomavirus 16 E5 Inhibits Interferon Signaling and Supports Episomal Viral Maintenance. *Journal of Virology*, **94**, e01582-19. https://doi.org/10.1128/jvi.01582-19

[40] Ren, S., Gaykalova, D.A., Guo, T., Favorov, A.V., Fertig, E.J., Tamayo, P., *et al*. (2020) HPV E2, E4, E5 Drive Alternative Carcinogenic Pathways in HPV Positive Cancers. *Oncogene*, **39**, 6327-6339. https://doi.org/10.1038/s41388-020-01431-8

[41] Yajid, A.I., Zakariah, M.A., Mat Zin, A.A. and Othman, N.H. (2017) Potential Role of E4 Protein in Human Papillomavirus Screening: a Review. *Asian Pacific Journal of Cancer Prevention*, **18**, 315-319.

[42] Bryant, D., Onions, T., Raybould, R., Flynn, Á., Tristram, A., Meyrick, S., *et al*. (2014) mRNA Sequencing of Novel Cell Lines from Human Papillomavirus Type-16 Related Vulval Intraepithelial Neoplasia: Consequences of Expression of HPV16 E4 and E5. *Journal of Medical Virology*, **86**, 1534-1541. https://doi.org/10.1002/jmv.23994

[43] Prescott, E.L., Brimacombe, C.L., Hartley, M., Bell, I., Graham, S. and Roberts, S. (2014) Human Papillomavirus Type 1 E1^E4 Protein Is a Potent Inhibitor of the Serine-Arginine (SR) Protein Kinase SRPK1 and Inhibits Phosphorylation of Host SR Proteins and of the Viral Transcription and Replication Regulator E2. *Journal of Virology*, **88**, 12599-12611. https://doi.org/10.1128/jvi.02029-14

[44] Peh, W.L., Brandsma, J.L., Christensen, N.D., Cladel, N.M., Wu, X. and Doorbar, J. (2004) The Viral E4 Protein Is Required for the Completion of the Cottontail Rabbit Papillomavirus Productive Cycle *in Vivo*. *Journal of Virology*, **78**, 2142-2151. https://doi.org/10.1128/jvi.78.4.2142-2151.2004

[45] Buck, C.B., Day, P.M. and Trus, B.L. (2013) The Papillomavirus Major Capsid Protein L1. *Virology*, **445**, 169-174. https://doi.org/10.1016/j.virol.2013.05.038

[46] Mahmoudvand, S., Shokri, S., Makvandi, M., Taherkhani, R., Rashno, M., Jalilian, F.A., *et al*. (2021) *In Silico* Prediction of T-Cell and B-Cell Epitopes of Human Papillomavirus Type 16 L1 Protein. *Biotechnology and Applied Biochemistry*, **69**, 514-525. https://doi.org/10.1002/bab.2128

[47] Wang, J.W. and Roden, R.B.S. (2013) L2, the Minor Capsid Protein of Papillomavirus. *Virology*, **445**, 175-186. https://doi.org/10.1016/j.virol.2013.04.017

[48] Campos, S. (2017) Subcellular Trafficking of the Papillomavirus Genome during Initial Infection: The Remarkable Abilities of Minor Capsid Protein L2. *Viruses*, **9**, Article No. 370. https://doi.org/10.3390/v9120370

[49] Van Doorslaer, K., Li, Z., Xirasagar, S., Maes, P., Kaminsky, D., Liou, D., *et al*. (2016) The Papillomavirus Episteme: A Major Update to the Papillomavirus Sequence Database. *Nucleic Acids Research*, **45**, D499-D506. https://doi.org/10.1093/nar/gkw879

[50] Pruitt, K., Brown, G., Tatusova, T., *et al*. (2002) Chapter 18. The Reference Sequence (RefSeq) Database. In: McEntyre, J. and Ostell, J., Eds., *The NCBI Handbook*, National Center for Biotechnology Information, Chapter 18. https://www.ncbi.nlm.nih.gov/books/NBK21091/

[51] Tamura, K., Stecher, G. and Kumar, S. (2021) MEGA11: Molecular Evolutionary Genetics Analysis Version 11. *Molecular Biology and Evolution*, **38**, 3022-3027. https://doi.org/10.1093/molbev/msab120

