Eukaryotic Circular Rep-Encoding Single-Stranded DNA (CRESS DNA) viruses: ubiquitous viruses with small genomes and a diverse host range

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Abstract

While single-stranded DNA (ssDNA) was once thought to be a relatively rare genomic architecture for viruses, modern metagenomics sequencing has revealed circular ssDNA viruses in most environments and in association with diverse hosts. In particular, circular ssDNA viruses encoding a homologous replication-associated protein (Rep) have been identified in the majority of eukaryotic supergroups, generating interest in the ecological effects and evolutionary history of circular Rep-encoding ssDNA viruses (CRESS DNA) viruses. This review surveys the explosion of sequence diversity and expansion of eukaryotic CRESS DNA taxonomic groups over the last decade, highlights similarities between the well-studied geminiviruses and circoviruses with newly identified groups known only through their genome sequences, discusses the ecology and evolution of eukaryotic CRESS DNA viruses, and speculates on future research horizons.

Keywords: CRESS DNA virus, single-stranded DNA, geminivirus, circovirus, nanovirus, genomovirus, smacovirus, bacilladnavirus

Defining CRESS DNA viruses

The term CRESS DNA viruses was coined in 2012 to refer to a group of single-stranded DNA (ssDNA) viruses encoding a replication-associated protein (Rep) that appears to be descended from a common ancestor. CRESS DNA stands for circular, Rep-encoding ssDNA and encompasses both prokaryotic and eukaryotic viruses, although the Reps of each of these groups have distinct characteristics (Koonin and Ilyina, 1993). Most ssDNA viruses are CRESS DNA viruses. Eleven out of thirteen ssDNA virus families established by the International Committee on the Taxonomy of Viruses (ICTV, http://ictv.global/report) contain circular genomes, with *Parvoviridae* and *Bidnaviridae* being the only exceptions. Seven of these eleven circular ssDNA virus families infect eukaryotic organisms (see Confirmed and potential host range and pathogenesis of eukaryotic CRESS DNA viruses, below), and among these only members of the *Anelloviridae* family do not encode a homologous Rep. The Rep of the six families of eukaryotic CRESS DNA viruses (Table 1; *Bacilladnaviridae*, *Circoviridae*, *Geminiviridae*, *Genomoviridae*, *Nanoviridae*, *Smacoviridae*) is distantly related to the Rep of bacterial (*Microviridae* and *Inoviridae*) and archaeal (*Pleolipoviridae*) CRESS DNA viruses; however, the Reps of these groups have distinct evolutionary histories (Koonin and Ilyina, 1993, Krupovic, 2013, Koonin et al., 2015, Rosario et al., 2012b). This review focuses on eukaryotic CRESS DNA viruses, for which an unforeseen diversity and distribution has been recognized and continues to expand.

Discovery of eukaryotic CRESS DNA viruses

Although the first eukaryotic CRESS DNA viruses were only identified as such in the 1970's, symptoms consistent with CRESS DNA viral infection were described over a millennium ago. The common yellowing symptom of CRESS DNA viral infection of euphorbia leaves was the inspiration for a Japanese poet in 752AD (Saunders et al., 2003), though the symptoms are not distinct enough for a definitive retrospective diagnosis. More definitively, plants with symptoms caused by geminiviruses were first observed more than 100 years ago. Abutilon mosaic virus is now known to be the cause of a pleasing mosaic pattern on the ornamental abutilon plant (Figure 1), which was highly coveted in Europe in the mid-1800s (reviewed in Wege et al., 2000). In animal hosts, the symptoms of psittacine beak and feather disease (now known to be caused by a circovirus) may have first been observed in Australia in 1888. An avid birder described parakeets which failed to grow back their feathers after their molt, leading to bizarre-looking, bald birds (Ashby, 1921). Eukaryotic CRESS DNA viruses very likely originated much longer ago than these human recordings imply, as several CRESS DNA viral genes have been found in the germ line of eukaryotic lineages that diverged at least a million years ago (see endogenized CRESS DNA viruses, below). Therefore, both historical records and modern molecular analyses support the ancient origin of eukaryotic CRESS DNA viruses.

Throughout history, the effects of viral infection were observed long before humans could isolate and identify the etiological agent, and CRESS DNA viruses were no exception. It wasn't until 1977 that scientists identified the first eukaryotic virus containing a circular ssDNA

genome, bean golden mosaic virus (*Geminiviridae*, Goodman, 1977a). Despite the earlier discovery of ssDNA viruses infecting bacteria (Sertic and Bulgakov, 1935) and mammals (Crawford, 1966), the overwhelming majority of DNA viruses were considered to be double-stranded at the time. Five years after the description of geminiviruses, porcine circovirus was the first animal-infecting circular ssDNA virus described (Tischer et al., 1982). Following these findings, the known diversity of geminiviruses rapidly increased, with 63 species identified by 1995 (Murphy et al., 1995). Largely these efforts were the result of pathologists determining the causative agent of economically important crop diseases. In contrast to the geminiviruses, awareness of other groups of eukaryotic CRESS DNA viruses did not expand significantly in terms of either diversity or detection until the 2000s -- only 3 circovirus species and 4 nanovirus species were recognized by 1999 (Regenmortel et al., 2000). Due to their lack of affiliation with human disease, CRESS DNA viruses were largely ignored by biomedical funding agencies, which instead directed efforts towards known pathogenic dsDNA, RNA, and retro-transcribing viruses. As a result, eukaryotic CRESS DNA viruses only recently gained recognition commensurate with their ubiquity, diversity, and impact.

The application of phi29 DNA polymerase and random hexamers (rolling circle amplification; RCA) for whole genome amplification of circular DNA templates (Dean et al., 2001) represented a turning point in the study of CRESS DNA viruses (reviewed in Rosario et al., 2012b). This method was so efficient that it was quickly adapted to clone and sequence complete geminivirus genomes, revolutionizing methodological approaches for detection of plant pathogens (Haible et al., 2006, Inoue-Nagata et al., 2004, Wyant et al., 2012). During this same time period, RCA was also being utilized in both clinical and environmental settings to obtain sufficient DNA concentrations for next-generation sequencing (Angly et al., 2006, Breitbart and Rohwer, 2005, Lasken and Egholm, 2003). Although the discovery of circular ssDNA viruses was not the intention of these endeavors, application of this method serendipitously resulted in the detection of a diversity of CRESS DNA viruses in unsuspected organisms and disparate environments (reviewed in Rosario et al., 2012b). Since RCA leads to a gross overrepresentation of viruses with circular genomes, this method cannot be used for quantitative analyses of viral communities (Kim and Bae, 2011, Roux et al., 2016). RCA is currently used in two distinct ways for discovering viruses with small circular genomes. The incorporation of RCA into standard metagenomics pipelines enables assembly of complete CRESS DNA genomes from both individual organisms and complex environmental communities (Li et al., 2010a, Rosario et al., 2009). However, caution must be used with assembly-based methods since RCA may lead to chimeric sequences (Tu et al., 2015). To verify assembled genomes, inverse PCR with abutting primers is recommended (Rosario et al., 2009). Alternatively, numerous studies have directly recovered unit length CRESS DNA viral genomes by applying RCA followed by restriction enzyme digestion, circumventing potential assembly errors (Inoue-Nagata et al., 2004, Rosario et al., 2012).

RCA has been instrumental in the recognition of the ubiquity and diversity of CRESS DNA viruses. The number of CRESS DNA viruses identified using this technique now far exceeds the number of well-characterized viral isolates obtained using classical methods. This is in stark contrast to historical situations where symptoms of viral infection were recognized long before

the etiological agent was identified. The explosion of CRESS DNA viral discovery through sequence-based methods has divorced viral sequences from much of their ecological context, including fundamental aspects such as host range.

We have now passed through the looking glass, where we are increasingly aware of the existence of incredible numbers of distinct viral species, without having any sense of the impact of these viruses.

Unity and diversity

While some eukaryotic CRESS DNA viruses have up to 10 open reading frames (ORFs), even the most compact genomes have two ORFs: one encoding the Rep and one encoding a capsid protein (CP). The conserved Rep serves as the anchor for this group of viruses, but the CP is highly divergent. Beyond the Rep and CP, protein content differs dramatically among CRESS DNA viruses.

Molecular biology of Rep

All eukaryotic CRESS DNA viruses encode a distinctive homologous Rep that is presumably conserved due to its essential function in viral genome replication through rolling circle replication (RCR). In fact, the Rep is often the only gene with homology among the divergent eukaryotic CRESS DNA viruses, and thus has been used extensively for phylogenetic analyses and higher-level taxonomic classification (Simmonds et al., 2017). The RCR mechanism (Figure 2) employed by eukaryotic CRESS DNA viruses (reviewed in Rosario et al., 2012b) has been elucidated based on *in vitro* studies performed with members representing only three of the eukaryotic CRESS DNA viral families, including the *Geminiviridae* (Hanley-Bowdoin et al., 2013, Jeske et al., 2001, Laufs et al., 1995), *Circoviridae* (Faurez et al., 2009, Steinfeldt et al., 2006), and *Nanoviridae* (Timchenko et al., 2000, Timchenko et al., 1999). In addition, the structure of several representative Reps from these three families has also been solved (Campos-Olivas et al., 2002, Vega-Rocha et al., 2007a, Vega-Rocha et al., 2007b). Briefly, the Rep binds to iterative sequences near an origin of replication (*ori*) distinguished by a conserved nonanucleotide motif at the apex of a hairpin structure. The Rep then nicks the covalently closed virion strand of the double-stranded replicative form of the viral genome within the nonanucleotide motif. After the exposed 3'-OH end is primed by a host polymerase, leading-strand synthesis proceeds until the Rep rejoins the virion strand at the initial nicking site.

The Reps of established and metagenomically identified eukaryotic CRESS DNA viruses stably contain a distinctive two functional domain organization, containing a HUH endonuclease domain towards the N-terminus and superfamily 3 (SF3) helicase domain at the C-terminus (Ilyina and Koonin, 1992, Koonin, 1993). Each of the eukaryotic CRESS DNA viral Rep domains is characterized by conserved motifs important for RCR (reviewed by (Rosario et al., 2017). The HUH endonuclease domain is characterized by RCR motifs I through III, which are important for RCR initiation and termination. The SF3 helicase domain contains Walker A, Walker B and motif C motifs that presumably allow the Rep to act as replicative helicase during RCR elongation (Gorbalenya et al., 1990, Gorbalenya and Koonin, 1993). A fourth motif corresponding to a

catalytic arginine finger conserved in various AAA+ family ATPases that may fuel helicase activity (Nagy et al., 2016) is also commonly found in the Rep SF3 helicase domain (Kazlauskas et al., 2017). This arginine finger has been identified in Reps encoded by members of *Bacilladnaviridae*, *Circoviridae*, *Nanoviridae*, and *Smacoviridae*, but not in *Geminiviridae* and *Genomoviridae* (Kazlauskas et al., 2017).

Intron-containing Reps

Many eukaryotic CRESS DNA viruses are known or predicted to express both spliced and non-spliced forms of the Rep. In mastreviruses (*Geminiviridae*), RepA (non-spliced form) and Rep (spliced form) are identical for the first ~200 N-terminal residues and are multifunctional proteins involved in virus genome replication, transcription, and gene regulation (Hefferon et al., 2006, Muñoz-Martín et al., 2003, Fondong, 2013). RepA has also been identified in other geminivirus genera including, *Becurtovirus*, *Capulavirus* and *Grablovirus* (Varsani et al., 2014, Varsani et al., 2017). The majority of the genomes representing the newly denoted family *Genomoviridae* also contain both RepA and the spliced Rep (Conceicao-Neto et al., 2015, Steel et al., 2016). Some members of the family *Circoviridae*, specifically porcine circoviruses (PCV), contain Rep and Rep', which is a spliced isoform of Rep with the C-terminus truncated and expressed in a different frame (Steinfeldt et al., 2006). Both proteins perform the nicking and joining activities during RCR and have sequence similarity to geminivirus and nanovirus Reps. One proposed mechanism for first appearance of spliced Reps in eukaryotic CRESS DNA viruses involves the endonuclease function of the Rep itself: site-specific endonucleases have been found in intron homing processes (Belfort and Perlman, 1995), implying that the Rep protein may have been involved in the acquisition of an intron (Gibbs et al., 2006).

Capsid proteins

All CRESS DNA virus groups that have been visualized by electron microscopy have icosahedral capsids, which are encoded by a capsid protein (CP). The CP protects the genome and is needed for the virus to move between individual hosts. The known capsids of CRESS DNA viruses vary in size (Table 1), and in the case of *Geminiviridae* in shape: the geminiviruses derive their name from their twinned icosahedral capsid (Figure 3), which packages a single genomic segment (Goodman, 1977b, Harrison et al., 1977).

