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Human Papillomavirus Genotypes in Invasive Cervical Carcinoma in HIV-Seropositive and HIV-Seronegative Women in Zimbabwe.

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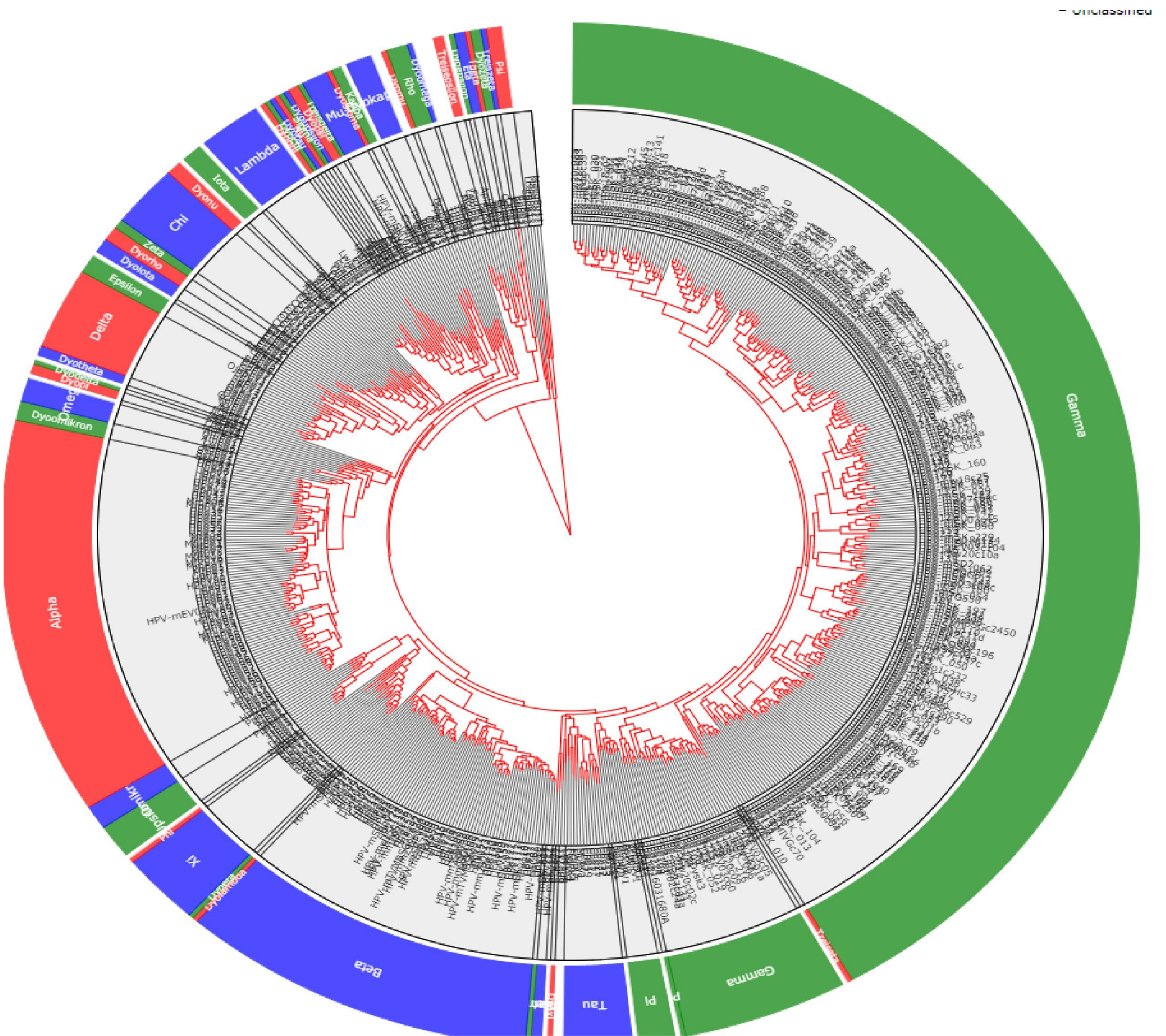
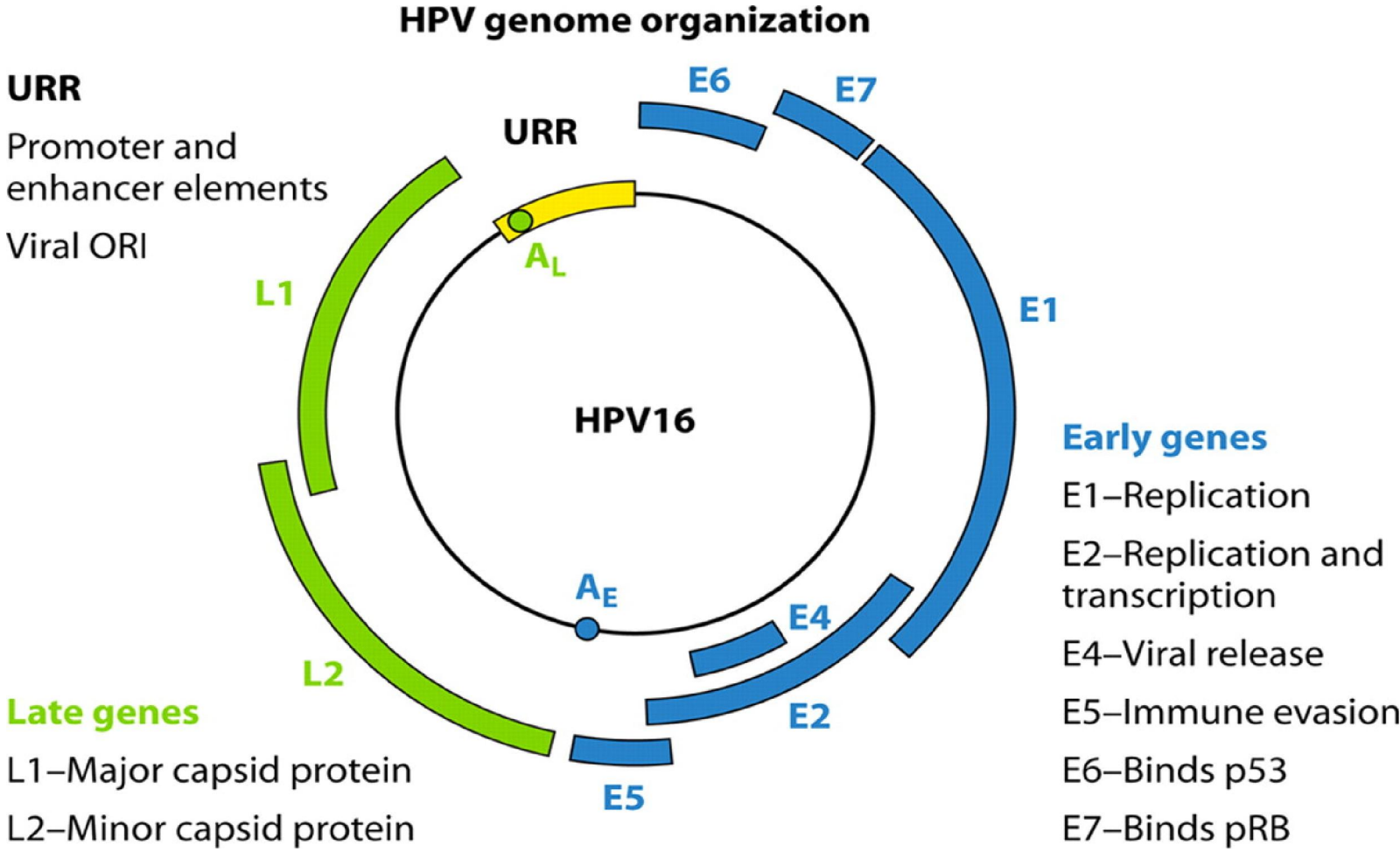
HPV genera and species