[52] Bernard, H., Burk, R.D., Chen, Z., van Doorslaer, K., Hausen, H.Z. and de Villiers, E. (2010) Classification of Papillomaviruses (PVs) Based on 189 PV Types and Proposal of Taxonomic Amendments. *Virology*, **401**, 70-79. https://doi.org/10.1016/j.virol.2010.02.002

[53] Ko, J., Park, H., Heo, L. and Seok, C. (2012) GalaxyWEB Server for Protein Structure Prediction and Refinement. *Nucleic Acids Research*, **40**, W294-W297. https://doi.org/10.1093/nar/gks493

[54] Murahwa, A.T., Tshabalala, M. and Williamson, A. (2020) Recombination between High-Risk Human Papillomaviruses and Non-Human Primate Papillomaviruses: Evidence of Ancient Host Switching among Alphapapillomaviruses. *Journal of Molecular Evolution*, **88**, 453-462. https://doi.org/10.1007/s00239-020-09946-0

[55] Egawa, N., Egawa, K., Griffin, H. and Doorbar, J. (2015) Human Papillomaviruses; Epithelial Tropisms, and the Development of Neoplasia. *Viruses*, **7**, 3863-3890. https://doi.org/10.3390/v7072802

[56] Hirsch-Behnam, A., Delius, H. and de Villiers, E. (1990) A Comparative Sequence Analysis of Two Human Papillomavirus (HPV) Types 2a and 57. *Virus Research*, **18**, 81-97. https://doi.org/10.1016/0168-1702(90)90091-o

[57] Egawa, K., Delius, H., Matsukura, T., Kawashima, M. and de Villiers, E. (1993) 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**, 789-799. https://doi.org/10.1006/viro.1993.1320

[58] Delius, H. and Hofmann, B. (1994) Primer-Directed Sequencing of Human Papillomavirus Types. In: Hausen, H., Ed., *Human Pathogenic Papillomaviruses*, Springer, 13-31. https://doi.org/10.1007/978-3-642-78487-3_2

[59] Hirt, L., Hirsch-Behnam, A. and de Villiers, E. (1991) Nucleotide Sequence of Human Papillomavirus (HPV) Type 41: An Unusual HPV Type without a Typical E2 Binding Site Consensus Sequence. *Virus Research*, **18**, 179-189. https://doi.org/10.1016/0168-1702(91)90017-p

[60] Müller, M., Kelly, G., Fiedler, M. and Gissmann, L. (1989) Human Papillomavirus Type 48. *Journal of Virology*, **63**, 4907-4908. https://doi.org/10.1128/jvi.63.11.4907-4908.1989

[61] Favre, M., Obalek, S., Jablonska, S. and Orth, G. (1989) Human Papillomavirus (HPV) Type 50, a Type Associated with Epidermodysplasia Verruciformis (EV) and Only Weakly Related to Other EV-Specific HPVs. *Journal of Virology*, **63**, Article No. 4910. https://doi.org/10.1128/jvi.63.11.4910-.1989

[62] Matsukura, T., Iwasaki, T. and Kawashima, M. (1992) Molecular Cloning of a Novel Human Papillomavirus (Type 60) from a Plantar Cyst with Characteristic Pathological Changes. *Virology*, **190**, 561-564. https://doi.org/10.1016/0042-6822(92)91254-r

[63] Kullander, J., Handisurya, A., Forslund, O., Geusau, A., Kirnbauer, R. and Dillner, J. (2007) Cutaneous Human Papillomavirus 88: Remarkable Differences in Viral Load. *International Journal of Cancer*, **122**, 477-480. https://doi.org/10.1002/ijc.23115

[64] Terai, M. and Burk, R.D. (2002) Identification and Characterization of 3 Novel Genital Human Papillomaviruses by Overlapping Polymerase Chain Reaction: CandHPV89, can-dHPV90, and candHPV91. *The Journal of Infectious Diseases*, **185**, 1794-1797. https://doi.org/10.1086/340824

[65] Forslund, O., Antonsson, A., Higgins, G., Ly, H., Delius, H., Hunziker, A., *et al*. (2003) Nucleotide Sequence and Phylogenetic Classification of Candidate Human Papilloma Virus Type 92. *Virology*, **312**, 255-260. https://doi.org/10.1016/s0042-6822(03)00391-x

