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SHORT COMMUNICATION

Molecular typing of bovine papillomaviruses in Costa Rica

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Abstract

Bovine papillomaviruses are related to cause fibroepithelial proliferations in the skin and mucosae and are associated with economic loss mainly related to poor body condition and reduced milk production. This study aimed to investigate the presence and types of bovine papillomaviruses (BPVs) in cattle sampled in different areas of Costa Rica using molecular techniques. A descriptive study with a non-probability convenience sampling was carried out. A total of 99 papillomatous lesions were collected from 63 animals in 32 farms, and analyzed by polymerase chain reaction, rolling circle amplification (RCA), sequencing, and restriction enzymes digestion. Seven bovine papillomavirus types (BPV1, BPV2, BPV4, BPV6, BPV7, BPV10, BPV11) and two putative novel viral variants (BPV-CR1 and BPV-CR2) were identified for the first time in Costa Rica. BPV6 was the most frequently detected virus in lesions (31.2%), followed by BPV2 (25%) and BPV1 (25%). BPV1 and BPV2 were the most widely distributed in the Country. Coinfections were recorded in two animals (BPV1 / BPV2 and BPV4 / BPV6). Restriction analyses allowed differentiating BPV1 from BPV2, BPV4, and BPV7, but failed to identify BPV6, BPV10, and BPV11. Results suggest that a great PVs diversity is harbored by bovines in Costa Rica and indicate the need for further investigations aimed to uncover PV diversity at the full genomic level.

Keywords Molecular epidemiology · Rolling circle amplification · Oncovirus · Molecular diagnosis

Introduction

Bovine papillomavirus (BPV) belongs to the family *Papillomaviridae*, including viruses with an 8 kb double-stranded DNA genome housing eight genes (Nair and Campo 2008). Globally, according to PaVE episteme (2021), 29 BPV types have been identified. Twenty six types have been allocated into genera *Deltapapillomavirus, Xipapillomavirus, Dyokappapapillomavirus, Dyoxipapillomavirus,* and *Epsilonpapillomavirus*, while BPV19, BPV21, and BPV27 are yet unclassified (Vazquez et al. 2012; Lunardi et al. 2013; Munday et al. 2015; Roperto et al. 2016; Araldi et al. 2017; Cardona-Alvarez et al. 2018; Yamashita-Kawanishi et al. 2020; PaVE episteme 2021). PVs classification is based on the nucleotide sequence of the gene encoding the L1 capsid protein. Depending on L1 homology level, new genera, species, types, subtypes, and variants (zur Hausen and De Villier 1994) are classified. BPV1 and BPV2 appear to be the most prevalent bovine viruses in the world (Vazquez et al. 2012; Munday et al. 2015). BPVs causes proliferation of epithelial tissues in the skin and mucous membranes, causing warts, benign or malignant tumors, particularly when

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environmental carcinogenic co-factors are present (Corteggio et al. 2013). The BPV E5, E6, and E7 oncoproteins are commonly associated with tumors etiology (Borzacchiello and Roberto 2008). Lesions can be few or multiple, and are usually located on the animal's face, neck, back, and trunk (Nair and Campo 2008). Warts can cause economic losses to farmers related to poor body condition and reduced milk production when lesions are in the udder, where they interfere with milking and induce mastitis (Wellenberg et al. 2002; Vazquez et al. 2012).

Diagnosis of BPV is mainly based on clinical observation, typically on the presence of proliferative lesions present in form of cauliflower, pedunculated, flat, or with atypical morphologies (Bastita et al. 2013). In the last decade, the use of molecular techniques, such as polymerase chain reaction (PCR), L1 gene sequencing (Lunardi et al. 2013; Araldi et al. 2014), rolling circle amplification (RCA) and enzymatic digestion, and sequencing of the entire viral genome have been increasingly used to identify and characterize PVs (Rector et al. 2004).

Although PV has been reported worldwide (Dolz et al. 2020), no molecular studies on bovine papillomatosis have been conducted in Costa Rica, and genotypes present in the Country are unknown. Therefore, this study aims to establish the BPV genotypes present in cattle in different areas of the Country using molecular techniques.

Materials and methods

Sampling

A descriptive study using a convenience non-probabilistic sampling method was conducted, to determine the presence of BPV genotypes in Costa Rican cattle. The snowball sampling method was used (potential subjects are identified in the population and asked to recruit others) to collect and analyze papillomatous lesions over one year, from cattle farms with different productive uses. The project was explained to producers and their consent was obtained. Before sampling, location of the farm (by georeferentiation), and identification of the animal were recorded and stored in a database. Papilloma samples were taken from different anatomical areas and one or more animals of a given farm when morphologically different. Samples were collected using a sterile scalpel, after cleaning the affected area with 2% iodine alcohol. Antibiotic was locally applied once the sample was taken. Immediately after sampling, specimens were divided into 2 aliquots. For each sample, one aliquot was placed in 1.5 ml Eppendorf tubes with 70% ethanol and stored at -20 °C, while the other was fixed in 10% buffered formalin for histological evaluations.