There is evidence for recombination among CRESS DNA viral CPs (e.g., the genus *Curtovirus* contains viruses descended from a recombinant begomovirus with a CP from a mastrevirus, which changed the vector specificity, Rybicki, 1994); however, some CP genes appear to have evolutionary linkages to those of RNA viruses (Kazlauskas et al., 2017, Krupovic et al., 2009, Lefeuvre et al., 2009, Roux et al., 2013). The capsid proteins of geminiviruses are structurally similar to that of a ssRNA plant virus, satellite tobacco necrosis virus, which is suggestive of a shared evolutionary history (Krupovic et al., 2009). The *Bacilladnaviridae* capsids are also suggested to be structurally similar to another group of ssRNA viruses, the nodaviruses (Kazlauskas et al., 2017) and the *Circoviridae* capsid proteins may have yet another common ancestor with capsids of RNA viruses (Gibbs and Weiller, 1999). In 2012, a RNA-DNA hybrid virus (RDHV) encoding a eukaryotic CRESS DNA viral Rep and a CP from unclassified ssRNA viruses similar to *Tombusviridae* was discovered from Boiling Spring Lake (Diemer and Stedman,

2012). This unique CRESS DNA virus group, named the cruciviruses (Quaiser et al., 2016), has been growing steadily since its initial discovery (Bistolas et al., 2017a, Dayaram et al., 2016, Hewson et al., 2013, Krupovic et al., 2015, Steel et al., 2016). The frequency of discovery of these viruses with a seeming RNA-DNA hybrid evolutionary history suggests that these recombination events are not vanishingly rare, and the mechanisms that could create these hybrids will continue to be explored in the coming years (Stedman, 2015). Capsid protein sequence diversity has not only come from RNA viruses, newly sequenced eukaryotic CRESS DNA viral genomes have shown to carry capsid protein sequences similar to ORF1, the putative capsid protein coding gene) of the ssDNA *Anelloviridae* (Lamberto et al., 2014).

In contrast to the homologous Rep protein shared among the eukaryotic CRESS DNA viruses, the CP can be highly divergent and is sometimes even unrecognizable by sequence similarity (e.g., Yoon et al., 2011). In public databases, some researchers have annotated the non-Rep-encoding ORF of CRESS DNA viruses as a CP by default; however, caution should be applied in interpreting and propagating these annotations without independent evidence that the ORF actually represents a capsid. One useful tool for identifying structural proteins within novel CRESS DNA viral genomes is the prediction of disorder patterns, which are conserved among CRESS DNA viral capsid proteins and can be used to complement similarity-based searches (Rosario et al., 2015a). While great strides have been made in understanding the evolution of eukaryotic CRESS DNA viruses based on the unifying Rep, deciphering the evolutionary histories of the CPs is clearly a more complex task that needs to be the subject of future studies.

Current taxonomy

Prior to 2015, the ICTV recognized three families of CRESS DNA viruses, namely *Geminiviridae* (approved in 1993), *Circoviridae* (approved in 1993), and *Nanoviridae* (approved in 2002). The number of CRESS DNA viral families has recently doubled with the addition of *Genomoviridae* (approved in 2015), *Bacilladnaviridae* (approved in 2017), and *Smacoviridae* (approved in 2017). The number of CRESS DNA viral genera increased more than five-fold (from 6 to 31) during the past five years and is currently distributed as follows (Table 2): *Geminiviridae* (9 genera), *Circoviridae* (2 genera), *Nanoviridae* (2 genera), *Genomoviridae* (9 genera), *Smacoviridae* (6 genera), and *Bacilladnaviridae* (3 genera). The majority of this increase is due to the advances in viral metagenomics (Simmonds et al., 2017), and one of the six families (*Smacoviridae*) has no cultured representatives. An exemplary geminivirus case study in this volume highlights the revolutionary changes metagenomics research has had on CRESS DNA virology (Claverie et al., 2018).

Geminiviridae

Geminiviruses are a group of plant-infecting viruses, encapsidated in twinned icosahedral capsids -- the structural feature that gave them the name gemini (Hanley-Bowdoin et al., 2013). *Geminiviridae* is currently the most speciose family of all viruses. Members of this viral family infect monocotyledons (monocots) and dicotyledons (dicots). Geminiviruses encompass both monopartite (six ORFs) and bipartite genomes (one segment, DNA-A, with five ORFs which is homologous to the monopartite genome, the other, DNA-B, with 2 ORFs, Rey et al., 2012). The monopartite genomes and DNA-As both encode a coat protein (CP) in the sense orientation and

four ORFs in anti-sense: the replication-associated protein (Rep), the replication-enhancer protein (REN) and transactivating protein (TraP) and an overlapping C4 protein which affects virulence (Hanley-Bowdoin et al., 2013). Monopartite genomes also encode a partially overlapping pre-coat protein which functions as a movement protein within the plant; bipartite geminiviruses have a DNA-B encoding a movement protein and a nuclear shuttle protein (Ho et al., 2014). Bipartite begomoviruses typically dominate in the New World (the Americas), while monopartite begomoviruses are the vast majority in the Old World (Ho et al., 2014); however, there are an increasing number of exceptions to this trend (e.g., Inoue-Nagata et al., 2016, Rosario et al., 2015b).

The largest genus within *Geminiviridae* is *Begomovirus*, which contains over three quarters of the current classified geminivirus species. Begomoviruses infect dicots and are transmitted by the whitefly *Bemisia tabaci*. *B. tabaci* is phloem-feeding and some biotypes have a very broad plant host range, including ornamental, vegetable, grain, legume, and cotton plants (De Barro et al., 2011). Possibly due to the very large number of identified species of begomoviruses, they comprise 90% of the viruses known to be transmitted by whiteflies (Jones, 2003). Species belonging to the second largest genus, *Mastrevirus*, are transmitted by leafhoppers (order Hemiptera, family Cicadellidae) and infect both monocot and dicot plants. The geminiviruses are usually transmitted by the vectors in a circulative, persistent and non-propagative manner (Blanc et al., 2014) – there is very little evidence that they replicate in their vectors despite being capable of transmission long after their initial acquisition (Czosnek et al., 2017). The long residence time of geminiviruses in their vectors has facilitated discovery efforts, as researchers have targeted insect vectors and their predators as a method for surveying viral diversity circulating among plants in a given region (vector-enabled metagenomics, (Dayaram et al., 2013b, Ng et al., 2011a, Rosario et al., 2012a).

Recent revisions to *Geminiviridae* family established the new genera *Becurtovirus*, *Eragrovirus*, *Turncurtovirus* (Varsani et al., 2014), *Capulavirus* and *Grablovirus* (Varsani et al., 2017). Geminiviruses are well studied in molecular virology because of the devastating effects of the well-characterized genera in important crops across temperate and tropic regions (Seal et al., 2006b). Frequent emergence and re-emergence of this geminiviruses in crops have attracted much research focus (Anderson et al., 2004), and the threat of unidentified geminiviruses emerging in crops is ever imminent (Claverie et al., 2018). Geminiviruses, as eukaryotic CRESS DNA viruses, have several evolutionary advantages that favor emergence (see Evolution, below), but a key ecological factor in the spread of begomoviruses specifically is the spread and abundance of their vectors (Seal et al., 2006a). Climate change and the increase of international trade have given rise to the expansion and invasion of vector populations to previously naïve parts of the world (for begomoviruses, the polyphagous *B. tabaci* Middle East-Asia minor 1), which both transport viruses to new areas and promote virus transmission in their invaded range (Varma et al., 2011).

Circoviridae

The family *Circoviridae* is notable because it contains the smallest known animal viruses, with nearly all members having genome sizes under 2kb. Prior to the recent taxonomic revisions of

the eukaryotic CRESS DNA viruses, *Circoviridae* was the catch-all for the animal infecting circular ssDNA viruses – including viruses affecting birds and mammals. As more and more diverse CRESS DNA sequences were identified, some of the sequences initially thought to represent circoviruses or 'circo-like' viruses based on low amino acid level similarities to the Rep of members of the *Circoviridae*, were assigned to other new CRESS DNA viral families. Notably, taxa without a Rep ORF were reassigned *Anelloviridae* (Rosario et al., 2017). Despite this culling, there is still tremendous diversity associated with *Circoviridae*, which is now composed of the genera *Circovirus* (established 1993) and *Cyclovirus* (established 2015). Members of the *Circoviridae* have been found in numerous vertebrate and invertebrate organisms (e.g., birds, fish, mammal, insects). Interestingly, members from the genus *Circovirus* seem to be mainly restricted to vertebrate hosts, whereas cycloviruses have been identified in both vertebrates and invertebrates (Rosario et al., 2017).

Although cycloviruses have been only identified through molecular analysis and no definitive host has not been identified for this genus, some members of *Circovirus* are well-recognized pathogens in animals. Porcine circovirus 2 causes porcine circovirus-associated disease (PCAD). This PCAD includes post-weaning multisystemic wasting syndrome, which causes devastating economical losses in the commercial hog industry, prompting widespread vaccination against a dominant strain of porcine circovirus 2 (Alarcon et al., 2013, Allan et al., 2012, Meng, 2013). Other circoviruses are known to infect livestock or human companion animals, for example, beak and feather disease virus (Harkins et al., 2014), and canine circovirus (Kapoor et al., 2012) .

Each genus in the family *Circoviridae* is distinguished by the genome organization. All genomes in the genus *Circovirus* encode the Rep protein in virion sense (positive sense), and CP in anti-sense, while the genomes in *Cyclovirus* have the flipped orientation: encoding the Rep in anti-sense and the CP in the virion sense predicted strands. The replication and transcription processes are thought to differ between two genera of *Circoviridae* due their difference in genome organization (Rosario et al., 2017). While all genomes contain these two ORFs, a third, overlapping ORF has been experimentally verified in some species, and others have potential additional ORFs (Bassami et al., 1998, Hamel et al., 1998).

Cycloviruses are found in a diverse range of samples: squirrels (Sato et al., 2015), cats (Zhang et al., 2014), humans (Li et al., 2010a), goats (Li et al., 2011), horses (Li et al., 2015a), bats (Wu et al., 2016), cows (Li et al., 2011), sheep (Li et al., 2010a), chickens (Li et al., 2011), cockroaches (Padilla-Rodriguez et al., 2013) and dragonflies (Rosario et al., 2012a). However, these are the hosts found in association with these viral sequences, the host range of all members of the genus remains unresolved without definitive experiments. Even the Dragonfly cyclovirus, which researchers are nearly certain infects an insect, may not infect the dragonflies from which it was isolated – the virus was present in the dragonfly gut, and dragonflies eat a variety of insects and the virus could have been infecting an insect the dragonfly had eaten (Rosario et al., 2011). Among eukaryotic CRESS DNA viruses, cycloviruses had seemed uniquely associated with invertebrates (Tijssen et al., 2016), but more recent work has shown that Rep sequences similar to members of the *Smacoviridae* and *Genomoviridae* are also associated with invertebrates (Rosario et al., 2018). Further complicating establishing definitive host range, phylogenetic

analysis of cycloviruses do not show sequences clustering according to their host of isolation, making inferences about host use unproductive (Rosario et al., 2017).

Nanoviridae

Family *Nanoviridae* contains two genera: *Babuvirus* and *Nanovirus*. All viruses in this family are multipartite, meaning they maintain their genomes in multiple segments of circular positive sense ssDNA that independently package into multiple, separate capsids. Genus *Babuvirus* contain three species, with either six or nine segments to their genome, that are known to infect tropical crops including bananas, abaca, taro and cardamom (Stainton et al., 2015). Genus *Nanovirus* contains eight species, seven of which have eight segments in their genomes, except for Subterranean clover stunt virus, which has six segments. All species from genus *Nanovirus* naturally infect legumes. Individual genomic segments are around 1 kb in size, usually carrying one identifiable ORF per segment (Sharman et al., 2008, Sicard et al., 2013). Similar to ORFs maintained in begomoviruses, nanoviruses usually encode a replication-associated protein, a capsid protein, a movement protein, a replication enhancer protein, and a nuclear shuttle protein, as well as one or more proteins of unknown function (Sicard et al., 2013). Nanoviruses are transmitted by aphids, usually causing stunt symptoms in infected plants, leading to agricultural losses throughout the tropics. Like the other plant infecting eukaryotic CRESS DNA virus family, *Geminiviridae*, the nanoviruses are also transmitted in a persistent, circulative and non-propagative manner (Blanc et al., 2014).