[66] Vasiljević, N., Hazard, K., Eliasson, L., Ly, H., Hunziker, A., de Villiers, E., *et al*. (2007) Characterization of Two Novel Cutaneous Human Papillomaviruses, HPV93 and HPV96. *Journal of General Virology*, **88**, 1479-1483. https://doi.org/10.1099/vir.0.82679-0

[67] Chen, Z., Schiffman, M., Herrero, R., DeSalle, R. and Burk, R.D. (2007) 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. https://doi.org/10.1016/j.virol.2006.10.022

[68] Nobre, R.J., Herráez-Hernández, E., Fei, J., Langbein, L., Kaden, S., Gröne, H., *et al*. (2009) E7 Oncoprotein of Novel Human Papillomavirus Type 108 Lacking the E6 Gene Induces Dysplasia in Organotypic Keratinocyte Cultures. *Journal of Virology*, **83**, 2907-2916. https://doi.org/10.1128/jvi.02490-08

[69] Ekström, J., Forslund, O. and Dillner, J. (2010) Three Novel Papillomaviruses (HPV109, HPV112 and HPV114) and Their Presence in Cutaneous and Mucosal Samples. *Virology*, **397**, 331-336. https://doi.org/10.1016/j.virol.2009.11.027

[70] Li, L., Barry, P., Yeh, E., Glaser, C., Schnurr, D. and Delwart, E. (2009) Identification of a Novel Human Gammapapillomavirus Species. *Journal of General Virology*, **90**, 2413-2417. https://doi.org/10.1099/vir.0.012344-0

[71] Egawa, N., Kawai, K., Egawa, K., Honda, Y., Kanekura, T. and Kiyono, T. (2012) Molecular Cloning and Characterization of a Novel Human Papillomavirus, HPV 126, Isolated from a Flat Wart-Like Lesion with Intracytoplasmic Inclusion Bodies and a Peculiar Distribution of Ki-67 and P53. *Virology*, **422**, 99-104. https://doi.org/10.1016/j.virol.2011.10.011

[72] Schowalter, R.M., Pastrana, D.V., Pumphrey, K.A., Moyer, A.L. and Buck, C.B. (2010) Merkel Cell Polyomavirus and Two Previously Unknown Polyomaviruses Are Chronically Shed from Human Skin. *Cell Host & Microbe*, **7**, 509-515. https://doi.org/10.1016/j.chom.2010.05.006

[73] Köhler, A., Gottschling, M., Manning, K., Lehmann, M.D., Schulz, E., Krüger-Corcoran, D., *et al*. (2011) Genomic Characterization of Ten Novel Cutaneous Human Papillomaviruses from Keratotic Lesions of Immunosuppressed Patients. *Journal of General Virology*, **92**, 1585-1594. https://doi.org/10.1099/vir.0.030593-0

[74] Bottalico, D., Chen, Z., Dunne, A., Ostoloza, J., McKinney, S., Sun, C., *et al*. (2011) The Oral Cavity Contains Abundant Known and Novel Human Papillomaviruses from the Betapapillomavirus and Gammapapillomavirus Genera. *The Journal of Infectious Diseases*, **204**, 787-792. https://doi.org/10.1093/infdis/jir383

[75] Ure, A.E. and Forslund, O. (2014) Characterization of Human Papillomavirus Type 154 and Tissue Tropism of Gammapapillomaviruses. *PLOS ONE*, **9**, e89342. https://doi.org/10.1371/journal.pone.0089342

[76] Li, J., Cai, H., Xu, Z., Wang, Q., Hang, D., Shen, N., *et al*. (2012) Nine Complete Genome Sequences of Cutaneous Human Papillomavirus Genotypes Isolated from Healthy Skin of Individuals Living in Rural He Nan Province, China. *Journal of Virology*, **86**, 11936-11936. https://doi.org/10.1128/jvi.01988-12

[77] Li, J., Pan, Y., Deng, Q., Cai, H. and Ke, Y. (2013) Identification and Characterization of Eleven Novel Human Gamma-Papillomavirus Isolates from Healthy Skin, Found at Low Frequency in a Normal Population. *PLOS ONE*, **8**, e77116. https://doi.org/10.1371/journal.pone.0077116