Histopathology

Formalin-fixed tissues were dehydrated with increasing alcohol concentrations and xylene in an automatic tissue processor, and paraffin-embedded. Sections (3 µm) were obtained with a microtome (RM2245, Leica Biosystems), and stained with hematoxylin and eosin (H.E.) in an automatic multistainer (ST5020, Leica Biosystems). Slides were then evaluated at light microscopy (Nikon Eclipse 80i) as previously described (Tore et al. 2017). Tissues were imaged using Nikon Eclipse 80i and digital computer images were recorded with a Nikon Ds-fi1 camera.

Molecular analysis (DNA extraction, amplification, and sequencing)

DNA was extracted from all samples using a DNeasy Blood and Tissue Kit (Qiagen, Hilden, Germany) following the manufacturer's protocol. A 478 bp conserved region in the gene encoding structural protein L1 was amplified by PCR using primers FAP59/FAP64 (5'-TAACWGTIGGICAYCCWTATT-3'/5'-CWATATCWVHCATITCICCATC-3'). PCR was performed with DreamTaq Master Mix 1X (Thermo Scientific, USA), 0.25 µM of each primer, 1.25 µL of DNA (100 ng/µL), and nuclease-free water (Thermo Scientific, USA) in a volume of 25 µL. The conditions for amplification were initial denaturation at 94 °C for 10 min, followed by 45 cycles of denaturation at 94 °C for 90 s, hybridization at 50 °C for 90 s, and extension for 90 s at 72 °C, with a final extension at 72 °C for 5 min (Roperto et al. 2008; Ogawa et al. 2004). Visualization of the PCR product was carried out by electrophoresis using a 1% agarose gel stained with GelRed (Thermo Scientific, USA). GeneRuler 100 bp DNA ladder (Thermo Scientific, USA) was used as the molecular weight marker. Selected PCR products were sent for sequencing to Macrogen, Seoul, Korea. Sequence editing was performed with Bioedit 7.2.5 software. Subsequently, the obtained sequence was compared with the sequences in GenBank using the BLASTn algorithm. Alignment of the sequences obtained in this study with 28 sequences representative of existing genotypes was also performed using ClustalW, to establish the level of homology of the L1 amplicons.

Circular DNA Replication (RCA)

Each genotype of BPV identified underwent complete genome amplification through the TempliPhi Amplification Kit (GE) (Rector et al. 2004). The DNA sample (5µL) was denatured at 95 °C for 3 min and placed on ice. In a second tube, 10 µL of the TempliPhi reaction buffer, 0.4 L of the

TempliPhi enzyme mixture, and 0.4 L of dNTP (10 mM) was added. The contents of both tubes were mixed and incubated for 18 h at 30ºC. The product was placed at 65 ºC for 10 min to inactivate the DNA polymerase and kept at -20ºC (Rector et al. 2004), until RCA products were digested with restriction enzymes such as *Escherichia coli* RY13 (EcoRI), *Bacillus amyloliquefaciens* HI (BamHI) and *Saccharomyces cerevisiae* I (SacI). RCA product (5µL) and 25µL of the reaction mixture of each enzyme were incubated at 37 ºC for 2 h. Cutting patterns were visualized by electrophoresis using 5µL of each digested sample, under the conditions described above for PCR. A 1 kb molecular weight marker (Thermo Scientific, USA) was used.

Data analysis

The results of the PCR and RCA were included in the database. The presence of genotypes by province was determined and the distribution of genotypes was georeferenced. Maximum likelihood phylogenetic trees were obtained with MEGA7 software, based on the GTR + I + G evolutionary model, which was the best suited model for our data by using the: "find best DNA/protein Models" option of MEGA7. Restriction enzymes cutting patterns identified by digesting RCA were established.

Results

A total of 99 papillomas from 63 animals and 32 farms were collected in five provinces (Alajuela 42, Guanacaste 28, Puntarenas 14, San José 13, and Limón 2). One papilloma was collected from 35 (55.6%) animals, two from 20 (31.7%), and three from eight (12.7%) bovines. Gross lesions consisted of multifocal exophytic proliferative and papillomatous cutaneous lesions, ranging from 1 to 5 cm and predominantly located in the udder (31.1%), head (21.1%), neck (21.1%), and belly (12.2%). Histologically, lesions were diagnosed as viral papillomas and were characterized by an exophytic, unencapsulated, delimitated neoplasm composed of single or multiple finger-like projections of thickened squamous epithelium sustained by a fibrovascular stroma with mild ectatic blood vessels and covered by orthokeratotic hyperkeratosis. Multifocally, the stratum granulosum showed increased keratohyalin granules and swelling scattered squamous cells with abundant clear cytoplasm and pyknotic nucleus surrounded by a clear halo (koilocytes) (Fig. 1).