The intriguing genomic compartmentalization of multipartite viruses has motivated scientists to study the cost of maintaining such a lifestyle. Due to their independent packaging, each segment must be independently transmitted to a new host for successful infection, and bottlenecks both in movement within plants and in aphid transmission pose obstacles to efficient infection of new hosts (Gallet et al., 2018). Further, instead of observing all segments at equal frequency, which is theoretically most efficient, researchers found that each virus maintains different segments at different frequencies, named the setpoint genome formula. Moreover, this setpoint genome formula varies with different hosts and has been proposed to be potentially beneficial for multipartite viruses (Sicard et al., 2013).

Genomoviridae

The first member of what would eventually be described as the family *Genomoviridae* is *Sclerotinia sclerotiorum* hypovirulence associated DNA virus 1 (SsHADV-1), isolated in 2010 (Yu et al., 2010). The genetic similarity between geminiviruses and SsHADV-1 was obvious from its isolation, and the family derives its name from 'geminivirus-like with no movement protein'. SsHADV-1 is the first and only known fungal infecting ssDNA virus (i.e., mycovirus), with all other identified mycoviruses containing double-stranded or single-stranded RNA genomes (Yu et al., 2010). In contrast to geminiviruses, SsHADV-1 purified virions and viral DNA, both dsDNA and ssDNA, are infectious to the fungal host (Yu et al., 2013). The virus-host pair SsHADV-1 and *S. sclerotiorum* have been proposed as a potential tool for genetic studies because of easy manipulation in PEG-mediated protoplast transfection assays (Yu et al., 2013). If its host range can be widened experimentally, SsHADV-1 may also be applicable as a biological control measure in inducing hypovirulence plant pathogenic fungi (Yu et al., 2010).

The classification of *Genomoviridae* viral genomes was done by maximum likelihood phylogenetic analysis on the Rep protein sequence alone. Five clades and 4 single branches were displayed in the phylogenetic tree – the group with SsDHAV-1 and eight other genera (Varsani and Krupovic, 2017). As SsHADV-1 has been characterized in the lab, it serves as the type species for genus *Gemycircularvirus*, which is named for Gemini-like myco-infecting circular virus (Rosario et al., 2012a). It currently contains 43 species, with other sequences assigned to *Gemycircularvirus* found associated with mammals, birds, insects, plants, fungus, sediments and sewage samples, but without definitive hosts (Steel et al., 2016, Sikorski et al., 2013c, Dayaram et al., 2012, Dayaram et al., 2015b, Male et al., 2015, Kraberger et al., 2013, Yu et al., 2010, Kraberger et al., 2015a). The established tradition for geminiviruses is to create genus names from abbreviations of the type species of each genus, and its host and symptoms – as in Bean golden mosaic virus - *Begomovirus*. Lacking this information, genomovirus genera all use the "gemy" prefix (Gemini-like, myco-infecting) with words from different languages to emphasize the circularity of the genomes (Table 2).

Smacoviridae

Another novel family discovered largely through metagenomics sequencing is *Smacoviridae* (smaco stands for small circular, Varsani and Krupovic, 2018). Although no member of this family has been cultured and smacoviruses have only been identified in fecal matter or dragonflies, the genomes of classified species have all been verified through PCR and Sanger sequencing. Smacovirus genera were established based on Rep phylogenetic analysis, with ≥40% Rep protein sequence identity required for members of the same genus. *Smacoviridae* is divided into six genera: *Bovismacovirus*, *Drosmacovirus*, *Huchismacovirus*, *Porprismacovirus*, *Cosmacovirus*, and *Dragsmacovirus*. The CPs of *Smacoviridae* are shared within the family, but not related to other CRESS DNA viruses (Varsani and Krupovic, 2018).

Bacilladnaviridae

Bacilladnaviridae contains 3 genera: *Protobacilladnavirus*, *Diatodnavirus*, and *Kieseladnavirus*. The first officially classified member of the *Bacilladnaviridae* family is the *Chaetoceros salsugineum* DNA virus 01 (CsalDNAV01), the first diatom-infecting DNA virus and only the second known diatom-infecting virus (the first was *Rhizosolenia setigera* RNA virus, Nagasaki et al., 2005). The sediment samples containing CsalDNAV01 were collected in 2003, but in the following years, another ten CRESS DNA viruses that infected other abundant *Chaetoceros* species and *Thalassionema* species were identified (Kimura and Tomaru, 2013, Kimura and Tomaru, 2015, Tomaru et al., 2008, Tomaru et al., 2011a, Tomaru et al., 2011b, Tomaru et al., 2012, Tomaru et al., 2013). Several characterized *Bacilladnaviridae* viruses have double-stranded DNA genomic segments of varying size and location, the properties of which are unknown (Kimura and Tomaru, 2015, Tomaru et al., 2013), which is unique thus far among eukaryotic CRESS DNA viruses.

The CPs of bacilladnaviruses show sequence and structure similarity to the CPs of nodaviruses, a group of ssRNA virus. Bacilladnaviruses have larger genomes sizes than other eukaryotic CRESS DNA viruses (~4.5-6kb, Kimura and Tomaru, 2015), but similar to the genome size of

nodaviruses. This larger genome size requires larger internal volume and the virion particle size (33-38 nm) of the nodavirus capsid structure accommodates the genome size (Kazlauskas et al., 2017).

As diatoms are an important player in marine and freshwater ecology, these host-virus systems are expected to provide insights into diatom-blooming dynamics, and should be more intensively researched in the coming years.

Evolutionary relationships among the eukaryotic CRESS DNA viral families

The homologous Rep protein of all eukaryotic CRESS DNA viruses allows for a straightforward analysis of the evolutionary history of this one ORF among all the diverse families mentioned above. However, ssDNA viruses frequently recombine, which interferes with accurate resolution of phylogenetic relationships (Martin et al., 2011). A recent publication accounted for the pervasive recombination in the Rep gene among unclassified eukaryotic CRESS DNA viruses, producing a dataset free of detectable recombination to build a robust Rep genealogy (Kazlauskas et al., 2018). Figure 4 shows our own analysis conducted with that recombinant-free dataset, which showed the same broad patterns as the publication. It reaffirms that the *Genomoviridae* Rep is closely related to that of *Geminiviridae*, and shows their reciprocal monophyly. *Nanoviridae* sequences form a clade with Reps from a group of satellites (discussed in Confirmed and potential pathogenesis of eukaryotic CRESS DNA viruses, below). This clade forms a larger monophyletic group with the *Smacoviridae* (and some unclassified Rep sequences), indicating that nanovirus Reps are the closest classified relatives to the smacoviruses. The recently established *Bacilladnaviridae* is roughly equally distant from all other named families of eukaryotic CRESS DNA viruses, foiling attempts to speculate with which other group of eukaryotic CRESS viruses it might share a recent common ancestor. Indeed, *Bacilladnaviridae* is fairly distant even from the black unclassified Rep sequences, suggesting either its sister taxon has yet to be sampled or that its closer relatives were unsuccessful over evolutionary time. Finally, it is important to note the preponderance of black taxa on the tree, and the groups they assemble into. While Rep similarity is not the sole determinant of eukaryotic CRESS DNA viral taxonomy, this is an indication that there are further cohesively evolving groups to be systematized within eukaryotic CRESS DNA viruses. These candidate groups have been given working names for the time being (see (Kazlauskas et al., 2018)). The diversity of these pathogens may not be completely sampled, but we know that the six named families cover just over half of the Rep diversity we do know about.

Ecology of eukaryotic CRESS DNA viruses

Distribution and sampling

We are not sure how close to the tip of the iceberg virologists are in terms of uncovering CRESS DNA viral diversity, but recent global efforts have doubled the number of eukaryotic CRESS DNA viral species in GenBank over the last 10 years (let alone the new strain sequences which add to our appreciation of the diversity within some eukaryotic CRESS DNA viral species). These abundant sequences come from a huge range of hosts and environments, and include both opportunistic sampling and intentional surveys.

While we have tried to be comprehensive in our survey of hosts and environments where researchers have identified eukaryotic CRESS DNA viral genomes (Table 3), our summary will be out of date soon after publication as further genomes are detected. Additionally, a list of places where eukaryotic CRESS DNA viruses have been detected suffers from the bias of not having a companion list of environments where researchers tried and failed to detect eukaryotic CRESS genomes. While the literature truly makes these viruses appear ubiquitous, the difficulty of proving a negative result means that a lack of CRESS DNA viruses would be hard to report. However, we note that there is a strong place in eukaryotic CRESS DNA viral discovery for negative controls; sequencing-based studies can be compromised by contaminated reagents (Salter et al., 2014) and CRESS DNA viral genomes have been found in commercially available DNA isolation spin columns (Naccache et al., 2013).

These many references evince the immerse efforts that virologists worldwide have made to sample and identify the potential eukaryotic CRESS DNA virus genomes. While the earth's virome may still be largely unknown, these efforts have better defined eukaryotic CRESS DNA viral diversity and prevalence, leading to improved systematics and a sense of their relatedness (see Figure 4, above). However, it has been increasingly frustrating that as genetic knowledge of these viruses increase, we lack commensurate information about these viruses' phenotype.

Confirmed and potential host range and pathogenesis of eukaryotic CRESS DNA viruses

The three oldest families of eukaryotic CRESS DNA viruses contain well-studied pathogens of plants and animals, though not all members of these families cause disease in all (or any) of the hosts they productively infect. Geminiviruses and nanoviruses infect plants, while circoviruses infect both vertebrates (mammals and birds) and invertebrates.

Plant infections

The speciose family *Geminiviridae* has members that can infect a wide range of plant hosts, from many plant families including Acanthaceae (e.g., Chinese violet), Amaranthaceae (e.g., sugar beet), Apocynaceae (e.g., golden trumpet), Asteraceae (e.g. zinnia), Bignoniaceae (e.g., yellow trumpetbush), Brassicaceae (e.g., cabbage), Capparaceae (e.g., spider flower), Caprifoliaceae (e.g., honeysuckle), Caricaceae (e.g. papaya), Convolvulaceae (e.g., sweet potato), Cucurbitaceae (e.g., squash), Cyperaceae (e.g., Nees weeping lovegrass), Dioscoreaceae (e.g., yam), Euphorbiaceae (e.g., cassava), Fabaceae (e.g., soybean), Gentianaceae (e.g., lisianthus), Lamiaceae (e.g., mint), Linderniaceae (e.g., false pimpernel), Malvaceae (e.g., cotton), Meliaceae (e.g., chinaberry tree), Moraceae (e.g., mulberry), Nyctaginaceae (e.g., red boerhavia), Oleaceae (e.g., Arabian jasmine), Onagraceae (e.g., Mexican primrose-willow), Oxalidaceae (e.g., pink woodsorrel), Papaveraceae (e.g., opium poppy), Passifloraceae (e.g., passionfruit), Phyllanthaceae (e.g., star gooseberry), Plantaginaceae (e.g., ribwort plaintain), Poaceae (e. g., maize), Polygalaceae (e.g., dainty butterfly bush), Rosaceae (e.g., rose), Rubiaceae (e.g., *Hedyotis uncinella*), Rutaceae (e.g., lemon), Sapindaceae (e.g., *Deinbollia borbonica*), Solanaceae (e.g, tomato), Urticaceae (e.g., ramie), Verbenaceae (e.g., pigeon berry), and Vitaceae (e.g., grapevine). The true host range of geminiviruses may be even larger, since there has been a sampling bias towards identifying

crop viruses and families without cultivated species that attract geminivirus insect vectors may also be susceptible to infection.

When infections are symptomatic, geminivirus cause yellowing of leaves (streaking, mosaicism (Figure 1), mottling) and distortions of the leaves (crumpling, curling, stunting, etc.), both of which interfere with the host plant's ability to conduct photosynthesis (Inoue-Nagata et al., 2016). Characterized geminiviruses are named for their plant host of isolation and symptoms, although many of these viruses infect more than one host and pose a series of symptoms, such that the species name may not reflect its predominant host or most typical symptoms in nature (Brown et al., 2015). Many affected plant species are economically and agriculturally important crops, so geminivirus infections can lead to economic losses and famine. For example, cassava is the third most important staple food for people living in the tropics, and more than 800 million people in Africa, Asia and Latin America depend on this plant for food and income (Legg et al., 2015). Cassava can withstand unfavorable soil conditions and drought, ensuring food security in marginal agricultural areas (Thresh and Cooter, 2005). In sub-Saharan Africa, cassava production is limited by a number of begomoviruses that cause cassava mosaic disease – the yellowing and distortion of the plant leaves prevents efficient starch production, and stunted tubers have sharply reduced yield compared to uninfected cassava (Alabi et al., 2011). The routine concern of cassava mosaic disease can worsen when the viruses evolve quickly (see Evolution, below), for instance when a recombinant between African cassava mosaic virus and East African mosaic virus (EACMV-UG) emerged, causing >90% crop loss in Uganda in 1997, leading some to starve in the resulting famine (Zhou et al., 1997).