- According to the most recent ICTV classification, the *Papillomaviridae* family includes two subfamilies *Firstpapilomavirinae* with more than 52 genera and *Secondpapillomavirinae* with one genus and one species"(Van Doorslaer et al., 2018) and a total of 133 species.
- Over 200 human papillomavirus (HPV) genotypes have been described with most falling into the **Alpha, Beta and Gamma** genera.
- HPVs associated with malignant anogenital cancers are found in the **Alpha-PV genus**.
- **Very little has been published on Beta and Gamma-PVs in genital infections and almost nothing is known about these viruses in Africa. There is no published information on genital Beta- and Gamma-PVs in South Africans.**
-



Background HPV Biology

- Papillomaviridae family
- Non-enveloped virus
- Double stranded circular DNA virus.
- Genome is approximately 8kb
- Typically it has 8 ORFs the early genes are for replication and transcription and the late are structural proteins.
- Establish productive infections in epithelial cells of the skin (cutaneous types) or mucous membranes (mucosotropic)



doi: 10.1128/CMR.05028-11 *Clin. Microbiol. Rev. April 2012 vol. 25no. 2 215-222*

BACKGROUND:

- Invasive cervical carcinoma (ICC) accounts for 23% of all cancer-related deaths in Zimbabwean women. Trials for a national program of genotype-specific human papillomavirus (HPV) vaccines are underway to prevent cervical carcinoma, but the distribution of HPV types among women with ICC according to HIV status is unknown.

METHODS:

To determine prevalence and distribution of high-risk HPV genotypes by HIV status in women with ICC.

We performed a cross-sectional study on women referred for ICC testing at 4 urban referral hospitals in Zimbabwe from June 2014 to December 2015.

Cervical biopsies were obtained for histology and HPV genotyping. HIV serology testing was performed. HPV testing was performed using MY09/MY11 polymerase chain reaction followed by typing using dot-blot hybridization.

RESULTS:

- Of 107 participants with histologically proven ICC, HIV prevalence was 49.5% (53/107). HIV-positive women tended to be younger (median age 44 years) than HIV-negative women (median age 59 years).
- HPV prevalence was 94% (101/107), ranging from 1 to 5 genotypes per participant.
- HPV 16 (81.5%), 18 (24%), 33 (13%), 35 (11%), 56 (9%), and 45 (7.4%) were the most prevalent genotypes among HIV-negative participants; HPV 16 (67.9%), 18 (43.4%), 56 (18.9%), 45 (15.1%), 33 (11.3%), and 58 (9.4%) were the most prevalent among HIV-positive participants. Eighty-three percent of women were infected with either HPV-16 or HPV-18.

TABLE 2. HPV Genotypes by HIV Status

		HIV Status Total n (%)	
HPV Genotype	**Total n (%)**	**Negative 54 (50.5)**	**Positive 53 (49.5)**
Any HPV	101 (94.4)	50 (93)	51 (96)
HR-HPV			
16	80 (74.8)	44 (81.4)	36 (67.9)
18	36 (33,6)	13 (24.1)	23 (43.4)
31	6 (5.6)	3 (5.6)	3 (5.7)
33	13 (12.1)	7 (13)	6 (11.3)
35	8 (7.5)	6 (11.1)	2 (3.8)
39	4 (3.7)	2 (3.7)	2 (3.8)
45	12 (11.2)	4 (7.4)	8 (15.1)
51	6 (5.6)	2 (3.7)	4 (7.5)
52	2 (1.9)	1 (1.9)	1 (1.9)
56	15 (14)	5 (9.3)	10 (18.9)
58	6 (5.6)	1 (1.9)	5 (9.4)
59	3 (2.8)	1 (1.9)	2 (3.8)
66	3 (2.8)	1 (1.9)	2 (3.8)
Low-risk HPV			
6		0 (0)	1 (1.9)
26		0 (0)	1 (1.9)
40		1 (1.9)	0 (0)
73		1 (1.9)	1 (1.9)
82		1 (1.9)	2 (3.8)

CONCLUSIONS:

- Effective vaccination programs against HPV 16 and HPV 18 could prevent up to 83% of cases of cervical cancer in Zimbabwe. HIV may influence distribution of some HPV genotypes given the significant increase in prevalence of HPV 18 among HIV-positive participants.

Human Papillomavirus Genotypes in Invasive Cervical Carcinoma in HIV-Seropositive and HIV-Seronegative Women in Zimbabwe

Washington Mudini, MB ChB (UZ),† Joel M. Palefsky, MD, FRCP (C),‡ Martin J. Hale, MB ChB (UR), LRCP LRCS (UK), FC Path (SA) Anat,*† Michael Z. Chirenje, MD (Liberia), MRCOG (UK), MSC (Gynae Oncology),§‖ Rudo Makunike-Mutasa, MB ChB (UZ), FRCPath (UK), MRCPath (UK),¶ Fiona Mutisi, HBMLS, (UZ),‖ Alltalents Murahwa, HBMLS (UZ), MPhil (UCT),# and Altini Mario, BDS, MDent, DSc (Medicine), FCPath (SA) Oral**

Background: Invasive cervical carcinoma (ICC) accounts for 23% of all cancer-related deaths in Zimbabwean women. Trials for a national program of genotype-specific human papillomavirus (HPV) vaccines are underway to prevent cervical carcinoma, but the distribution of HPV types among women with ICC according to HIV status is unknown.