A total of 84 papillomas from 56 animals tested positive by FAP59/FAP64 PCR while 15 samples from 7 bovines were PCR negative. Negative samples were re-analyzed, first by RCA and subsequently by PCR, resulting in 6 additional samples obtained from 4 animals while 9 papillomas from 3 animals were persistently negative.

Nucleotide sequencing allowed to identify 7 BPV genotypes (BPV1, BPV2, BPV4, BPV6, BPV7, BPV10, and BPV11) showing nucleotide identities between 99–100% with reference genotypes deposited in GenBank. Interestingly 2 samples (BPV-CR1 and BPV-CR2) showed levels of nucleotide identity respectively differing by more than 2% and 10% from the closest known types suggesting their designation as novel BPV type (BPV-CR2) and variant (BPV-CR1).

Access numbers for Costa Rican and reference genotypes sequences are shown in Table 1. Phylogenetic analysis matched the results obtained by BLASTN (Fig. 2).

The most commonly genotype found in lesions was BPV6 (31.2%), which was found in 2 provinces (Alajuela and Guanacaste), while BPV2 (25.0%) was found in 4 provinces (San José, Alajuela, Guanacaste, and Puntarenas) and BPV1 (25.0%) in all 5 provinces. The genotypes BPV4, BPV7, BPV10, and BPV11 were only found in 1 province each. Six different BPV genotypes were determined in cattle from Alajuela province, where most of the samples originated.

The distribution of BPV genotypes found in 32 bovine papillomas is shown in Fig. 3. The presence of a single genotype was determined in 88.5% (23/26) of farms, while in three farms two genotypes were detected. BPV6 was found in 34.6% (9/26), BPV2 in 23.1% (6/26), and BPV1 in 23.1% (6/26) of farms. These three genotypes were the most prevalent in the different provinces. Finally, two co-infections, BPV1/BPV2 (San José) and BPV4/BPV6 (Alajuela) were found, respectively, in two animals, while BPV1/BPV6 was found in the same farm, but on different animals, in Alajuela. BPV-CR1 was found in San José and BPV-CR2 in Alajuela.

The enzymatic digestion cut-off pattern of the seven genotypes identified is shown in Table 2. BPV1, BPV2, BPV4, and BPV7 cuts were recorded in areas of a high molecular weight (> 4 Kb). For BPV1, BPV4, and BPV7 a cut close to 7 Kb was established in the presence of EcoRI. For BPV1, BPV2, BPV4, and BPV7 the highest weight cut with BamHI was close to 6 Kb, and in the case of BPV1, BPV2, and BPV4 the SacI enzyme generated cuts in the region close to 7 kb. No cutting pattern was obtained for the BPV6, BPV10, and BPV11 genotypes.

Discussion

In this paper we report the identification of 9 BPV types in Costa Rica: BPV1 and BPV2 belonging to the genus *Deltapapillomavirus*, BPV4, BPV6, BPV10 and BPV11 belonging to the genus *Xipapillomavirus*, and BPV7 to *Dyoxipapillomavirus* (Lunardi et al. 2013; Figueirêdo et al 2020). This is the first report of BPV in Costa Rica and, in general, in