Eighty-eight percent of classified geminiviruses are begomoviruses (Table 2), leading to an understandable bias in the literature towards this genus. Much of the work on geminivirus pathogenicity has been done in begomovirus-dicot host systems, including the model Arabidopsis (Hanley-Bowdoin et al., 2013), but many discoveries have also been made through field surveys. For instance, the symptoms of geminivirus infections can be altered by the presence of satellites. To date, four groups geminivirus associated satellites have been described, including alphasatellites, betasatellites, gammasatellites, and deltasatellites. The majority of described satellite species are found in association with monopartite begomoviruses (Zerbini et al., 2017). However, alphasatellites, betasatellites, and deltasatellites have been found with bipartite begomoviruses (Fiallo-Olivé et al., 2012, Lozano et al., 2016). Notably, alphasatellites have also been found with mastreviruses (Kumar et al., 2014), and thus geminivirus associated satellites are not limited to members of the genus *Begomovirus*. All four kinds of satellites are circular ssDNA with a stem-loop origin of replication (see Molecular biology of Rep, above).

The protein-coding alphasatellites and betasatellites are the best studied geminivirus-associated satellites. Alphasatellites are ~1300 nt, roughly half the length of a geminivirus genome (or genomic segment in the case of the bipartite begomoviruses). They encode their own Rep protein and autonomously replicate. Their Rep protein is closely related to that of nanoviruses, and the nonanucleotide in their stem-loop origin of replication matches that of nanoviruses as well (Rosario et al., 2012b). However, when coinfecting with either a geminivirus

or nanovirus, an alphasatellite can be encapsidated and transmitted. The roles that alphasatellites play in the infection dynamics have not been definitively determined, with some research suggesting they reduce begomovirus titer, thus prolonging the length of infection (Idris et al., 2011), while others suggest they help suppress silencing (Nawaz-ul-Rehman et al., 2010). Recently alphasatellites have been classified in to a virus family, *Alphasatellitidae* (included with *Nanoviridae* in Figure 4), with two genera reflecting their associated hosts: *Geminialphasatellitinae* and *Nanoalphasatellitinae* (Briddon et al., 2018). The most frequently encountered satellites, at least in the Old World, are betasatellites, which hijack both the capsids and replication initiation processes of their coinfecting geminiviruses (Sattar et al., 2013). A betasatellite is also usually half the size of a geminivirus genome (~1300nt) and has a stem-loop that is recognized by a geminivirus Rep (they encode the predominant begomovirus nonanucleotide (Rosario et al., 2016). It encodes a single protein, bC1, which can affect symptom severity and affect host silencing (functions thoroughly reviewed/listed in (Sattar et al., 2013, Zhou, 2013)). Geminivirus betasatellites are currently classified within the family *Tolecusatellitidae*, genus *Betasatellite*.

The remaining two groups of satellites are comparatively poorly studied and encompass non-protein encoding satellite molecules. Gammasatellites and deltasatellites are smaller (~700nt) than alphasatellites and betasatellites and seem to be largely restricted to the New World (Fiallo-Olivé et al., 2012, Fiallo-Olivé et al., 2016, Lozano et al., 2016, Rosario et al., 2016). Deltasatellites have been isolated from plants infected with either monopartite or bipartite begomoviruses (Fiallo-Olivé et al., 2012, Lozano et al., 2016). On the other hand, gammasatellites were discovered from the begomovirus whitefly vector through molecular analysis and, thus, have not been associated with a particular geminivirus (Rosario et al., 2016). The effects of these non-protein coding satellites on begomovirus infection are not yet known, though deltasatellites may decrease begomovirus accumulation in the host plant (Fiallo-Olivé et al., 2016). The nonanucleotide in the origin of replication for all identified gammasatellites and deltasatellites matches that of the begomoviruses (Fiallo-Olivé et al., 2016, Rosario et al., 2016). Gammasatellites were named based on the Greek alphabetical order since they were discovered after alpha and betasatellites. However, the first report of deltasatellites was almost simultaneous to that of gammasatellites and their name comes from their apparent derivation from betasatellites (delta, in the sense of a change from betasatellites). Currently there is no formal taxonomic classification for either gammasatellites or deltasatellites. Since both groups refer to small, non-protein coding satellites, it remains to be determined if both groups will be merged or will remain separate. Further phylogenetic analyses and biological characterization of these small satellites should shed light on this issue.

Nanovirus pathogenicity has been understudied compared to geminiviruses. They are known to infect a smaller number of plant families: Arecaceae (coconut), Caricaceae (papaya), Fabaceae (cow vetch, fava bean, pea, sophora root, subterranean clover), Musaceae (abaca, banana), Solanaceae (tobacco) and Zingiberaceae (cardamom), though they have been found to be most problematic in leguminous hosts (Fabaceae). This known host range has the same caveat that symptomatic crops have disproportionately been sampled and uncultivated plants may also be susceptible to nanoviruses. The most pronounced symptoms of nanovirus infection are

stunting, yellowing and leaf rolling, sometimes followed by necrosis (Abraham et al., 2012). Members of genus *Nanovirus* are transmitted by two aphid vectors, *Aphis craccivora* (Koch) and *Acyrthosiphou pisian* (Harris, and alphasatellites can associate with their already multipartite genomes (Kraberger et al., 2018). Nanoviruses have been reported in countries throughout North and Eastern Africa, Europe, the Middle East, China, Japan and Australia (Abraham et al., 2010, Abraham et al., 2012, Babin et al., 2000, Gaafar et al., 2017, Grigoras et al., 2010a, Grigoras et al., 2014, Kraberger et al., 2018, Kumari et al., 2009, Makkouk and Kumari, 2009, Vetten, 2008).

The symptoms of banana bunchy top virus, the type species of genus *Babuvirus* was first reported in Fiji in 1889 (Magee, 1927, Stover, 1972) and has been recognized as a pathogen that affects banana production worldwide (Dale, 1987) transmitted by the banana aphid (*Pentalonia nigronervosa*, Magee, 1927). Infected plants show significant reduction in size, and produce stunted fruits or fail to fruit (Hooks et al., 2008). Efforts to control banana bunchy top virus are complicated by asymptomatic infections, the virus' ability to infect other uncultivated hosts and long incubation periods, but molecular surveillance has helped earlier identification of infected plants (Allen, 1978, Dale and Harding, 1998, Hooks et al., 2008).

Animal infections

The family *Circoviridae*, genus *Circovirus* contains well-studied pathogens like porcine circovirus 2 (PCV2) and beak and feather disease virus (BFDV). Since cycloviruses are largely known only from metagenomics efforts, and their hosts are unknown, it is premature to discuss their pathogenicity. The host-virus interactions of porcine circoviruses in particular are well studied, starting with PCV1. Although PCV1 is not pathogenic in its typical porcine hosts, it was characterized as contaminant in a pig kidney cell line (PK-15) and studied for its unusual genomic architecture (Tischer et al., 1974). PCV2 contributes to several virulent diseases of pigs, notably post-weaning multisystemic wasting syndrome in piglets – a fatal disease that became epidemic in the late 1990s (Allan et al., 1999, Harding and Clark, 1997, Nayar et al., 1997). Retrospective studies found PCV2-antibodies in serum from Belgium as early as 1969 (Sanchez et al., 2001). Subsequently it was recognized that PCV2 is the leading causative agent for a collection of syndromes known as porcine circovirus associated disease (PCAD), including respiratory diseases, enteric diseases (porcine dermatitis and nephropathy syndrome) and reproductive problems (Opriessnig et al., 2007). PCV efficiently spreads horizontally through contact with respiratory, oral, urinary secretions and feces Magar et al., 2000, (Gillespie et al., 2009, Rose et al., 2012), and in rare cases, can transmit vertically from mother to piglets (Maldonado et al., 2005, Shen et al., 2010). PCV2 infects components of the immune system (Choi and Chae, 1999, Vincent et al., 2003), leading to depleted levels of lymphocytes in infected animals. PCV2 is now endemic globally and antibodies are found in up to 100% of pigs (Walker et al., 2000), but a much smaller percentage show symptoms of PCAD. This is likely because PCAD seems polymicrobial, and requires co-infection by PCV2 and another microbe – an RNA virus, another ssDNA virus (including porcine parvovirus, which has a linear genome), or even a bacterial infection (Rose et al., 2012).The initial epidemics of PCV2 were caused by one strain (PCV2a) and widespread vaccination was implemented to prevent piglets from succumbing to PCAD. In the wake of this successful intervention, the prevalent genotype shifted

to PCV2b, which is thought to be less virulent (Rose et al., 2012). Vaccination against PCV2b has led to another strain replacement, with PCV2d (Opriessnig et al., 2017).

The etiological agent for psittacine beak and feather disease is BFDV. Infected birds can exhibit many kinds of symptoms: peracute, acute, chronic and subclinical, depending on their age. Neonates and fledglings (young birds) typically show peracute and acute symptoms with high mortality rates (Doneley, 2003, Ritchie et al., 1989, Schoemaker et al., 2000). In chronic cases in more mature birds, beak and feather deformities are observed (Figure 5) and most birds become immunocompromised and become susceptible to secondary infections (Pass and Perry, 1984, Ritchie et al., 1989). Chronic symptoms include lethargy, depression, and diarrhea, which helps shed BFDV virions (Fogell et al., 2016). There is currently no cure, treatment or vaccine available for psittacine beak and feather disease (Regnard et al., 2017, Robino et al., 2014). Just as for PCV, BFDV can transmit horizontally through contact with infected secretions, for instance on nesting material (Gerlach, 1994, Ritchie et al., 2003b), and rarely transmit vertically (Rahaus et al., 2008, Todd, 2004). BFDV is endemic to Australia and has become a global concern due to legal and illegal trades of psittacine species (parrots, cockatoos, parakeets, Raidal et al., 2015). Phylogenetic analyses have confirmed the historical record, and shown that BFDV originated from Australia and then spread to the rest of the world (Harkins et al., 2014, Pass and Perry, 1984, Raidal et al., 2015). BFDV can infect at least 60 species within the order Psittaciformes (Harkins et al., 2014), and it is considered capable of emerging in other parrot species, including many “exotic” endangered species (Raidal et al., 2015, Sarker et al., 2015b, Sarker et al., 2015a).

Potential pathogens

Because of the lack of biological characterization among the newly identified CRESS DNA viruses, it is difficult to identify their roles in the biosphere. While viruses must use host resources to replicate, not all viruses significantly impact the fitness of their hosts, and the effects of some viral infections help their hosts survive and reproduce (Roossinck, 2011). Therefore, even if a eukaryotic CRESS DNA virus found in association with a host truly infects that host, it may not cause detectable disease symptoms. Indeed, one of the consequences of sequencing-based surveys of ecosystems is that a large number and diversity of viruses are uncovered in healthy plants – the methods are ideal for detecting benign or latent viruses (Roossinck et al., 2010).

It is nevertheless intriguing to many researchers that sequenced eukaryotic CRESS DNA viruses may have an impact on disease, especially in humans. There are several human diarrhea cases associated CRESS DNA viral discoveries, though these viruses may be present in human waste because they infect food ingested by the study subjects (Table 3). Others have found eukaryotic CRESS DNA viral genomes isolated from human cerebrospinal fluids. The tentatively named cyclovirus-Vietnam (CyCV-VN) was first found in patients with acute central nervous system infections in Vietnam, but was then also detected in fecal samples from humans, pigs and poultry (Tan et al., 2013). That same year, human cyclovirus VS5700009 (closely related to CyCV-VN (Sasaki et al., 2015)) was independently found in the cerebrospinal fluid of patients with unexplained paraplegia in Malawi (Smits et al., 2013). Others have subsequently screened

for CyCV-VN in cerebrospinal fluid of diseased patients without finding it: in northern Vietnam, Cambodia, Nepal and The Netherlands (Le et al., 2014). CyCV-VN still exists in association with humans – it was found in healthy children's feces and pig feces in Africa (Garigliany et al., 2014) and in the blood but not cerebrospinal fluid samples of immunodeficient Italian men (Macera et al., 2016). There is still a lack of evidence for any disease-causing properties and follow up studies concerning CyCV-VN, and many aspects of Koch's postulates remain unfulfilled for this potential human pathogen.

Outside of looking for human (and other animal) pathogens, researchers would like to understand the current role and potential of eukaryotic CRESS DNA viruses in our ecosystems, such as the ocean. As some eukaryotic CRESS DNA viruses can infect diatoms, they could possibly be used as biological control agents to stop the onset of some algal blooms. A number of bacilladnaviruses were found infecting the most abundant genus of diatoms, *Chaetoceros* (Kimura and Tomaru, 2013, Kimura and Tomaru, 2015, Nagasaki et al., 2005, Tomaru et al., 2008, Tomaru et al., 2011a, Tomaru et al., 2011b, Toyoda et al., 2012, Tomaru et al., 2013), which means these viruses could potentially be used worldwide to cure locations of toxic, anoxic algal overgrowth. Since so many eukaryotic CRESS DNA viruses have been discovered in association with aquatic invertebrates (ctenophores, sea stars, sea urchins, etc.), these viruses may play important roles in food web dynamics and biogeochemistry in aquatic systems (Rosario et al., 2015a).