Methods: To determine prevalence and distribution of high-risk HPV genotypes by HIV status in women with ICC, we performed a cross-sectional study on women referred for ICC testing at 4 urban referral hospitals in Zimbabwe from June 2014 to December 2015. Cervical biopsies were obtained for histology and HPV genotyping. HIV serology testing was performed. HPV testing was performed using MY09/MY11 polymerase chain reaction followed by typing using dot-blot hybridization.

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Conclusions: Effective vaccination programs against HPV 16 and HPV 18 could prevent up to 83% of cases of cervical cancer in Zimbabwe. HIV may influence distribution of some HPV genotypes given the significant increase in prevalence of HPV 18 among HIV-positive participants.

Key Words: cervical cancer, HPV, HIV, Zimbabwe, dot-blot hybridization

(*J Acquir Immune Defic Syndr* 2018;79:e1–e6)

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CHARACTERISATION AND EVOLUTIONARY DYNAMICS OF TEN NOVEL *GAMMAPAPILLOMAVIRUS* TYPES FROM SOUTH AFRICAN PENILE SWABS

Alltalents Tutsirayi Murahwa

PhD Medical Virology (UCT) , MPhil (MED) Immunology (UZ), Hons BMLS (UZ)

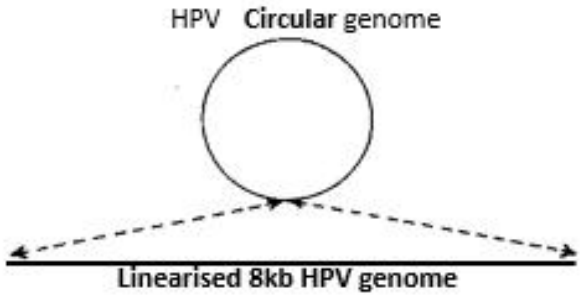
National Research Foundation

INSTITUTE OF INFECTIOUS DISEASE AND MOLECULAR MEDICINE

Poliomyelitis Research Foundation

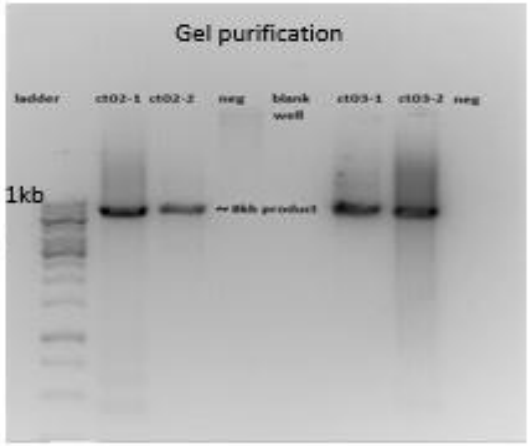
NATIONAL HEALTH LABORATORY SERVICE

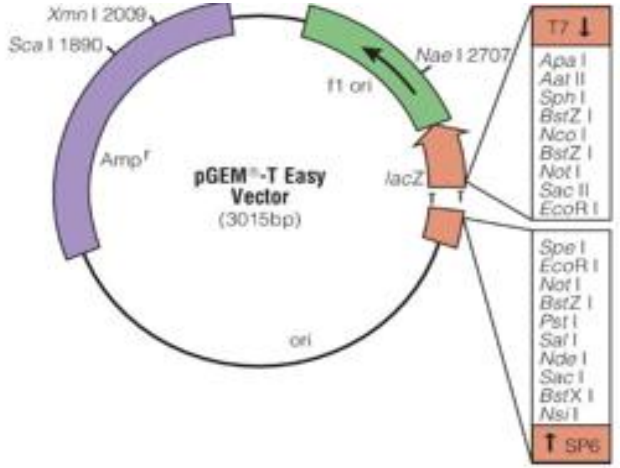
Laboratory workflow



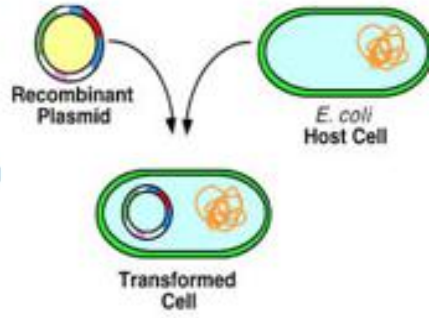
Kapa long range PCR

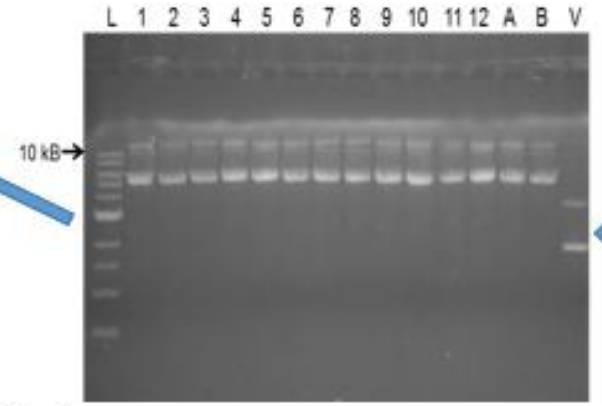
Touch down approach





pGEM T easy vector/
Topo XL vector





Plasmid purifications (lanes 1-12, A, B) run on 0.8% agarose gel. The NEB 1kb DNA ladder (L) and the non-recombinant vector (3.5kb p CR-XL-TOPO vector) were included (V).

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journal homepage: www.elsevier.com/locate/pvr

Discovery, characterisation and genomic variation of six novel *Gammapapillomavirus* types from penile swabs in South Africa

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[b] Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa
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[d] SAMRC Gynaecological Cancer Research Centre, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

ARTICLE INFO