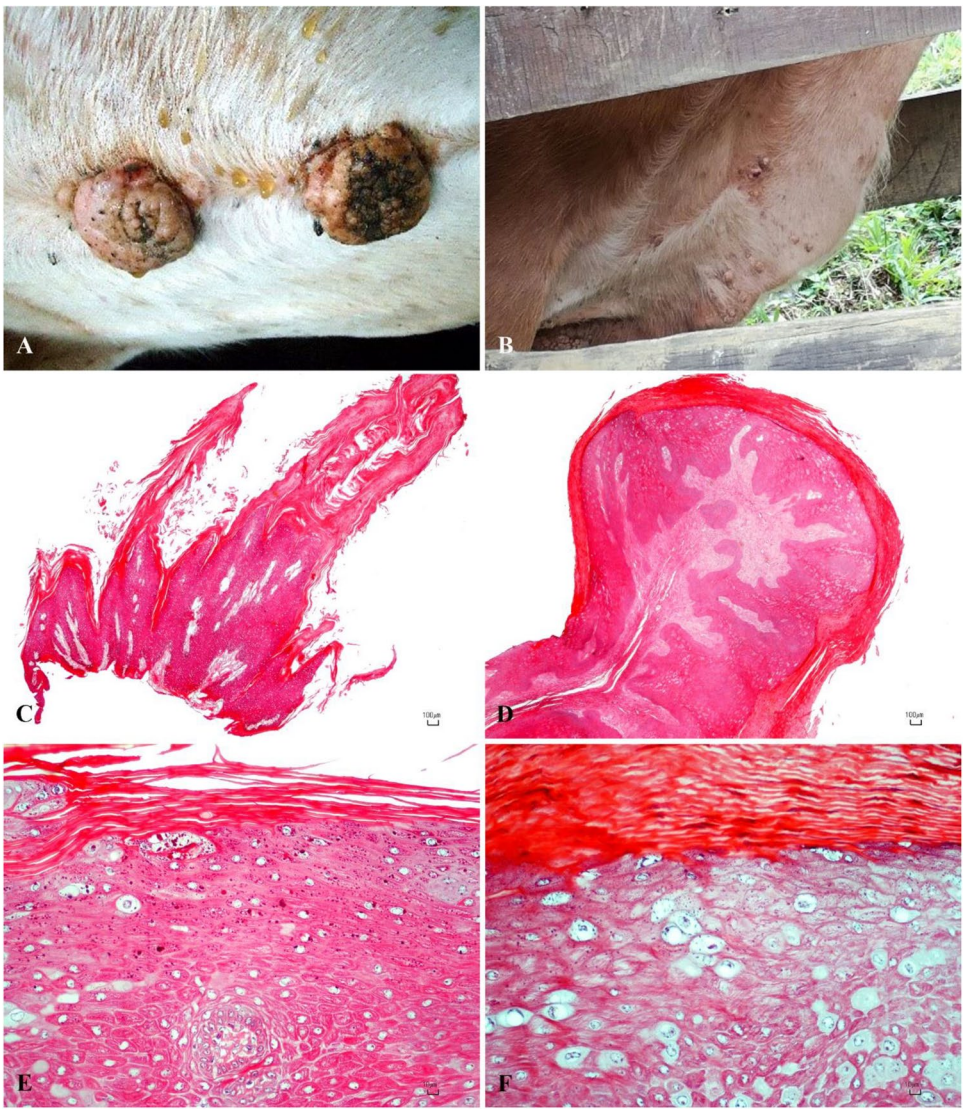

Fig. 1 Gross and microscopical features of viral papillomas in Costa Rica bovines. A-B: multifocal exophytic smooth (A) to crusty (B) cutaneous papillomas. C-D: Single (C) or multiple finger-like exophytic projections of hyperkeratotic squamous epithelium on delicate connective tissue cores. H.E. Bar 100 µm. E–F: giant keratohyalin granules in the stratum granulosum (E) and multiple koilocites in the upper stratum spinosum (F). H.E. Bar 10 µm

Table 1 BPV genotypes detected in a selected group of 32 bovine papillomas in Costa Rica

Genotype	n (%)	Homology (bp)	Reference (GenBank)	Accession Number
BPV1	8 (25.0)	100% (429/429)	KC595244.2	MT385853
BPV2	8 (25.0)	100% (431/431)	LC426022.1	MT385854
BPV4	1 (3.1)	99% (430/434)	X05817.1	TM385855
BPV6	10 (31.2)	100% (428/428)	AB845589.1	TM385856
BPV7	1 (3.1)	99% (439/440)	HM245431.1	TM385857
BPV10	1 (3.1)	100% (428/428)	MH729199.1	TM385858
BPV11	1 (3.1)	99% (430/431)	JQ897976.1	TM385859
BPV-CR1	1 (3.1)	92% (391/425)	MT674614.1	MZ292466
BPV-CR2	1 (3.1)	86% (368/426)	JF834524.1	MZ292467

Central America. Additionally, 2 potentially novel BPV types were identified.

Most papillomas (91%) were PCR positive, confirming the presence of the virus in the lesions. Negative results (9% of the cases) could be due to the sensitivity of the technique used, which is consistent with 54–100% sensitivity reports for FAP59/FAP64 PCR (Ogawa et al. 2004; Silva et al. 2013).

Alajuela province provided most of the animals for the study, showing the owners' concern about the problem in