[78] Johansson, H. and Forslund, O. (2014) Complete Genome Sequences of Three Novel Human Papillomavirus Types, 175, 178, and 180. *Genome Announcements*, **2**, e00443-14. https://doi.org/10.1128/genomea.00443-14

[79] Arroyo Mühr, L.S., Bzhalava, D., Lagheden, C., Eklund, C., Johansson, H., Forslund, O., *et al*. (2015) Does Human Papillomavirus-Negative Condylomata Exist? *Virology*, **485**, 283-288. https://doi.org/10.1016/j.virol.2015.07.023

[80] Ahola, H., Bergman, P., Ström, A.C., Moreno-Lopéz, J. and Pettersson, U. (1986) Organization and Expression of the Transforming Region from the European Elk Papillomavirus (EEPV). *Gene*, **50**, 195-205. https://doi.org/10.1016/0378-1119(86)90324-0

[81] Terai, M., DeSalle, R. and Burk, R.D. (2002) Lack of Canonical E6 and E7 Open Reading Frames in Bird Papillomaviruses: *Fringilla coelebs* Papillomavirus and *Psittacus erithacus timneh* Papillomavirus. *Journal of Virology*, **76**, 10020-10023. https://doi.org/10.1128/jvi.76.19.10020-10023.2002

[82] Ogawa, T., Tomita, Y., Okada, M. and Shirasawa, H. (2007) Complete Genome and Phylogenetic Position of Bovine Papillomavirus Type 7. *Journal of General Virology*, **88**, 1934-1938. https://doi.org/10.1099/vir.0.82794-0

[83] Bennett, M.D., Reiss, A., Stevens, H., Heylen, E., Van Ranst, M., Wayne, A., *et al*. (2010) The First Complete Papillomavirus Genome Characterized from a Marsupial Host: A Novel Isolate from *Bettongia penicillata*. *Journal of Virology*, **84**, 5448-5453. https://doi.org/10.1128/jvi.02635-09

[84] Isegawa, N., Ohta, M., Shirasawa, H., Tokita, H., Yamaura, A. and Simizu, B. (1995) Nucleotide-Sequence of a Canine Oral Papillomavirus Containing a Long Noncoding Region. *International Journal of Oncology*, **7**, 155-159. https://doi.org/10.3892/ijo.7.1.155

[85] Yuan, H., Ghim, S., Newsome, J., Apolinario, T., Olcese, V., Martin, M., *et al*. (2007) An Epidermotropic Canine Papillomavirus with Malignant Potential Contains an E5 Gene and Establishes a Unique Genus. *Virology*, **359**, 28-36. https://doi.org/10.1016/j.virol.2006.08.029

[86] Tobler, K., Favrot, C., Nespeca, G. and Ackermann, M. (2006) Detection of the Prototype of a Potential Novel Genus in the Family Papillomaviridae in Association with Canine Epidermodysplasia Verruciformis. *Journal of General Virology*, **87**, 3551-3557. https://doi.org/10.1099/vir.0.82305-0

[87] Lange, C.E., Tobler, K., Ackermann, M., Panakova, L., Thoday, K.L. and Favrot, C. (2009) Three Novel Canine Papillomaviruses Support Taxonomic Clade Formation. *Journal of General Virology*, **90**, 2615-2621. https://doi.org/10.1099/vir.0.014498-0

[88] Lange, C.E., Tobler, K., Lehner, A., Vetsch, E. and Favrot, C. (2011) A Case of a Canine Pigmented Plaque Associated with the Presence of a Chi-Papillomavirus. *Veterinary Dermatology*, **23**, 76-80, e18-9. https://doi.org/10.1111/j.1365-3164.2011.01007.x

[89] Yuan, H., Luff, J., Zhou, D., Wang, J., Affolter, V., Moore, P., *et al*. (2012) Complete Genome Sequence of Canine Papillomavirus Type 9. *Journal of Virology*, **86**, 5966-5966. https://doi.org/10.1128/jvi.00543-12