Keywords:
Gammapapillomavirus
Penile

ABSTRACT

Six novel human papillomaviruses from penile swabs were characterised. Multiple full genome clones for each novel type were generated, and complete genome sizes were: HPV211 (7253bp), HPV212 (7208bp), HPV213 (7096bp), HPV214 (7357), HPV215 (7186bp) and HPV216 (7233bp). Phylogenetically the novel papillomaviruses all clustered with *Gammapapillomaviruses*: HPV211 is most closely related to HPV168 (72% identity in the L1 nucleotide sequence) of the Gamma-8 species, HPV212 is most closely related to HPV144 (82.9%) of the Gamma-17 species, HPV213 is most closely related to HPV153 (71.8%) of the Gamma-13 species, HPV214 is most closely related to HPV103 (75.3%) of the Gamma-6 species, HPV215 and HPV216 are most closely related to HPV129 (76.8% and 79.2% respectively) of the Gamma-9 species. The novel HPV types demonstrated the classical genomic organisation of *Gammapapillomavirusess*, with seven open reading frames (ORFs) encoding five early (E1, E2, E4, E6 and E7) and two late (L1 and L2) proteins. Typical of *Gammapapillomavirusess* the novel types all lacked the E5 ORF and HPV214 also lacked the E6 ORF. HPV212 had nine unique variants, HPV213 had five and HPV215 had four variants. Conserved domains observed among the novel types are the Zinc finger Binding Domain and PDZ domains. A retinoblastoma binding domain (pRB) binding domain in E7 protein was additionally identified in HPV214. This study expands the knowledge of the rapidly growing *Gammapapillomavirus* genus.

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VIRUSES

Complete Genome Sequences of Four Novel Human *Gammapapillomavirus* Types, HPV-219, HPV-220, HPV-221, and HPV-222, Isolated from Penile Skin Swabs from South African Men

Alltalents T. Murahwa,[a] Tracy L. Meiring,[a] Zizipho Z. A. Mbulawa,[a,b] Anna-Lise Williamson[a,c]

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ABSTRACT Four novel human gammapapillomaviruses were characterized from penile specimens using genome amplification, cloning, and sequencing. The HPV-219 L1 gene showed 87% nucleotide identity to that of HPV-213 of species gamma-13, HPV-220 had 72% identity to L1 of HPV-212 (gamma-17), HPV-221 had 80% identity to L1 of HPV-142 (gamma-10), and HPV-222 had 73% nucleotide identity to L1 of HPV-162 (gamma-19).