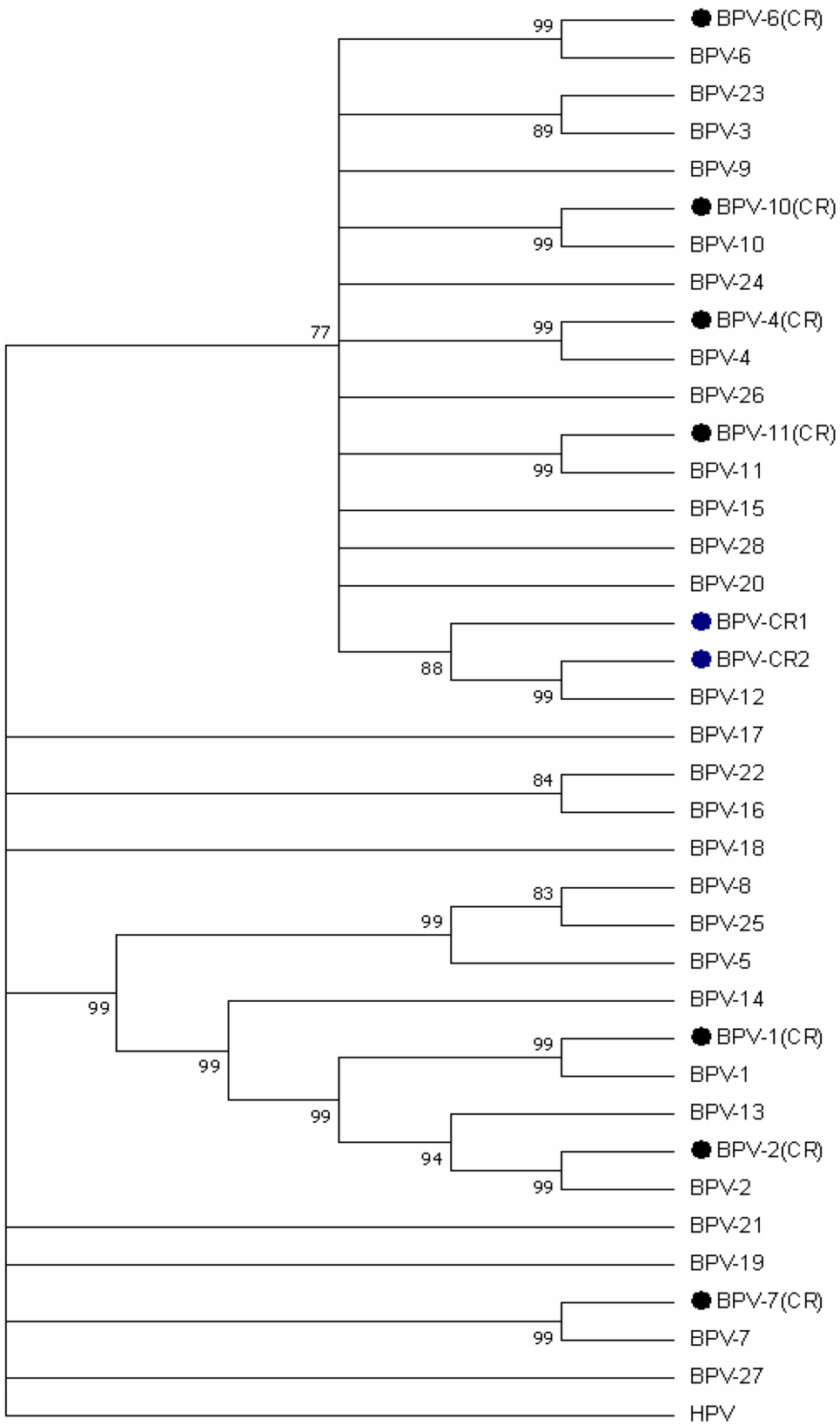

Fig. 2 Cladogram built by the Maximum Likelihood method, using the General Time Reversible method, with Bootstrap support obtained with 1000 replications from PCR products for the L1 BPV genes found in Costa Rica