[90] Lange, C.E., Tobler, K., Schraner, E.M., Vetsch, E., Fischer, N.M., Ackermann, M., *et al*. (2013) Complete Canine Papillomavirus Life Cycle in Pigmented Lesions. *Veterinary Microbiology*, **162**, 388-395. https://doi.org/10.1016/j.vetmic.2012.10.012

[91] Erdélyi, K., Bálint, Á., Dencső, L., Dán, Á. and Ursu, K. (2008) Characterisation of the First Complete Genome Sequence of the Roe Deer (*Capreolus capreolus*) Papillomavirus. *Virus Research*, **135**, 307-311. https://doi.org/10.1016/j.virusres.2008.03.002

[92] Rogovskyy, A.S., Chen, Z., Burk, R.D. and Bankhead, T. (2014) Characterization of the North American Beaver (*Castor canadensis*) Papillomavirus Genome. *Veterinary*

Microbiology, **168**, 214-220. https://doi.org/10.1016/j.vetmic.2013.11.011

[93] Stevens, H., Heylen, E., De Keyser, K., Maes, R., Kiupel, M., Wise, A., *et al*. (2013) Complete Genome Sequence of the *Crocuta crocuta* Papillomavirus Type 1 (CcrPV1) from a Spotted Hyena, the First Papillomavirus Characterized in a Member of the Hyaenidae. *Genome Announcements*, **1**, e00062-12. https://doi.org/10.1128/genomea.00062-12

[94] Ure, A.E., Elfadl, A.K., Khalafalla, A.I., Gameel, A.A.R., Dillner, J. and Forslund, O. (2011) Characterization of the Complete Genomes of Camelus Dromedarius Papillomavirus Types 1 and 2. *Journal of General Virology*, **92**, 1769-1777. https://doi.org/10.1099/vir.0.031039-0

[95] Wood, C.E., Tannehill-Gregg, S.H., Chen, Z., Doorslaer, K.V., Nelson, D.R., Cline, J.M., *et al*. (2010) Novel Betapapillomavirus Associated with Hand and Foot Papillomas in a Cynomolgus Macaque. *Veterinary Pathology*, **48**, 731-736. https://doi.org/10.1177/0300985810383875

[96] Van Doorslaer, K., Rector, A., Vos, P. and Van Ranst, M. (2006) Genetic Characterization of the *Capra hircus* Papillomavirus: A Novel Close-to-Root Artiodactyl Papillomavirus. *Virus Research*, **118**, 164-169. https://doi.org/10.1016/j.virusres.2005.12.007

[97] Lecis, R., Tore, G., Scagliarini, A., Antuofermo, E., Dedola, C., Cacciotto, C., *et al*. (2014) *Equus asinus* Papillomavirus (EaPV1) Provides New Insights into Equine Papillomavirus Diversity. *Veterinary Microbiology*, **170**, 213-223. https://doi.org/10.1016/j.vetmic.2014.02.016

[98] Ghim, S., Rector, A., Delius, H., Sundberg, J.P., Jenson, A.B. and Van Ranst, M. (2004) Equine Papillomavirus Type 1: Complete Nucleotide Sequence and Characterization of Recombinant Virus-Like Particles Composed of the EcPV-1 L1 Major Capsid Protein. *Biochemical and Biophysical Research Communications*, **324**, 1108-1115. https://doi.org/10.1016/j.bbrc.2004.09.154

[99] Rector, A., Tachezy, R., Van Doorslaer, K., MacNamara, T., Burk, R.D., Sundberg, J.P., *et al*. (2005) 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. https://doi.org/10.1016/j.virol.2004.10.033

[100] Schulz, E., Gottschling, M., Bravo, I.G., Wittstatt, U., Stockfleth, E. and 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. *Journal of General Virology*, **90**, 626-633. https://doi.org/10.1099/vir.0.008011-0

[101] Munday, J.S., Dunowska, M., Hills, S.F. and Laurie, R.E. (2013) Genomic Characterization of *Felis catus* Papillomavirus-3: A Novel Papillomavirus Detected in a Feline Bowenoid *in Situ* Carcinoma. *Veterinary Microbiology*, **165**, 319-325. https://doi.org/10.1016/j.vetmic.2013.04.006