Human Reference clones

Show 10 entries

Search: Murahwa

Virus name	Genus name	Species name	GenBank ID	Date submitted	Submitted by	Reference
HPV211	Gamma	Gamma-8	MF509816	2016-06-19	T. Meiring	Murahwa et al, 2019
HPV212	Gamma	Gamma-17	MF509817	2016-06-19	T. Meiring	Murahwa et al, 2019
HPV213	Gamma	Gamma-13	MF509818	2016-06-19	T. Meiring	Murahwa et al, 2019
HPV214	Gamma	Gamma-6	MF509819	2016-06-19	T. Meiring	Murahwa et al, 2019
HPV215	Gamma	Gamma-9	MF509820	2016-06-19	T. Meiring	Murahwa et al, 2019
HPV216	Gamma	Gamma-9	MF509821	2016-06-19	T. Meiring	Murahwa et al, 2019
HPV219	Gamma	Gamma-13	MH172376	2017-10-10	T. Meiring	Murahwa et al, 2018
HPV220	Gamma	Gamma-17	MH172377	2017-10-10	T. Meiring	Murahwa et al, 2018
HPV221	Gamma	Gamma-10	MH172378	2017-10-10	T. Meiring	Murahwa et al, 2018
HPV222	Gamma	Gamma-19	MH172379	2017-10-10	T. Meiring	Murahwa et al, 2018

Showing 1 to 10 of 10 entries (filtered from 226 total entries)

Previous Next

[a] Assignments are tentative and not official, but might be recommendations to the papillomavirus working group and ICTV

Recent News

The Carina Eklund Symposium: 30 years of HPV research

April 29, 2019

In April 2019, it has been 30 years since Project Coordinator Carina Eklund started working at Professor Joakim Dillner's research group at Karolinska Insitute. At that time, viruses causing cancer was not a mainstream issue. Thirty years later, they are well on their way to use HPV as a target for global elimination of cervical cancer. To commemorate the occasion, Professor Joakim Dillner arranged a One-day symposium dedicated to the [...]

» Read more

Biobank of HPV types

The International Human Papillomavirus (HPV) Reference Center confirms DNA sequences of novel HPV types after the whole genomes have been cloned, assigns HPV type numbers, deposits and maintains the reference clones, as well as distributes samples of the reference material for research use.

Menu

- Aims
- Services

Murahwa et al. BMC Genomics (2019) 20:368
https://doi.org/10.1186/s12864-019-5735-9

BMC Genomics

RESEARCH ARTICLE Open Access

Evolutionary dynamics of ten novel *Gamma-PVs*: insights from phylogenetic incongruence, recombination and phylodynamic analyses

Alltalents T. Murahwa[1,2], Fredrick Nindo[3], Harris Onywera[1,2], Tracy L. Meiring[1,2], Darren P. Martin[2,3] and Anna-Lise Williamson[1,2,4*]