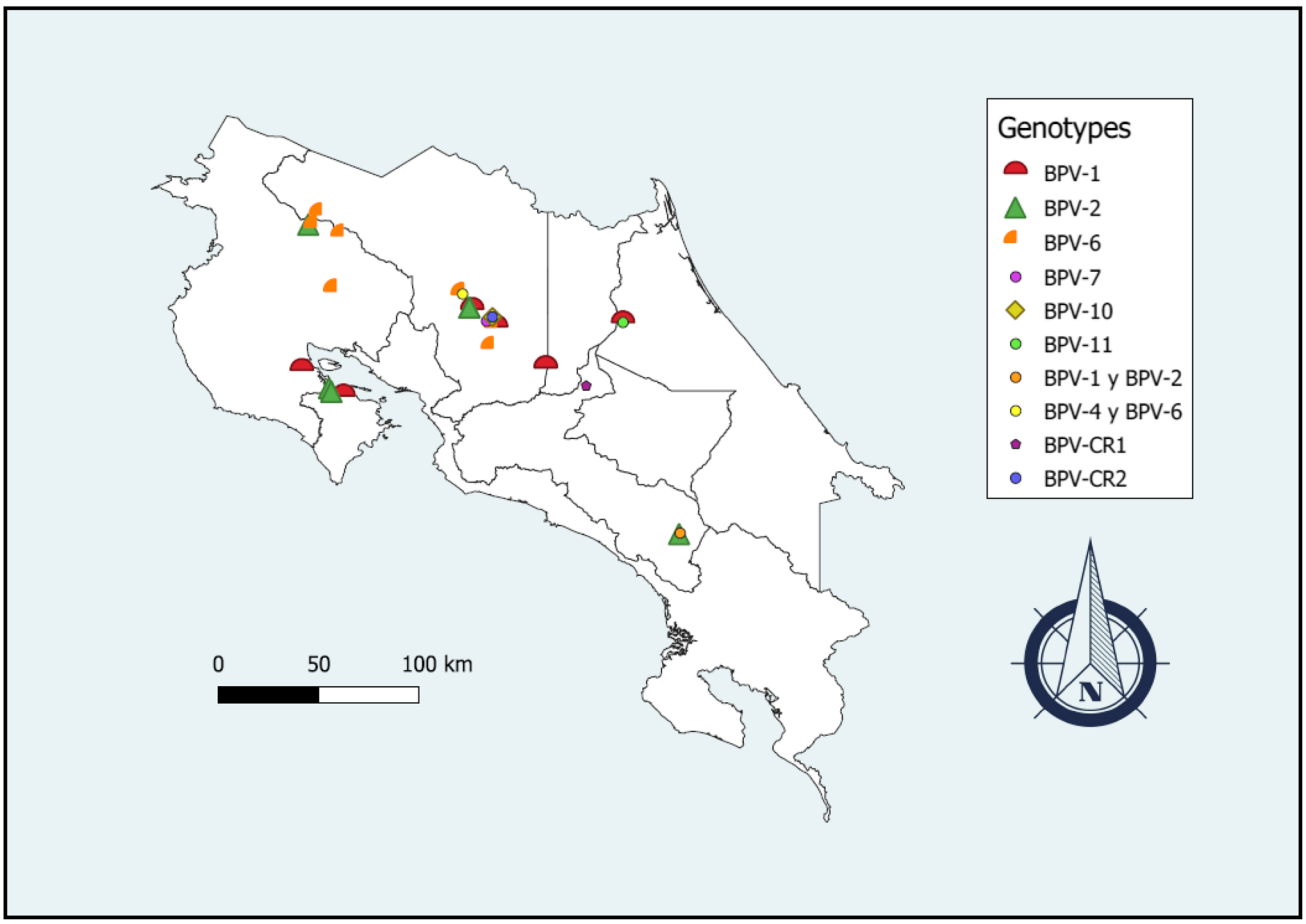

Fig. 3 Distribution of BPV genotypes detected in different regions of Costa Rica in 2018

Table 2 Enzymatic digestion cutting patterns of BPV genotypes detected and identified in Costa Rica

Genotypes	EcoRI	BamHI	SacI
BPV1	1	1	1
BPV2	0	2	1
BPV4	2	1	1
BPV6	0	0	0
BPV7	1	2	0
BPV10	0	0	0
BPV11	0	0	0

the area. In this province, 7 out of 9 genotypes were found. Besides the abundance of samples obtained from Alajuela, the high PV prevalence in this region can be explained by the high concentration of dairy cattle, mostly belonging to breeds in which udders papillomas are usually reported (Vasquez et al. 2012; Módolo et al. 2017; Violet et al. 2017).

BPV1 was found in five provinces, indicating a wide distribution in Costa Rica, followed by BPV2, which was found in four provinces. These two genotypes are also mentioned in the world literature as the most prevalent genotypes (Vasquez et al. 2012). Although BPV6 was the most frequently detected genotype in the samples (31.2%), it was only detected in samples from Alajuela and Guanacaste, which are areas with the greatest livestock activity in Costa Rica.

Coinfections were only detected in 2 farms, and this is consistent with reports from Pompeo et al. (2009) and Carvalho et al. (2012; 2013). However, it is the first time that BPV4 and BPV6 are reported as coinfecting viruses.

BPV-CR1 and BPV-CR2 were not identified and it is possible that we found in this investigation a new variant and a new type of BPV, according to their homology (92% for BPV-CR1 and 86% for BPV-CR2), using the GenBank reference MT674614.1 and JF834524.1, respectively (zur Hausen and De Villier 1994; Figueirêdo et al 2020). It should be noticed that at the moment this paper was being submitted PV sequence MT674603 was deposited in the genbank, related to a L1 ORF rescued in Brazil from a papillomatous lesion of a bovine (Figueirêdo et al. 2020), and this could

indicate a larger geographical distribution of this virus posing a potential threat to animal productions in South and Central America. However, since full genome sequencing is not available both in the case of BPV-CR2 and MT674603, it is not possible to establish whether the two sequences are indicative of the same viral type.

Sequencing of the full BPV-CR1 and BPV-CR2 genomes is required to elucidate the taxonomy and evolution of these novel Central America papillomaviruses. Establishing the genotypes present in a region is paramount to developing effective BPVs vaccines since vaccines against a single BPV type could not be effective against another, and that would lead to the high percentage of prophylactic and diagnostic failures (Vazquez et al. 2012).