[102] Van Doorslaer, K., Ould M'hamed Ould Sidi, A., Zanier, K., Rybin, V., Deryckère, F., Rector, A., *et al*. (2009) Identification of Unusual E6 and E7 Proteins within Avian Papillomaviruses: Cellular Localization, Biophysical Characterization, and Phylogenetic Analysis. *Journal of Virology*, **83**, 8759-8770. https://doi.org/10.1128/jvi.01777-08

[103] Chen, Z., van Doorslaer, K., DeSalle, R., Wood, C.E., Kaplan, J.R., Wagner, J.D., *et al*. (2009) Genomic Diversity and Interspecies Host Infection of *A*12 Macaca Fascicularis Papillomaviruses (MfPVs). *Virology*, **393**, 304-310.

https://doi.org/10.1016/j.virol.2009.07.012

[104] Ostrow, R.S., Liu, Z., Schneider, J.F., McGlennen, R.C., Forslund, K. and Faras, A.J. (1993) The Products of the E5, E6, or E7 Open Reading Frames of RhPV 1 Can Individually Transform NIH 3T3 Cells or in Cotransfections with Activated Ras Can Transform Primary Rodent Epithelial Cells. *Virology*, **196**, 861-867. https://doi.org/10.1006/viro.1993.1547

[105] Van Doorslaer, K., Rector, A., Jenson, A.B., Sundberg, J.P., Van Ranst, M. and Ghim, S. (2007) Complete Genomic Characterization of a Murine Papillomavirus Isolated from Papillomatous Lesions of a European Harvest Mouse (*Micromys minutus*). *Journal of General Virology*, **88**, 1484-1488. https://doi.org/10.1099/vir.0.82615-0

[106] Joh, J., Jenson, A.B., King, W., Proctor, M., Ingle, A., Sundberg, J.P., *et al*. (2010) Genomic Analysis of the First Laboratory-Mouse Papillomavirus. *Journal of General Virology*, **92**, 692-698. https://doi.org/10.1099/vir.0.026138-0

[107] Tan, C., Tachezy, R., Van Ranst, M., Chan, S., Bernard, H. and 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. https://doi.org/10.1006/viro.1994.1064

[108] Smits, S.L., Raj, V.S., Oduber, M.D., Schapendonk, C.M.E., Bodewes, R., Provacia, L., *et al*. (2013) Metagenomic Analysis of the Ferret Fecal Viral Flora. *PLOS ONE*, **8**, e71595. https://doi.org/10.1371/journal.pone.0071595

[109] Lange, C.E., Favrot, C., Ackermann, M., Gull, J., Vetsch, E. and Tobler, K. (2011) Novel Snake Papillomavirus Does Not Cluster with Other Non-Mammalian Papillomaviruses. *Virology Journal*, **8**, Article No. 436. https://doi.org/10.1186/1743-422x-8-436

[110] Christensen, N.D., Cladel, N.M., Reed, C.A. and Han, R. (2000) Rabbit Oral Papillomavirus Complete Genome Sequence and Immunity Following Genital Infection. *Virology*, **269**, 451-461. https://doi.org/10.1006/viro.2000.0237

[111] Groff, D.E. and Lancaster, W.D. (1985) Molecular Cloning and Nucleotide Sequence of Deer Papillomavirus. *Journal of Virology*, **56**, 85-91. https://doi.org/10.1128/jvi.56.1.85-91.1985

[112] Varsani, A., Kraberger, S., Jennings, S., Porzig, E.L., Julian, L., Massaro, M., *et al*. (2014) A Novel Papillomavirus in Adélie Penguin (*Pygoscelis adeliae*) Faeces Sampled at the Cape Crozier Colony, Antarctica. *Journal of General Virology*, **95**, 1352-1365. https://doi.org/10.1099/vir.0.064436-0

[113] Tachezy, R., Rector, A., Havelkova, M., Wollants, E., Fiten, P., Opdenakker, G., *et al*. (2002) 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 Microbiology*, **2**, Article No. 19. https://doi.org/10.1186/1471-2180-2-19

[114] Bergin, I.L., Bell, J.D., Chen, Z., Zochowski, M.K., Chai, D., Schmidt, K., *et al*. (2012) Novel Genital Alphapapillomaviruses in Baboons (*Papio hamadryas anubis*) with Cervical Dysplasia. *Veterinary Pathology*, **50**, 200-208. https://doi.org/10.1177/0300985812439725