Abstract

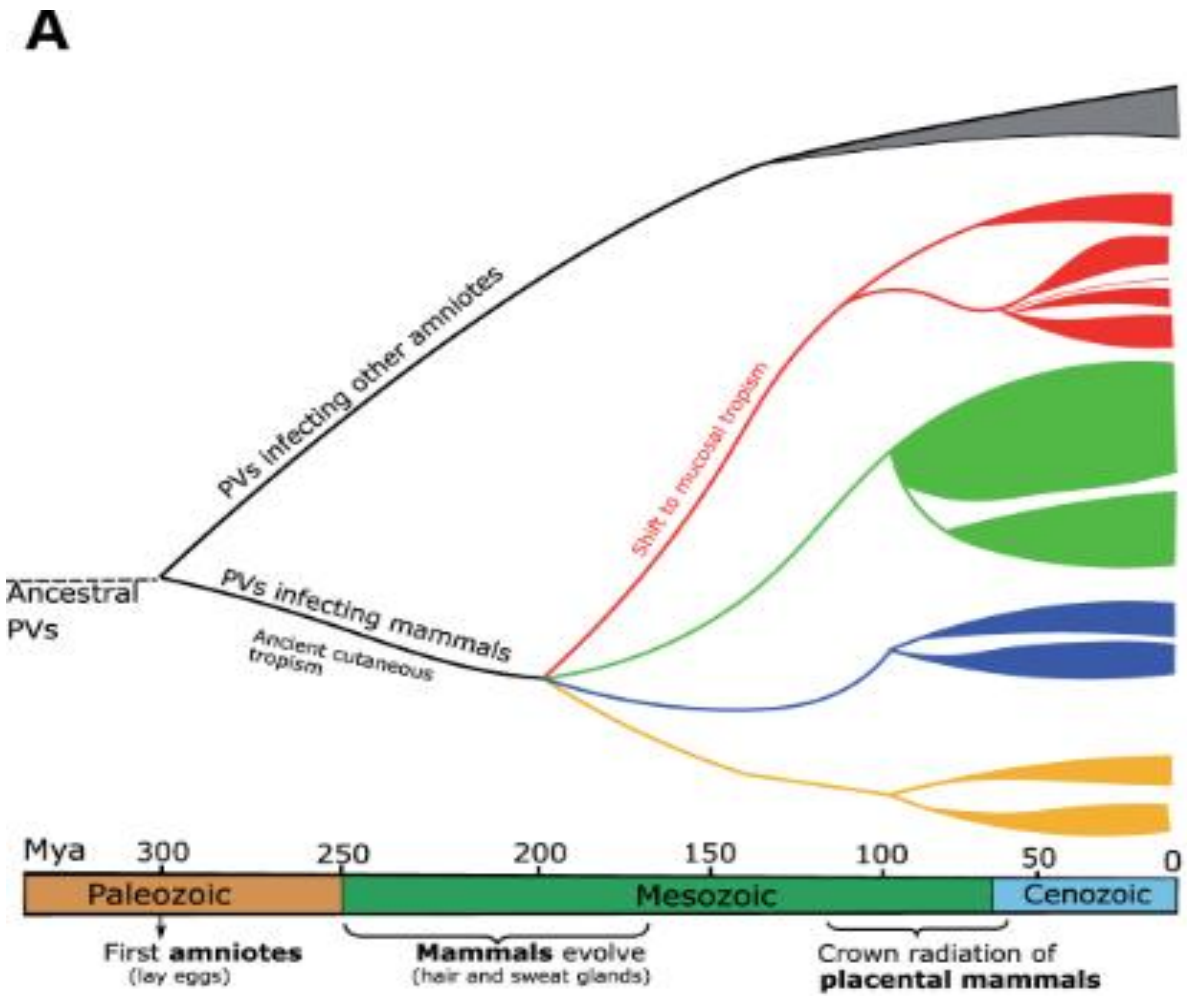
Background: Human papillomaviruses (HPVs) are genetically diverse, belonging to five distinct genera: Alpha, Beta, Gamma, Mu and Nu. All papillomaviruses have double stranded DNA genomes that are thought to evolve slowly because they co-opt high-fidelity host cellular DNA polymerases for their replication. Despite extensive efforts to catalogue all the HPV species that infect humans, it is likely that many still remain undiscovered. Here we use the sequences of ten novel *Gammapapillomaviruses* (*Gamma-PVs*) characterized in previous studies and related HPVs to analyse the evolutionary dynamics of these viruses at the whole genome and individual gene scales.

Results: We found statistically significant incongruences between the phylogenetic trees of different genes which imply gene-to-gene variation in the evolutionary processes underlying the diversification of Gamma-PVs. We were, however, only able to detect convincing evidence of a single recombination event which, on its own, cannot explain the observed incongruences between gene phylogenies. The divergence times of the last common ancestor (LCA) of the Alpha, Beta, Mu, Nu and Gamma genera was predicted to have existed between 49.7–58.5 million years ago, before splitting into the five main lineages. The LCA of the Gamma-*PVs* at this time was predicted to have existed between 45.3 and 67.5 million years ago: approximately at the time when the simian and tarsier lineages of the primates diverged.

Conclusion: Consequently, we report here phylogenetic tree incongruence without strong evidence of recombination.