Author contributions Conceptualization: Ramsés Alfaro Mora; Methodology: Ramsés Alfaro Mora, Gaby Dolz, Ruth Castro-Vásquez; Formal Analysis an investigation: Ramsés Alfaro Mora, Ruth Castro-Vásquez; Rosanna Zobba, Elisabetta Antuofermo, Alberto Alberti; Writing: Ramsés Alfaro Mora; Writing review and editing: Gaby Dolz, Giovanni Pietro, Alberto Alberti; Funding: Gaby Dolz, Resources: Gaby Dolz, Giovanni Pietro, Alberto Alberti; Supervision: Gaby Dolz, Alberto Alberti. All authors read and approved the final manuscript.

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Data availability All data generated or analyzed during this study are included in this article.

Declarations

Ethics approval and consent to participate This study was carried out in accordance with Law 7451 Animal Welfare, and was approved by the Bioethics and Animal Welfare Commission of the National University of Costa Rica (UNA-EMV-CBBA-ACUE-005–2018).

Consent to participate Not applicable

Consent for publication Not applicable

Conflict of interest The authors have no conflicts of intere to declare.

References

Araldi RP, Carvlh RF, Melo TC, Diniz NS, Sant´Ana TA, Mazzuchelli-de-Souza J, Spadacci-Morena DD, Beçak W, Stocco RC (2014) Bovine papillomavirus in beef cattle: first description of BPV-12 and putative type BAPV8 in Brazil. Genet Mol Res 13:5644–5653. https://doi.org/10.4238/2014.July.25.20

Araldi R, Reis S, Carvalho R, Caldas M, Mazzuchelli J, Fiusa R, Grando D, Peppino F, de Cassia R, Beçak W (2017) Papillomaviruses: a systematic review. Genet Mol Biol 40:1–21. https://doi.org/10.1590/1678-4685-GMB-2016-0128

Batista M, Silva M, Pontes N, Reis M, Corteggio A, Castro R, Borzacchiello G, Balbino V, Freitas A (2013) Molecular epidemiology of bovine papillomatosis and the identification of a putative new virus type in Brazilian cattle. Vet J 197:368–373. https://doi.org/10.1016/j.tvjl.2013.01.019

Borzacchiello G, Roperto F (2008) Bovine papillomaviruses, papillomas and cancer in cattle. Vet Res 39:1–10. https://doi.org/10.1051/vetres:2008022

Cardona-Álvarez J, Montes-Vergara D, Álvarez-Peñate J (2018) Caracterizaciónclínica, histopatológica e histoquímica del papiloma cutáneo en bovinos (Bos Taurus) del departamento de Córdoba, Colombia. Revista U.D.C.A. Actualidad y Divulgación Científica. 21: 137-146. https://doi.org/10.31910/rudca.v21.n1.2018.672

Carvalho C, Batista M, Silva M, Balbino V, Freitas A (2012) Detection of bovine papillomavirus types, co-infection and a putative new BPV11 subtype in cattle. Transbound Emerg Dis 59:441–447. https://doi.org/10.1111/j.1865-1682.2011.01296.x

Carvalho R, Sakata S, Giovanni D, Brandão P, Richtzenhain L, Pozzi C, Arcaro J, Miranda M, Mazzuchelli-de-Souza J, Melo T, Comecale G, Assaf S, Beçak W, Stocco R (2013) Bovine papillomavirus in Brazil: detection of coinfection of unusual types by a PCR-RFLP method. Biomed Res Int 2013:270898. https://doi.org/10.1155/2013/270898

Corteggio A, Altamura G, Roperto F, Borzacchiello G (2013) Bovine papillomavirus E5 and E7 oncoproteins in naturally occurring tumors: are two better than one? Infect Agent Cancer 8:1. https://doi.org/10.1186/1750-9378-8-1

Davis L, Dibner M, Battey J (1986) Section 5–4-restriction endonucleases (Res) and their use. Basic methods in molecular biology (pp 51–57). New York: Elsevier

Dolz G, Lecis R, Solórzano-Morales A, Aguilar-Vargas F, Solórzano-Scott T, Peña R, Zobba R, Tore G, Pittau M, Alberti A (2020) Leopardus wiedii Papillomavirus type 1, a novel papilomavirus species in the tree ocelot, suggests Felidae Lambdapapollomavirus polyphyletic origin and host-independent evolution. Infect Genet Evol 81:104239. https://doi.org/10.1016/j.meegid.2020.104239

Figueirêdo R, Santos G, Oliveira L, Santos L, Barreto D, Cândido A, Campos A, Azevedo E, Batista M (2020) High genotypic diversity, putative new type and intra-genotype variants of bovine papillomavirus in Northeast Brazil. Pathogens 9:748. https://doi.org/10.3390/pathogens9090748