Endogenized eukaryotic CRESS DNA viruses

Viruses have played many roles in eukaryotic evolution, but the age of genomic sequencing has revealed that eukaryotic genomes have more, and more diverse endogenized viral sequences than previously thought. Some viral genomic architectures lend themselves to frequent endogenization, such as retroviruses, which comprise ~8% of the human genome. Human endogenized retroviruses are genomic fossils, which have evolved at the slower rate of human evolution since their integration, and thus provide good information on the deep evolutionary history of retroviruses. Genomic fossils provide information on host jumps, host-virus interactions and even can indicate that arms races took place with the host (Hayward and Katzourakis, 2015). There have been some documented benefits to endogenized retroviruses as well, as eukaryotes have incorporated the viral genes and proteins into their functional systems. The best known example of an endogenized retroviral protein evolving to serve a critical function for the host would be the cooption of syncitin for host placenta morphogenesis, something that has occurred multiple independent times in the evolution of mammals (Mi et al., 2000). While some viruses routinely integrate into their hosts' genomes, and their occasional invasion of the germ line would be mechanistically understandable (retroviruses, some large DNA viruses), genomic fossils are being discovered in eukaryotes that are related to all types of lytic viruses, including RNA and ssDNA viruses. These sequences stand in opposition to our current understanding of these viruses' replication and inability to integrate into host genomes. Regardless they exist, even if they are the product of very small chance events (see several hypothetical mechanisms in (Krupovic and Forterre, 2015)), given many chances over the long arc of evolutionary time. The study of endogenized viruses comprises a major part of paleovirology, which not only allow us to know more about the origin

and evolutionary history of viruses, but also how virus integration may affected the evolutionary history of their hosts (Feschotte and Gilbert, 2012).

Many endogenized partial eukaryotic CRESS DNA viral genomes (most often a sequence with homology to Rep) have been founds in all eukaryotic supergroups (Kryukov et al., 2018). One of the earliest examples was a geminivirus Rep homolog in several tobacco species genomes, suggesting an integration event in a common ancestor more than a million years ago (Bejarano et al., 1996, Ashby et al., 1997). Other groups have found multiple cases of circovirus-like sequences in animal host genomes (Belyi et al., 2010, Malik et al., 2010, Katzourakis and Gifford, 2010). Comprehensive searches in eukaryotic genomes have found endogenized CRESS DNA virus-like sequences inside genomes of plants, fungi, animals and protists, suggesting these may have been hosts for eukaryotic CRESS DNA viruses in the past (Liu et al., 2011). More recent studies have found many endogenized circovirus-like elements inside host genomes (Dennis et al., 2018a). A thorough scan of ~4000 eukaryotic genomes with all non-retroviral virus sequences found sequences homologous to ssDNA viruses endogenized in all eukaryotic supergroups, but nearly half of the hits were in plant genomes (Kryukov et al., 2018). It is not yet known how active these virus-like sequences are within their hosts, and if they affect their hosts' fitness. Some of the more conserved sequences suggest that either the endogenization event was relatively recent, or selection has maintained the function of the sequence (Filloux et al., 2015). One study has reported geminivirus-like endogenized sequences in yam that are active, producing small RNA transcripts (Filloux et al., 2015).

Since so many eukaryotic CRESS DNA viruses do not have a definitive host, endogenized homologous sequences can give researchers an idea of what kind of host these viruses used to or could still infect (Aiewsakun and Katzourakis, 2015). These genomic fossils may point researchers towards fruitful hosts for isolating viruses that can be brought into the lab and characterized. This has already begun for those studying endogenous circoviral elements (Dennis et al., 2018b). Researchers have found endogenous sequences in host genomes cluster with exogenous contemporary viruses infecting similar hosts such as birds compared to mammals or fish (Dennis et al., 2018a). Endogenized cyclovirus elements have further confirmed their potential infectivity of insects, as endogenous sequences are similar to those found associated with dragonflies abdomen and larvae samples (Dayaram et al., 2013b, Dayaram et al., 2014, Rosario et al., 2011, Rosario et al., 2012a).

In addition to informing host use, these genomic fossils help provide depth to evolutionary studies of eukaryotic CRESS DNA viruses. The integrated Rep sequence in tobacco plants, for instance, indicates that geminivirus-like viruses were present in South America (where the tobacco plants diversified) at least 1.8 million years ago (Lefeuvre et al., 2011). This contradicts what researchers assumed from the modern distribution of whitefly-transmitted geminiviruses, where the begomoviruses in the New World appear descended from the more diverse Old World begomoviruses (Nawaz-ul-Rehman and Fauquet, 2009). These genomic fossils can inform where and when the ancestors of all circulating related viruses existed, even if the fast evolution of eukaryotic CRESS DNA viruses and coalescence have eliminated all traces of that history from their current sequences. As more eukaryotic genomes are sequenced, the greater

the opportunity will be to identify more endogenized eukaryotic CRESS DNA virus-like elements, and eukaryotic CRESS DNA paleovirology is likely to grow in the upcoming decade.

Evolution

Eukaryotic CRESS DNA viruses evolve quickly

Evolutionary study of eukaryotic CRESS DNA viruses is not restricted to paleovirology and untangling the deep phylogenetic relationships among families. Some eukaryotic CRESS DNA viruses are emergent pathogens, and the year-to-year evolution of these viruses impacts food security. For instance, novel begomoviruses have been a persistent emerging problem in crops including tomato (Ribeiro et al., 2003). Like emergent RNA viruses, eukaryotic CRESS DNA viruses have been shown to evolve quickly, and to do so even in datasets that remove statistically detectable recombination (the effects of recombination are discussed below). Representative lineages have been measured evolving quickly over a period of years: *Geminiviridae*: Tomato yellow leaf curl virus (TYLCV, Duffy and Holmes, 2009), Maize streak virus (MSV, van der Walt et al., 2008) and Sugarcane streak Reunion virus (Harkins et al., 2009a), *Nanoviridae*: Faba bean yellow necrotic virus (Grigoras et al., 2010b). Many more species have been able to have their rates of evolution estimated by computational methods, including members of *Circoviridae* (Firth et al., 2009, Kundu et al., 2012) and *Geminiviridae* (Duffy and Holmes, 2008, Harkins et al., 2009b). These high substitution rates do not cause commensurate change in protein-coding genes over long periods of evolutionary time. This is expected as part of the generalizable time-dependence of substitution rates – selection to retain function and saturation, especially of third codon positions, affect the measurable substitution rate over longer timespans (Aiewsakun and Katzourakis, 2016). This time dependence explains how mastreviruses may have diverged with their hosts, despite substitution rates calculated from that are orders of magnitude slower than observable mastrevirus evolution (Wu et al., 2008).

What is less understandable is how eukaryotic CRESS DNA viruses achieve these high, RNA virus-like substitution rates. RNA virus mutation rates drive their high substitution rates, but ssDNA viruses replicate with their host polymerases that are not thought to have high error rates (Duffy et al., 2008). As it is easier to measure the mutation rate of CRESS DNA viruses of bacteria than of eukaryotes (due to difficulty knowing and controlling generation times), no rigorous mutation rates have been measured for eukaryotic CRESS DNA viruses. Phages phiX174 and M13 have both been shown to mutate more rapidly than that of the *Escherichia coli* DNA polymerase that replicate their genomes (Cuevas et al., 2009, Sanjuán et al., 2010), and phiX174 avoids host DNA repair (Cuevas et al., 2011), but their ssDNA virus mutation rates are still 10 to 100-fold lower than the RNA virus mutation rates that explain their high substitution rates. Eukaryotic CRESS DNA viruses may have similar mutation rates to their phage counterparts, but the lack of mechanistic insight with phage offers nothing to assist in understanding how eukaryotic CRESS DNA viruses achieve the mutation rates necessary for their fast rates of evolution.

Circovirus researchers had noted fifteen years ago that unpaired single-stranded DNA bases could be oxidatively damaged, leading to high rates of transition for cytosines and adenines, which could bolster the baseline mutation rate of BFDV (Ritchie et al., 2003a). Phylogenetic and experimental studies of geminiviruses confirmed that cytosine to thymine transitions were elevated compared to the other kinds of transitions (Tomato yellow leaf curl China virus, Ge et al., 2007), TYLCV (Duffy and Holmes, 2008), East African cassava mosaic virus (EACMV, Duffy and Holmes, 2009), Sugarcane streak Reunion virus (Harkins et al., 2009a)), but other substitution biases with the potential to be due to oxidative damage (i.e., guanine to thymine transversions) were more frequently observed than the predicted adenine transitions (TYLCV (Duffy and Holmes, 2008), EACMV (Duffy and Holmes, 2009), MSV (van der Walt et al., 2008)). In begomoviruses, these substitution biases are strand-specific, indicating that the oxidative damage might occur while eukaryotic CRESS DNA viruses are encapsidated. That the cytosine transitions occur on the packaged, virion strand was cleanly demonstrated by an examination of begomovirus codon usage, which is biased towards thymine-ending codons in the mRNA for virion sense CP, but adenine-ending codons for antisense Rep, which correspond to thymines in the virion complement of the Rep gene (Cardinale et al., 2013). While it seems likely that oxidative damage contributes to higher CRESS DNA virus mutation rates, it does not appear that it explains all of the difference between expected mutation rates and measured substitution rates. This open question would benefit greatly from accurate measurement of mutation rate within eukaryotic hosts. Data indicate that geminivirus mutation rates might be very high in plants (Arguello-Astorga et al., 2007), and eukaryotic CRESS DNA viruses have highly diverse populations within single hosts (Sánchez-Campos et al., 2018, Sarker et al., 2014). It would be helpful if technological advances helped the field move from high mutation frequencies to accurately measured mutation rates.

Recombination

Long before high mutation rates were implied in eukaryotic CRESS DNA viruses, they were known to be capable of frequent recombination, and successful recombinant viruses were often isolated (Lefeuvre and Moriones, 2015). Even in the small, 1 kb segments of nanoviruses, statistically detectable recombination is found (Grigoras et al., 2014, Hyder et al., 2011). Recombination can bring more genetic change into a genome at once than a point mutation, which can cause large, swift phenotypic changes. As mentioned earlier, the genus *Curtovirus* was the result of a successful recombination between ancestors with a begomovirus-like Rep and a mastrevirus-like CP (Rybicki, 1994) – this caused a change in vector from whitefly to leafhopper, a phenotype that could not be conferred with a point mutation. A similar whole-gene recombination birthed the recently emerged porcine circovirus 3, which has a PCV Rep and an avian circovirus CP (Franzo et al., 2018). In chunks of whole genes (or more than one gene) or smaller portions of the genome, statistically detectable recombination is prevalent in eukaryotic CRESS DNA viruses. Undetectable recombination between nearly identical viruses also likely occurs as well, making the frequent recombination observed a conservative estimate of its occurrence.

Both mutation and recombination are known to occur more often in hot spots, and beyond their non-random occurrence, natural selection purges most mutations (and products of

recombination) such that surviving sequences show clear signals of regions where recombination is well-tolerated (Lefeuvre et al., 2007). For instance, across eukaryotic CRESS DNA viruses, recombination in intergenic regions is favored compared to recombination within a protein-coding gene. The canalization of recombination hot spots is more pronounced within family and genus. Despite nucleotide dissimilarity, the same regions are recombination hot spots within *Geminiviridae* (Lefeuvre et al., 2009), and separately, within *Circovirus* (Stenzel et al., 2014). The ambisense nature of many eukaryotic CRESS DNA viruses may be one reason for frequent recombination. When a gene is simultaneously replicated and transcribed, the interaction of the enzymes causes a pausing, and paused polymerases are associated with template switching recombination events (Martin et al., 2011). The best data that supports this idea is that there are more recombination breakpoints detected in the antisense genes in ambisense genomes – the orientation where it would be easiest to have replication and transcription approach each other from opposite directions (Martin et al., 2011). While eukaryotic CRESS DNA viruses are able to recombine quite often, mutation still accounts for most of the diversity seen in begomovirus populations worldwide (Lima et al., 2017a).

The multipartite plant CRESS DNA viruses also can experience reassortment (previously called pseudorecombination), wherein a segment from one virus can be used in a successful infection of another. The sequence similarity of the origin of replication in the Rep-encoding segment and the reasserted segment determines whether the segments can productively infect the host – the Rep protein must still be able to recognize the new segment's intergenic region including its stem-loop origin and nonanucleotide (Martin et al., 2011).