Keywords: Human papillomavirus, Gamma-PVs, Most recent common ancestor, Phylogenetic incongruence, Recombination, Molecular divergence

Global scenario of PV evolution



Crown-group	Characteristics of the Phenotype
	-Essentially cutaneous PVs -Productive and asymptomatic infections
Alpha-Omikron	-Essentially mucosal PVs -Productive infections -Some of them carcinogenic potential (e.g. HPV16 and HPV18)
Beta-XI	-Cutaneous PVs -Mainly asymptomatic -Some of them proliferative infections (e.g. HPV4)
Delta-Zeta	-Cutaneous PVs -Productive infections -Some of them carcinogenic potential (e.g. EcPV2)
Lambda-Mu	-Mucosal and cutaneous PVs -Productive and asymptomatic infections

Journal of Medical Virology 87:478–484 (2015)

Frequency of *Betapapillomavirus* Infections Among HIV Infected and Uninfected Black Zimbabweans With Cutaneous Lesions

Alltalents T. Murahwa,[1,2]* Faith C. Muchemwa,[1] Kerina Duri,[1] Russell B. Kanyera,[1] Mqondisi Tshabalala,[1] Monalisa T. Manhanzva,[2] Munyaradzi P. Mapingure,[3] and Babill Stray-Pedersen[4]

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Human papillomavirus (HPV) types from the *Betapapillomavirus* (β-HPV) genus are plentiful in non-melanoma skin cancers and warts among Caucasians, but there is paucity of information among black Africans. To determine the frequency of β-HPV genotypes in cutaneous infections among Black Zimbabweans, a cross-sectional study was carried out in which blood samples and skin biopsies were collected from patients infected and uninfected with HIV attending a referral hospital. We included 144 participants (72 infected and 72 uninfected with HIV) with clinically apparent cutaneous warts (n = 34), suspected non-melanoma skin cancers (n = 98) and Kaposi sarcoma (KS) (n = 18). The skin biopsies were analyzed for HPV DNA presence and type. β-HPV DNA was identified

KEY WORDS: human papillomavirus; non-melanoma skin cancers; cutaneous warts; Kaposi sarcoma

INTRODUCTION

Human papillomavirus (HPV) is the most commonly implicated virus in many human malignancies with 5.2% of all cancers being attributable to HPV infection [Parkin and Bray, 2006]. The World Health Organization estimated that about 9–13% (~630 million) of the world population has an HPV [Pagluisi, 2001]. The involvement of HPV in cervical, penile, oral, genital, and oropharyngeal cancers and cutaneous lesions such as skin warts, squamous cell carcinomas and basal cell carcinomas has been

Journal of Medical Virology 86:1556–1559 (2014)

Presence of *Betapapillomavirus* in Kaposi Sarcoma Lesions

Alltalents T. Murahwa,[1,2] Faith C. Muchemwa,[1]* Kerina Duri,[1] Margaret Z. Borok,[3] Russell B. Kanyera,[1] Monalisa T. Manhanzva,[2] Munyaradzi P. Mapingure,[4] and Babill Stray-Pedersen[5]

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Human herpes virus 8 (HHV 8) is recognized as the necessary cause of Kaposi sarcoma (KS) and in the recent past the human papillomavirus (HPV) has been linked to the development of cutaneous basal cell and squamous cell carcinomas. In a cross sectional study investigating Beta-HPV infections in skin lesions, an unexpected occurrence of HPV DNA was found in KS lesions of HIV infected individuals. Of the 18 KS cases included in the study 16 (89%) had HPV DNA detected. The most common *Betapapillomavirus* types were HPV14 [15 cases (83.3%)], HPV12 [8 cases (44.4%)], and HPV24 [7 cases (39%)]. Multiple Beta-HPV types were detected in 10 (62.5%) of the participants with HPV DNA positive lesions; of these 7 had a CD4+ count below 350 cells/μl and 3 had CD4+

occurrence of KS is significantly associated with HIV infection, several studies have shown increased incidence of KS among HIV infected individuals and the synergistic interactions between these two viruses [Cattelan et al., 2001; Newton et al., 2006; Sullivan et al., 2008].

HPV is the most commonly implicated virus in many human malignancies, 5.2% of all cancers are attributable to HPV infection [Parkin and Bray, 2006]. The involvement of HPV in cervical, penile, oral, genital, and laryngeal cancers and cutaneous lesions such as skin warts, squamous cell carcinomas (SCC), and basal cell carcinomas (BCC) has been documented extensively [Alba and Cararach, 2009]. There is an increasing body of evidence linking HPV to non-melanoma skin cancers [Plasmeijer et al., 2011; Viarisio et al., 2011]. Several molecular epide-

Conclusion

- Discovery of more HPV viruses will enable a better understanding of both prophylactic and therapeutic strategies.

- Embracing next generation sequencing technologies is key to this goal.