Lunardi M, Alfieri AA, Otonel RA, de Alcântara BK, Rodrigues WB, de Miranda AB, Alfieri AF (2013) Genetic characterization of novel bovine papillomavirus member of the Deltapapillomavirus genus. Vet Microbiol 162:207–2013. https://doi.org/10.1016/j.vetmic.2012.08.030

Módolo D, Pinheiro R, Mazzuchelli-de-Souza J, Pereira A, Carvalho D, Zanphorlin L, Beçak W, Menossi M, Stocco R, Carvalho R (2017) Integrated analysis of recombinant BPV-1 L1 protein for the production of a bovine paillomavirus VLP vaccine. Vaccine 35:1590–1593. https://doi.org/10.1016/j.vaccine.2017.02.007

Munday JS, Thomson N, Dunowska M, Knight CG, Laurie RE, Hills S (2015) Genomic characterisation of the feline sarcoide-associated papillomavirus and proposed classification as Bos Taurus papillomavirus type 14. Vet Microbiol 177:289–295. https://doi.org/10.1016/j.vetmic.2015.03.019

Nair L, Campo MS (2008) Bovine papillomaviruses: their role in the aetiology of cutaneous tumours of bovids and equids. Vet Dermatol 19:243–254. https://doi.org/10.1111/j.1365-3164.2008.00683.x

Ogawa T, Tomita Y, Okada M, Shinozaki K, Kubonoya H, Kaiho I, Shirasawa H (2004) Broad-spectrum detertion of papillomaviruses in bovine teat papilomas and healthy teat skin. J Gen Virol 85:2191–2197. https://doi.org/10.1099/vir.0.80086-0

PaVE Papillomavirus Episteme (2021) Available online: https://pave.niaid.nih.gov/ (accessed on 25 may 2021)

Pompeo M, Lunardi C, Alfieri A, Arellano R, Sartori O, Pelegrinelli M, Fernandes A (2009) Multiple bovine papillomavirus infection

associated with cutaneous papillomatosis in brazilian cattle herds. Braz Arch Biol Technol 52:93–98. https://doi.org/10.1590/S1516-89132009000700013

Rector A, Tachezy R, Van Ranst M (2004) A sequence-independent strategy for detection and cloning of circular DNA virus genomes by using multiply primed rolling-circle amplification. J Virol 78:4993–4998. https://doi.org/10.1128/JVI.78.10.4993-4998.2004

Roperto S, Brun R, Paolini F, Urraro C, Russo V, Borzacchiello G, Pagnini U, Raso C, Rizzo C, Roperto F, Venuti A (2008) Detection of bovine papillomavirus type 2 in the peripheral blood of cattle with urinary bladder tumours: possible biological role. J Gen Virol 89:3027–3033. https://doi.org/10.1099/vir.0.2008/004457-0

Roperto S, Munday JS, Corrado F, Goria M, Roperto F (2016) Detection of bovine papillomavirus type 14 DNA sequences in urinary bladder tumors in cattle. Vet Microbiol 190:1–4. https://doi.org/10.1016/j.vetmic.2016.04.007

Silva M, Batista M, Pontes N, Santos E, Coutinho L, Castro R, Balbino V, Freitas A (2013) Comparison of two PCR strategies for the detection of bovine papillomavirus. J Virol Methods 192:55–58. https://doi.org/10.1016/j.jviromet.2013.04.017

Tore G, Cacciotto C, Anfossi AG, Dore GM, Antuofermo E, Scagliarini A, Burrai GP, Pau S, Zedda MT, Masala G et al (2017) Host cell tropism, genome characterization, and evolutionary features of OaPV4, a novel Deltapapillomavirus identified in sheep fibropapilloma. Vet Microbiol 204:151–158. https://doi.org/10.1016/j.vetmic.2017.04.024

Vázquez R, Duch E, Gómez D, Duato G, Benítez R (2012) Papilomatosis Bovina: Epidemiología y diversidad de papilomavirus bovinos (BPV). Rev Complut Cienc Vet 6:19–57

Violet L, Montes D, Cardona J (2017) Frecuencia de papilomatosis en bovinos (Bos Taurus) del departamento de Córdoba, Colombina. Rev Colomb Cienc Anim 9:294–300. https://doi.org/10.24188/recia.v9.n2.2017.611

Wellenberg G, van der Poel W, Van Oirschot J (2002) Viral infection and bovine mastitis: a review. Vet Microbiol 88:27–45. https://doi.org/10.1016/S0378-1135(02)00098-6

Yamashita-Kawanishi N, Tsuzuki M, Kasuya F, Chang HW, Haga T (2020) Genomic characterization of a novel bovine papillomavirus type 28. Virus Genes: 1–6. https://doi.org/10.1007/s11262-020-01779-9

Zur Hausen H, De Villier EM (1994) Human Papilloma Viruses. Annu Rev Microbiol 48:427–447. https://doi.org/10.1146/annurev.mi.48.100194.002235