Migration

Researchers have studied the epidemiology of eukaryotic CRESS DNA virus spread around the globe to understand the current patterns of infection and to help prevent pathogens from moving into key agricultural areas. The Old World-New World biogeography of begomoviruses means that it has been easy to see when a virus from the Old World (Tomato yellow leaf curl virus, TYLCV) has migrated into the Americas, as it did to Hispaniola the early 1990s (Mabvakure et al., 2016). From there, it spread throughout the Caribbean, into Central and North America and at the same time was re-introduced to the west coast of Mexico from Asia (Duffy and Holmes, 2007). The only New World begomovirus that has successfully migrated out of the Americas is Squash leaf curl virus, which is now a problem in Cucurbit production throughout Asia Minor (Lapidot et al., 2014).

Modern phylogenetic software packages have made it possible to examine the likely pathways viruses take as they spread worldwide. Phylogeographic analyses have been conducted for members of the three most well-characterized families with a focus in the geminiviruses MSV and Panicum streak virus (Varsani et al., 2009), TYLCV (Lefeuvre et al., 2010, Mabvakure et al., 2016), East African cassava mosaic virus (De Bruyn et al., 2012), and Sweet potato leaf curl virus (Kim et al., 2018). Livestock trading among countries has been shown to be significant in PCV2 phylogeography (Firth et al., 2009, Vidigal et al., 2012), and the pet trade undoubtedly helped the spread of BFDV out of Australia (Harkins et al., 2014), but banana bunchy top virus (BBTV) has appeared to rarely move long distances, suggesting the modern banana trade is not

responsible for the current distribution of BBTV (Stainton et al., 2015). As increased sampling reveals more about the location of related eukaryotic CRESS DNA viruses that are not associated with diseases, some of these same techniques might be applied to viruses that are not necessarily pathogens, but for now the largest datasets that cover the longest periods of sampling are all from pathogens in *Geminiviridae, Circoviridae* and *Nanoviridae*.

Conclusions

Eukaryotic CRESS DNA viruses have been on the vanguard of the transition from detailed, molecular characterization of novel viruses to taxonomy by sequence similarity alone. Their small genome size, prevalence and affinity for rolling-circle replication allow easy molecular surveillance and high return on sampling effort. Virologists can now appreciate their incredible sequence diversity: varied genomic organization, divergence of the homologous Rep protein and novel viral proteins, which are sometimes unlike anything else previously sequenced (part of viral "dark matter," Krishnamurthy and Wang, 2017). There is also no sign that the diversity of eukaryotic CRESS DNA viruses has been thoroughly explored, and there is the strong potential for even more novel species, genera and families to be discovered with increased sampling.

The burgeoning number of families of eukaryotic CRESS DNA viruses reflects some of the extant diversity of this widespread group of viruses. While each of these families (and genera) have important idiosyncrasies, the shared evolutionary of their Rep protein provides important unity within this group that is deserving of recognition by ICTV as a higher level of taxonomy.

The sharp, recent expansion of our knowledge of eukaryotic CRESS DNA viral diversity was partially a function of how little attention was paid to this genomic architecture for several decades. The diversity of all viral groups will likely expand as more affordable sequencing facilitates larger surveys. However, CRESS DNA viruses have served as the canaries in the metagenomics mine for how cheap sequencing and expensive molecular virology skews our understanding of viruses towards bioinformatics and away from host-virus interactions and ecology. Without dedicated effort to cultivate and study representatives of these families in the laboratory, virologists will still know comparatively less about this widespread, diverse and intriguing viral group.

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References

Abraham, A.D., Bencharki, B., Torok, V., Katul, L., Varrelmann, M., Josef Vetten, H., 2010. Two distinct nanovirus species infecting faba bean in Morocco. Arch. Virol. 155, 37-46.

Abraham, A.D., Varrelmann, M., Josef Vetten, H., 2012. Three Distinct Nanoviruses, One of Which Represents a New Species, Infect Faba Bean in Ethiopia. Plant Dis. 96, 1045-1053.

Aiewsakun, P., Katzourakis, A., 2015. Endogenous viruses: Connecting recent and ancient viral evolution. Virology 479-480, 26-37.

Aiewsakun, P., Katzourakis, A., 2016. Time-Dependent Rate Phenomenon in Viruses. J. Virol. 90, 7184-7195.

Al Rwahnih, M., Alabi, O.J., Westrick, N.M., Golino, D., Rowhani, A., 2017. Description of a Novel Monopartite Geminivirus and Its Defective Subviral Genome in Grapevine. Phytopathology 107, 240-251.

Alabi, O., Rayapati, N., Kumar, L., 2011. Cassava mosaic disease: A curse to food security in Sub-Saharan Africa. Online. APS*net* Features. doi:10.1094/APSnetFeature-2011-0701.

Alarcon, P., Rushton, J., Wieland, B., 2013. Cost of post-weaning multi-systemic wasting syndrome and porcine circovirus type-2 subclinical infection in England - an economic disease model. Prev. Vet. Med. 110, 88-102.

Allan, G., Krakowka, S., Ellis, J., Charreyre, C., 2012. Discovery and evolving history of two genetically related but phenotypically different viruses, porcine circoviruses 1 and 2. Virus Res. 164, 4-9.

Allan, G.M., Mc Neilly, F., Meehan, B.M., Kennedy, S., Mackie, D.P., Ellis, J.A., Clark, E.G., Espuna, E., Saubi, N., Riera, P., Bøtner, A., Charreyre, C.E., 1999. Isolation and characterisation of circoviruses from pigs with wasting syndromes in Spain, Denmark and Northern Ireland. Vet. Microbiol. 66, 115-123.

Allen, R.N., 1978. Spread of bunchy top disease in established banana plantations. Australian J. Ag. Res. 29, 1223-1233.

Anderson, P.K., Cunningham, A.A., Patel, N.G., Morales, F.J., Epstein, P.R., Daszak, P., 2004. Emerging infectious diseases of plants: pathogen pollution, climate change and agrotechnology drivers. Trends Ecol. Evol. 19, 535-544.

Angly, F.E., Felts, B., Breitbart, M., Salamon, P., Edwards, R.A., Carlson, C., Chan, A.M., Haynes, M., Kelley, S., Liu, H., Mahaffy, J.M., Mueller, J.E., Nulton, J., Olson, R., Parsons, R., Rayhawk, S., Suttle, C.A., Rohwer, F., 2006. The Marine Viromes of Four Oceanic Regions. PLOS Biol. 4, e368.

Arguello-Astorga, G., Ascencio-Ibáñez, J.T., Dallas, M.B., Orozco, B.M., Hanley-Bowdoin, L., 2007. High-Frequency Reversion of Geminivirus Replication Protein Mutants during Infection. J. Virol. 81, 11005-11015.

Ashby, E., 1921. Notes on Psephotus haematonotus, the Red-rumped Grass Parrakeet. The Avicultural Magazine 12, 131-133.

Ashby, M.K., Warry, A., Bejarano, E.R., Khashoggi, A., Burrell, M., Lichtenstein, C.P., 1997. Analysis of multiple copies of geminiviral DNA in the genome of four closely related Nicotiana species suggest a unique integration event. Plant Mol. Biol. 35, 313-321.

Babin, M., Ortíz, V., Castro, S., Romero, J., 2000. First Detection of Faba bean necrotic yellow virus in Spain. Plant Dis. 84, 707-707.

Bassami, M.R., Berryman, D., Wilcox, G.E., Raidal, S.R., 1998. Psittacine Beak and Feather Disease Virus Nucleotide Sequence Analysis and Its Relationship to Porcine Circovirus, Plant Circoviruses, and Chicken Anaemia Virus. Virology 249, 453-459.

Basso, M.F., da Silva, J.C.F., Fajardo, T.V.M., Fontes, E.P.B., Zerbini, F.M., 2015. A novel, highly divergent ssDNA virus identified in Brazil infecting apple, pear and grapevine. Virus Res. 210, 27-33.

Bejarano, E.R., Khashoggi, A., Witty, M., Lichtenstein, C., 1996. Integration of multiple repeats of geminiviral DNA into the nuclear genome of tobacco during evolution. Proc. Natl. Acad. Sci. U. S. A. 93, 759-764.

Belabess, Z., Dallot, S., El-Montaser, S., Granier, M., Majde, M., Tahiri, A., Blenzar, A., Urbino, C., Peterschmitt, M., 2015. Monitoring the dynamics of emergence of a non-canonical recombinant of Tomato yellow leaf curl virus and displacement of its parental viruses in tomato. Virology 486, 291-306.

Belfort, M., Perlman, P.S., 1995. Mechanisms of Intron Mobility. J. Biol. Chem. 270, 30237-30240.

Belyi, V.A., Levine, A.J., Skalka, A.M., 2010. Sequences from ancestral single-stranded DNA viruses in vertebrate genomes: the parvoviridae and circoviridae are more than 40 to 50 million years old. J. Virol. 84, 12458-12462.

Bernardo, P., Muhire, B., Francois, S., Deshoux, M., Hartnady, P., Farkas, K., Kraberger, S., Filloux, D., Fernandez, E., Galzi, S., Ferdinand, R., Granier, M., Marais, A., Monge Blasco, P., Candresse, T., Escriu, F., Varsani, A., Harkins, G.W., Martin, D.P., Roumagnac, P., 2016. Molecular characterization and prevalence of two capulaviruses: Alfalfa leaf curl virus from France and Euphorbia caput-medusae latent virus from South Africa. Virology 493, 142-153.

Bistolas, K.S.I., Besemer, R.M., Rudstam, L.G., Hewson, I., 2017a. Distribution and Inferred Evolutionary Characteristics of a Chimeric ssDNA Virus Associated with Intertidal Marine Isopods. Viruses 9, 361.

Bistolas, K.S.I., Jackson, E.W., Watkins, J.M., Rudstam, L.G., Hewson, I., 2017b. Distribution of circular single-stranded DNA viruses associated with benthic amphipods of genus Diporeia in the Laurentian Great Lakes. Freshwater Biol. 62, 1220-1231.

Bistolas, K.S.I., Rudstam, L.G., Hewson, I., 2017c. Gene expression of benthic amphipods (genus: Diporeia) in relation to a circular ssDNA virus across two Laurentian Great Lakes. PeerJ 5.

Blanc, S., Drucker, M., Uzest, M., 2014. Localizing viruses in their insect vectors. Annu. Rev. Phytopathol. 52, 403-425.

Blinkova, O., Victoria, J., Li, Y., Keele, B.F., Sanz, C., Ndjango, J.B., Peeters, M., Travis, D., Lonsdorf, E.V., Wilson, M.L., Pusey, A.E., Hahn, B.H., Delwart, E.L., 2010. Novel circular DNA viruses in stool samples of wild-living chimpanzees. J. Gen. Virol. 91, 74-86.

Borzak, R., Sellyei, B., Szekely, C., Doszpoly, A., 2017. Molecular Detection and Genome Analysis of Circoviruses of European Eel (*Anguilla anguilla*) and Sichel (Pelecus cultratus). Acta Vet. Hung. 65, 262-277.

Breitbart, M., Benner, B.E., Jernigan, P.E., Rosario, K., Birsa, L.M., Harbeitner, R.C., Fulford, S., Graham, C., Walters, A., Goldsmith, D.B., Berger, S.A., Nejstgaard, J.C., 2015. Discovery, Prevalence, and Persistence of Novel Circular Single-Stranded DNA Viruses in the Ctenophores Mnemiopsis leidyi and Beroe ovata. Front. Microbiol. 6, 1427.