[115] Rector, A., Van Doorslaer, K., Bertelsen, M., Barker, I.K., Olberg, R., Lemey, P., *et al*. (2005) Isolation and Cloning of the Raccoon (*Procyon lotor*) Papillomavirus Type 1 by Using Degenerate Papillomavirus-Specific Primers. *Journal of General Virology*, **86**, 2029-2033. https://doi.org/10.1099/vir.0.80874-0

[116] Van Bressem, M., Cassonnet, P., Rector, A., Desaintes, C., Van Waerebeek, K., Al-

faro-Shigueto, J., *et al*. (2007) Genital Warts in Burmeister's Porpoises: Characterization of *Phocoena spinipinnis* Papillomavirus Type 1 (PsPV-1) and Evidence for a Second, Distantly Related PSPV. *Journal of General Virology*, **88**, 1928-1933. https://doi.org/10.1099/vir.0.82694-0

[117] Rector, A., Mostmans, S., Van Doorslaer, K., McKnight, C.A., Maes, R.K., Wise, A.G., *et al*. (2006) Genetic Characterization of the First Chiropteran Papillomavirus, Isolated from a Basosquamous Carcinoma in an Egyptian Fruit Bat: The *Rousettus aegyptiacus* Papillomavirus Type 1. *Veterinary Microbiology*, **117**, 267-275. https://doi.org/10.1016/j.vetmic.2006.06.010

[118] Mengual-Chuliá, B., Domenis, L., Robetto, S. and Bravo, I.G. (2014) A Novel Papillomavirus Isolated from a Nasal Neoplasia in an Italian Free-Ranging Chamois (*Rupicapra r. rupicapra*). *Veterinary Microbiology*, **172**, 108-119. https://doi.org/10.1016/j.vetmic.2014.05.006

[119] Smits, S.L., Schapendonk, C.M.E., van Leeuwen, M., Kuiken, T., Bodewes, R., Stalin Raj, V., *et al*. (2013) Identification and Characterization of Two Novel Viruses in Ocular Infections in Reindeer. *PLOS ONE*, **8**, e69711. https://doi.org/10.1371/journal.pone.0069711

[120] Giri, I., Danos, O. and Yaniv, M. (1985) Genomic Structure of the Cottontail Rabbit (Shope) Papillomavirus. *Proceedings of the National Academy of Sciences*, **82**, 1580-1584. https://doi.org/10.1073/pnas.82.6.1580

[121] Stevens, H., Rector, A., Van Der Kroght, K. and Van Ranst, M. (2008) Isolation and Cloning of Two Variant Papillomaviruses from Domestic Pigs: Sus Scrofa Papillomaviruses Type 1 Variants A and B. *Journal of General Virology*, **89**, 2475-2481. https://doi.org/10.1099/vir.0.2008/003186-0

[122] Rector, A., Bossart, G.D., Ghim, S., Sundberg, J.P., Jenson, A.B. and 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. *Journal of Virology*, **78**, 12698-12702. https://doi.org/10.1128/jvi.78.22.12698-12702.2004

[123] Rector, A., Stevens, H., Lacave, G., Lemey, P., Mostmans, S., Salbany, A., *et al*. (2008) Genomic Characterization of Novel Dolphin Papillomaviruses Provides Indications for Recombination within the Papillomaviridae. *Virology*, **378**, 151-161. https://doi.org/10.1016/j.virol.2008.05.020

[124] Rehtanz, M., Ghim, S., Rector, A., Van Ranst, M., Fair, P.A., Bossart, G.D., *et al*. (2006) Isolation and Characterization of the First American Bottlenose Dolphin Papillomavirus: Tursiops Truncatus Papillomavirus Type 2. *Journal of General Virology*, **87**, 3559-3565. https://doi.org/10.1099/vir.0.82388-0

[125] Stevens, H., Rector, A., Bertelsen, M.F., Leifsson, P.S. and Van Ranst, M. (2008) Novel Papillomavirus Isolated from the Oral Mucosa of a Polar Bear Does Not Cluster with Other Papillomaviruses of Carnivores. *Veterinary Microbiology*, **129**, 108-116. https://doi.org/10.1016/j.vetmic.2007.11.037