Breitbart, M., Rohwer, F., 2005. Method for discovering novel DNA viruses in blood using viral particle selection and shotgun sequencing. BioTechniques 39, 729-736.
Briddon, R.W., Martin, D.P., Roumagnac, P., Navas-Castillo, J., Fiallo-Olivé, E., Moriones, E., Lett, J.-M., Zerbini, F.M., Varsani, A., 2018. Alphasatellitidae: a new family with two subfamilies for the classification of geminivirus- and nanovirus-associated alphasatellites. Arch. Virol. 163, 2587-2600.
Brown, J.K., Zerbini, F.M., Navas-Castillo, J., Moriones, E., Ramos-Sobrinho, R., Silva, J.C., Fiallo-Olive, E., Briddon, R.W., Hernandez-Zepeda, C., Idris, A., Malathi, V.G., Martin, D.P., Rivera-Bustamante, R., Ueda, S., Varsani, A., 2015. Revision of Begomovirus taxonomy based on pairwise sequence comparisons. Arch. Virol. 160, 1593-1619.
Campos-Olivas, R., Louis, J.M., Clerot, D., Gronenborn, B., Gronenborn, A.M., 2002. The structure of a replication initiator unites diverse aspects of nucleic acid metabolism. Proc. Natl. Acad. Sci. U. S. A. 99, 10310-10315.
Capella-Gutierrez, S., Silla-Martinez, J.M., Gabaldon, T., 2009. trimAl: a tool for automated alignment trimming in large-scale phylogenetic analyses. Bioinformatics 25, 1972-1973.
Cardinale, D., DeRosa, K., Duffy, S., 2013. Base Composition and Translational Selection are Insufficient to Explain Codon Usage Bias in Plant Viruses. Viruses 5, 162.
Castrignano, S.B., Nagasse-Sugahara, T.K., Garrafa, P., Monezi, T.A., Barrella, K.M., Mehnert, D.U., 2017. Identification of circo-like virus-Brazil genomic sequences in raw sewage from the metropolitan area of Sao Paulo: evidence of circulation two and three years after the first detection. Mem. Inst. Oswaldo Cruz 112, 175-181.
Castrignano, S.B., Nagasse-Sugahara, T.K., Kisielius, J.J., Ueda-Ito, M., Brandao, P.E., Curti, S.P., 2013. Two novel circo-like viruses detected in human feces: complete genome sequencing and electron microscopy analysis. Virus Res. 178, 364-373.
Cheung, A.K., Ng, T.F., Lager, K.M., Alt, D.P., Delwart, E.L., Pogranichniy, R.M., 2014. Unique circovirus-like genome detected in pig feces. Genome Announc. 2, e00251-14.
Cheung, A.K., Ng, T.F., Lager, K.M., Bayles, D.O., Alt, D.P., Delwart, E.L., Pogranichniy, R.M., Kehrli, M.E., 2013. A divergent clade of circular single-stranded DNA viruses from pig feces. Arch. Virol. 158, 2157-2162.
Cheung, A.K., Ng, T.F.F., Lager, K.M., Alt, D.P., Delwart, E., Pogranichniy, R.M., 2015. Identification of several clades of novel single-stranded circular DNA viruses with conserved stem-loop structures in pig feces. Arch. Virol. 160, 353-358.
Choi, C., Chae, C., 1999. In-situ hybridization for the detection of porcine circovirus in pigs with postweaning multisystemic wasting syndrome. J. Comp. Pathol. 121, 265-270.
Claverie, S., Bernardo, P., Kraberger, S., Hartnady, P., Lefeuvre, P., Lett, J.M., Galzi, S., Filloux, D., Harkins, G.W., Varsani, A., Martin, D.P., Roumagnac, P., 2018. From Spatial Metagenomics to Molecular Characterization of Plant Viruses: A Geminivirus Case Study. Adv. Virus. Res. 101, 55-83.
Conceicao-Neto, N., Zeller, M., Heylen, E., Lefrere, H., Mesquita, J.R., Matthijnssens, J., 2015. Fecal virome analysis of three carnivores reveals a novel nodavirus and multiple gemycircularviruses. Virol. J. 12, 6.
Crawford, L.V., 1966. A minute virus of mice. Virology 29, 605-612.
Cuevas, J.M., Duffy, S., Sanjuán, R., 2009. Point Mutation Rate of Bacteriophage ΦX174. Genetics 183, 747-749.

Cuevas, J.M., Pereira-Gomez, M., Sanjuan, R., 2011. Mutation rate of bacteriophage PhiX174 modified through changes in GATC sequence context. Infect. Genet. Evol. 11, 1820-1822.
Cui, L.B., Wu, B.Y., Zhu, X.J., Guo, X.L., Ge, Y.Y., Zhao, K.C., Qi, X., Shi, Z.Y., Zhu, F.C., Sun, L.X., Zhou, M.H., 2017. Identification and genetic characterization of a novel circular single-stranded DNA virus in a human upper respiratory tract sample. Arch. Virol. 162, 3305-3312.
Czosnek, H., Hariton-Shalev, A., Sobol, I., Gorovits, R., Ghanim, M., 2017. The Incredible Journey of Begomoviruses in Their Whitefly Vector. Viruses 9, 273.
Dale, J.L., 1987. Banana Bunchy Top: An Economically Important Tropical Plant Virus Disease, in: Maramorosch, K., Murphy, F.A., Shatkin, A.J. (Eds.), Advances in Virus Research. Academic Press, pp. 301-325.
Dale, J.L., Harding, R.M., 1998. Banana bunchy top disease: current and future stratified for control., in: Hadidi, E.A., Khetarpal, R.K., Koganezawa, H. (Eds.), Plant Virus Disease Control. APS Press, St. Paul, MN, USA, pp. pp. 659-669.
Dayaram, A., Galatowitsch, M., Harding, J.S., Arguello-Astorga, G.R., Varsani, A., 2014. Novel circular DNA viruses identified in Procordulia grayi and Xanthocnemis zealandica larvae using metagenomic approaches. Infect. Genet. Evol. 22, 134-141.
Dayaram, A., Galatowitsch, M.L., Arguello-Astorga, G.R., van Bysterveldt, K., Kraberger, S., Stainton, D., Harding, J.S., Roumagnac, P., Martin, D.P., Lefeuvre, P., Varsani, A., 2016. Diverse circular replication-associated protein encoding viruses circulating in invertebrates within a lake ecosystem. Infect. Genet. Evol. 39, 304-316.
Dayaram, A., Goldstien, S., Arguello-Astorga, G.R., Zawar-Reza, P., Gomez, C., Harding, J.S., Varsani, A., 2015a. Diverse small circular DNA viruses circulating amongst estuarine molluscs. Infect. Genet. Evol. 31, 284-295.
Dayaram, A., Goldstien, S., Zawar-Reza, P., Gomez, C., Harding, J.S., Varsani, A., 2013a. Novel ssDNA virus recovered from estuarine Mollusc (Amphibola crenata) whose replication associated protein (Rep) shares similarities with Rep-like sequences of bacterial origin. J. Gen. Virol. 94, 1104-1110.
Dayaram, A., Opong, A., Jaschke, A., Hadfield, J., Baschiera, M., Dobson, R.C.J., Offei, S.K., Shepherd, D.N., Martin, D.P., Varsani, A., 2012. Molecular characterisation of a novel cassava associated circular ssDNA virus. Virus Res. 166, 130-135.
Dayaram, A., Potter, K.A., Moline, A.B., Rosenstein, D.D., Marinov, M., Thomas, J.E., Breitbart, M., Rosario, K., Arguello-Astorga, G.R., Varsani, A., 2013b. High global diversity of cycloviruses amongst dragonflies. J. Gen. Virol. 94, 1827-1840.
Dayaram, A., Potter, K.A., Pailes, R., Marinov, M., Rosenstein, D.D., Varsani, A., 2015b. Identification of diverse circular single-stranded DNA viruses in adult dragonflies and damselflies (Insecta: Odonata) of Arizona and Oklahoma, USA. Infect. Genet. Evol. 30, 278-287.
De Barro, P.J., Liu, S.S., Boykin, L.M., Dinsdale, A.B., 2011. Bemisia tabaci: a statement of species status. Annu. Rev. Entomol. 56, 1-19.
De Bruyn, A., Villemot, J., Lefeuvre, P., Villar, E., Hoareau, M., Harimalala, M., Abdoul-Karime, A.L., Abdou-Chakour, C., Reynaud, B., Harkins, G.W., Varsani, A., Martin, D.P., Lett, J.-M., 2012. East African cassava mosaic-like viruses from Africa to Indian ocean islands: molecular diversity, evolutionary history and geographical dissemination of a bipartite begomovirus. BMC Evol. Biol. 12, 228.

Dean, F.B., Nelson, J.R., Giesler, T.L., Lasken, R.S., 2001. Rapid Amplification of Plasmid and Phage DNA Using Phi29 DNA Polymerase and Multiply-Primed Rolling Circle Amplification. Genome Res. 11, 1095-1099.

Decaro, N., Martella, V., Desario, C., Lanave, G., Circella, E., Cavalli, A., Elia, G., Camero, M., Buonavoglia, C., 2014. Genomic characterization of a circovirus associated with fatal hemorrhagic enteritis in dog, Italy. PLoS One 9, e105909.

Dennis, T.P.W., de Souza, W.M., Marsile-Medun, S., Singer, J.B., Wilson, S.J., Gifford, R.J., 2018a. The evolution, distribution and diversity of endogenous circoviral elements in vertebrate genomes. Virus Res, in press.

Dennis, T.P.W., Flynn, P.J., Marciel de Souza, W., Singer, J.B., Moreau, C.S., Wilson, S.J., Gifford, R.J., 2018b. Insights into circovirus host range from the genomic fossil record. J. Virol. 92, e00145-18.

Diemer, G.S., Stedman, K.M., 2012. A novel virus genome discovered in an extreme environment suggests recombination between unrelated groups of RNA and DNA viruses. Biol. Direct 7, 13.

Doneley, R.J., 2003. Acute beak and feather disease in juvenile African Grey parrots--an uncommon presentation of a common disease. Aust. Vet. J. 81, 206-207.

Du, Z.G., Tang, Y.F., Zhang, S.B., She, X.M., Lan, G.B., Varsani, A., He, Z.F., 2014. Identification and molecular characterization of a single-stranded circular DNA virus with similarities to Sclerotinia sclerotiorum hypovirulence-associated DNA virus 1. Arch. Virol. 159, 1527-1531.

Duffy, S., Holmes, E.C., 2007. Multiple Introductions of the Old World Begomovirus Tomato yellow leaf curl virus into the New World. Appl. Environ. Microbiol. 73, 7114.

Duffy, S., Holmes, E.C., 2008. Phylogenetic evidence for rapid rates of molecular evolution in the single-stranded DNA begomovirus tomato yellow leaf curl virus. J. Virol. 82, 957-965.

Duffy, S., Holmes, E.C., 2009. Validation of high rates of nucleotide substitution in geminiviruses: phylogenetic evidence from East African cassava mosaic viruses. J. Gen. Virol. 90, 1539-1547.

Duffy, S., Shackelton, L.A., Holmes, E.C., 2008. Rates of evolutionary change in viruses: patterns and determinants. Nat. Rev. Genet. 9, 267.

Dunlap, D.S., Ng, T.F.F., Rosario, K., Barbosa, J.G., Greco, A.M., Breitbart, M., Hewson, I., 2013. Molecular and microscopic evidence of viruses in marine copepods. Proc. Natl. Acad. Sci. U. S. A. 110, 1375-1380.

Eaglesham, J.B., Hewson, I., 2013. Widespread detection of circular replication initiator protein (rep)-encoding ssDNA viral genomes in estuarine, coastal and open ocean net plankton. Mar. Ecol.-Prog. Ser. 494, 65-72.

Edgar, R.C., 2004. MUSCLE: multiple sequence alignment with high accuracy and high throughput. Nucl Acids Res. 32.

Fahsbender, E., Hewson, I., Rosario, K., Tuttle, A.D., Varsani, A., Breitbart, M., 2015. Discovery of a novel circular DNA virus in the Forbes sea star, Asterias forbesi. Arch. Virol. 160, 2349-2351.

Faurez, F., Dory, D., Grasland, B., Jestin, A., 2009. Replication of porcine circoviruses. Virol J. 6, 60.

Feschotte, C., Gilbert, C., 2012. Endogenous viruses: insights into viral evolution and impact on host biology. Nat. Rev. Genet. 13, 283-296.
Fiallo-Olivé, E., Martínez-Zubiaur, Y., Moriones, E., Navas-Castillo, J., 2012. A novel class of DNA satellites associated with New World begomoviruses. Virology 426, 1-6.
Fiallo-Olivé, E., Tovar, R., Navas-Castillo, J., 2016. Deciphering the biology of deltasatellites from the New World: maintenance by New World begomoviruses and whitefly transmission. New Phytol. 212, 680-692.
Filloux, D., Murrell, S., Koohapitagtam, M., Golden, M., Julian, C., Galzi, S., Uzest, M., Rodier-Goud, M., D'Hont, A., Vernerey, M.S., Wilkin, P., Peterschmitt, M., Winter, S., Murrell, B., Martin, D.P., Roumagnac, P., 2015. The genomes of many yam species contain transcriptionally active endogenous geminiviral sequences that may be functionally expressed. Virus Evol. 1, vev002.
Firth, C., Charleston, M.A., Duffy, S., Shapiro, B., Holmes, E.C., 2009. Insights into the Evolutionary History of an Emerging Livestock Pathogen: Porcine Circovirus 2. J. Virol. 83, 12813.
Fogell, D.J., Martin, R.O., Groombridge, J.J., 2016. Beak and feather disease virus in wild and captive parrots: an analysis of geographic and taxonomic distribution and methodological trends. Arch. Virol. 161, 2059-2074.
Fondong, V.N., 2013. Geminivirus protein structure and function. Mol Plant Pathol 14, 635-649.
Fontenele, R.S., Abreu, R.A., Lamas, N.S., Alves-Freitas, D.M.T., Vidal, A.H., Poppiel, R.R., Melo, F.L., Lacorte, C., Martin, D.P., Campos, M.A., Varsani, A., Ribeiro, S.G., 2018. Passion Fruit Chlorotic Mottle Virus: Molecular Characterization of a New Divergent Geminivirus in Brazil. Viruses 10, e169.
Franz, A., Makkouk, K.M., Vetten, H.J., 1998. Acquisition, Retention and Transmission of Faba Bean Necrotic Yellows Virus by Two of its Aphid Vectors, Aphis craccivora (Koch) and Acyrthosiphon pisum (Harris). J. Phytopathol. 146, 347-355.
Franzo, G., Segales, J., Tucciarone, C.M., Cecchinato, M., Drigo, M., 2018. The analysis of genome composition and codon bias reveals distinctive patterns between avian and mammalian circoviruses which suggest a potential recombinant origin for Porcine circovirus 3. PLoS One 13, e0199950.
Gaafar, Y., Timchenko, T., Ziebell, H., 2017. First report of Pea necrotic yellow dwarf virus in The Netherlands. New Dis. Rep. 35, 23.
Gallet, R., Fabre, F., Thébaud, G., Sofonea, M.T., Sicard, A., Blanc, S., Michalakis, Y., 2018. Small bottleneck size in a highly multipartite virus during a complete infectious cycle. J. Virol. 92, e00139-18.
Garigliany, M.M., Hagen, R.M., Frickmann, H., May, J., Schwarz, N.G., Perse, A., Jost, H., Borstler, J., Shahhosseini, N., Desmecht, D., Mbunkah, H.A., Daniel, A.M., Kingsley, M.T., Campos Rde, M., de Paula, V.S., Randriamampionona, N., Poppert, S., Tannich, E., Rakotozandrindrainy, R., Cadar, D., Schmidt-Chanasit, J., 2014. Cyclovirus CyCV-VN species distribution is not limited to Vietnam and extends to Africa. Sci. Rep. 4, 7552.
Ge, L., Zhang, J., Zhou, X., Li, H., 2007. Genetic Structure and Population Variability of Tomato Yellow Leaf Curl China Virus. J. Virol. 81, 5902-5907.
Ge, X.Y., Li, J.L., Peng, C., Wu, L.J., Yang, X.L., Wu, Y.Q., Zhang, Y.Z., Shi, Z.L., 2011. Genetic diversity of novel circular ssDNA viruses in bats in China. J. Gen. Virol. 92, 2646-2653.

Gerlach, H., 1994. Circoviridae-psittacine beak and feather disease virus, in: Ritchie, B.W., Harrison, G.J., Harrison, L.R. (Eds.), Avian medicine: principles and application. Wingers Publishing Incorporation, Lake Worth, FL, pp. 894-903.
Gibbs, M.J., Smeianov, V.V., Steele, J.L., Upcroft, P., Efimov, B.A., 2006. Two families of rep-like genes that probably originated by interspecies recombination are represented in viral, plasmid, bacterial, and parasitic protozoan genomes. Mol. Biol. Evol. 23, 1097-1100.
Gibbs, M.J., Weiller, G.F., 1999. Evidence that a plant virus switched hosts to infect a vertebrate and then recombined with a vertebrate-infecting virus. Proc. Natl. Acad. Sci. U. S. A. 96, 8022-8027.
Gillespie, J., Opriessnig, T., Meng, X.J., Pelzer, K., Buechner-Maxwell, V., 2009. Porcine Circovirus Type 2 and Porcine Circovirus-Associated Disease. J. Vet. Intern. Med. 23, 1151-1163.
Goodman, R.M., 1977a. Infectious DNA from a whitefly-transmitted virus of Phaseolus vulgaris. Nature 266, 54.
Goodman, R.M., 1977b. Single-stranded DNA genome in a whitefly-transmitted plant virus. Virology 83, 171-179.
Gorbalenya, A.E., Koonin, E.V., 1993. Helicases: amino acid sequence comparisons and structure-function relationships. Curr. Opin. Struct. Biol. 3, 419-429.
Gorbalenya, A.E., Koonin, E.V., Wolf, Y.I., 1990. A new superfamily of putative NTP-binding domains encoded by genomes of small DNA and RNA viruses. FEBS Lett. 262, 145-148.
Grigoras, I., Ginzo, A.I.d.C., Martin, D.P., Varsani, A., Romero, J., Mammadov, A.C., Huseynova, I.M., Aliyev, J.A., Kheyr-Pour, A., Huss, H., Ziebell, H., Timchenko, T., Vetten, H.-J., Gronenborn, B., 2014. Genome diversity and evidence of recombination and reassortment in nanoviruses from Europe. J. Gen. Virol. 95, 1178-1191.
Grigoras, I., Gronenborn, B., Vetten, H.J., 2010a. First Report of a Nanovirus Disease of Pea in Germany. Plant Dis. 94, 642-642.
Grigoras, I., Timchenko, T., Grande-Perez, A., Katul, L., Vetten, H.J., Gronenborn, B., 2010b. High Variability and Rapid Evolution of a Nanovirus. J. Virol. 84, 9105-9117.
Guindon, S., Gascuel, O., 2003. A Simple, Fast and Accurate Algorithm to Estimate Large Phylogenies by Maximum Likelihood. Syst. Biol. 52.
Haible, D., Kober, S., Jeske, H., 2006. Rolling circle amplification revolutionizes diagnosis and genomics of geminiviruses. J. Virol. Meth. 135, 9-16.
Hamel, A.L., Lin, L.L., Nayar, G.P.S., 1998. Nucleotide Sequence of Porcine Circovirus Associated with Postweaning Multisystemic Wasting Syndrome in Pigs. J. Virol. 72, 5262-5267.
Hanley-Bowdoin, L., Bejarano, E.R., Robertson, D., Mansoor, S., 2013. Geminiviruses: masters at redirecting and reprogramming plant processes. Nat. Rev. Microbiol. 11, 777-788.
Hanna, Z.R., Runckel, C., Fuchs, J., DeRisi, J.L., Mindell, D.P., Van Hemert, C., Handel, C.M., Dumbacher, J.P., 2015. Isolation of a Complete Circular Virus Genome Sequence from an Alaskan Black-Capped Chickadee (Poecile atricapillus) Gastrointestinal Tract Sample. Genome Announc 3, e01081-15.
Harding, J.C.S., Clark, E.G., 1997. Recognizing and diagnosing postweaning multisystemic wasting syndrome (PMWS). Swine Health Prod. 5, 201-203.
Harkins, G.W., Delport, W., Duffy, S., Wood, N., Monjane, A.L., Owor, B.E., Donaldson, L., Saumtally, S., Triton, G., Briddon, R.W., Shepherd, D.N., Rybicki, E.P., Martin, D.P., Varsani,

A., 2009a. Experimental evidence indicating that mastreviruses probably did not co-diverge with their hosts. Virol. J. 6, 104.
Harkins, G.W., Martin, D.P., Christoffels, A., Varsani, A., 2014. Towards inferring the global movement of beak and feather disease virus. Virology 450-451, 24-33.
Harkins, G.W., Martin, D.P., Duffy, S., Monjane, A.L., Shepherd, D.N., Windram, O.P., Owor, B.E., Donaldson, L., van Antwerpen, T., Sayed, R.A., Flett, B., Ramusi, M., Rybicki, E.P., Peterschmitt, M., Varsani, A., 2009b. Dating the origins of the maize-adapted strain of maize streak virus, MSV-A. J. Gen. Virol. 90, 3066-3074.
Harrison, B.D., Barker, H., Bock, K.R., Guthrie, E.J., Meredith, G., Atkinson, M., 1977. Plant viruses with circular single-stranded DNA. Nature 270, 760.
Hayward, A., Katzourakis, A., 2015. Endogenous retroviruses. Curr Biol 25, R644-646.
Hefferon, K.L., Moon, Y.S., Fan, Y., 2006. Multi-tasking of nonstructural gene products is required for bean yellow dwarf geminivirus transcriptional regulation. FEBS J. 273, 4482-4494.
Hewson, I., Eaglesham, J.B., Hook, T.O., LaBarre, B.A., Sepulveda, M.S., Thompson, P.D., Watkins, J.M., Rudstam, L.G., 2013. Investigation of viruses in Diporeia spp. from the Laurentian Great Lakes and Owasco Lake as potential stressors of declining populations. J. Great Lakes Res. 39, 499-506.
Heydarnejad, J., Kamali, M., Massumi, H., Kvarnheden, A., Male, M.F., Kraberger, S., Stainton, D., Martin, D.P., Varsani, A., 2017. Identification of a Nanovirus-Alphasatellite Complex in Sophora alopecuroides. Virus Res. 235, 24-32.
Ho, E.S., Kuchie, J., Duffy, S., 2014. Bioinformatic analysis reveals genome size reduction and the emergence of tyrosine phosphorylation site in the movement protein of New World bipartite begomoviruses. PLoS One 9, e111957.
Hooks, C.R.R., Wright, M.G., Kabasawa, D.S., Manandhar, R., Almeida, R.P.P., 2008. Effect of banana bunchy top virus infection on morphology and growth characteristics of banana. Ann. Appl. Biol. 153, 1-9.
Hyder, M.Z., Shah, S.H., Hameed, S., Naqvi, S.M., 2011. Evidence of recombination in the Banana bunchy top virus genome. Infect. Genet. Evol. 11, 1293-1300.
Idris, A.M., Shahid, M.S., Briddon, R.W., Khan, A.J., Zhu, J.-K., Brown, J.K., 2011. An unusual alphasatellite associated with monopartite begomoviruses attenuates symptoms and reduces betasatellite accumulation. J. Gen. Virol. 92, 706-717.
Ilyina, T.V., Koonin, E.V., 1992. Conserved sequence motifs in the initiator proteins for rolling circle DNA replication encoded by diverse replicons from eubacteria, eucaryotes and archaebacteria. Nucleic Acids Res. 20, 3279-3285.
Inoue-Nagata, A.K., Albuquerque, L.C., Rocha, W.B., Nagata, T., 2004. A simple method for cloning the complete begomovirus genome using the bacteriophage ϕ29 DNA polymerase. J. Virol. Meth. 116, 209-211.
Inoue-Nagata, A.K., Lima, M.F., Gilbertson, R.L., 2016. A review of geminivirus diseases in vegetables and other crops in Brazil: current status and approaches for management. Hort. Bras. 34, 8-18.
Jackson, E.W., Bistolas, K.S.I., Button, J.B., Hewson, I., 2016. Novel Circular Single-Stranded DNA Viruses among an Asteroid, Echinoid and Holothurian (Phylum: Echinodermata). PLoS One 11, 9.

Jeske, H., Lütgemeier, M., Preiß, W., 2001. DNA forms indicate rolling circle and recombination-dependent replication of Abutilon mosaic virus. EMBO J. 20, 6158-6167.
Jones, D.R., 2003. Plant Viruses Transmitted by Whiteflies. Eur. J. Plant Pathol. 109, 195-219.
Kapoor, A., Dubovi, E.J., Henriquez-Rivera, J.A., Lipkin, W.I., 2012. Complete genome sequence of the first canine circovirus. J. Virol. 86, 7018.
Kaszab, E., Marton, S., Forro, B., Bali, K., Lengyel, G., Banyai, K., Feher, E., 2018. Characterization of the genomic sequence of a novel CRESS DNA virus identified in Eurasian jay (Garrulus glandarius). Arch. Virol. 163, 285-289.
Katzourakis, A., Gifford, R.J., 2010. Endogenous viral elements in animal genomes. PLoS Genet. 6, e1001191.
Kazlauskas, D., Dayaram, A., Kraberger, S., Goldstien, S., Varsani, A., Krupovic, M., 2017. Evolutionary history of ssDNA bacilladnaviruses features horizontal acquisition of the capsid gene from ssRNA nodaviruses. Virology 504, 114-121.
Kazlauskas, D., Varsani, A., Krupovic, M., 2018. Pervasive Chimerism in the Replication-Associated Proteins of Uncultured Single-Stranded DNA Viruses. Viruses 10.
Kemenesi, G., Kurucz, K., Zana, B., Foldes, F., Urban, P., Vlaschenko, A., Kravchenko, K., Budinski, I., Szodoray-Paradi, F., Bucs, S., Jere, C., Csosz, I., Szodoray-Paradi, A., Estok, P., Gorfol, T., Boldogh, S., Jakab, F., 2018. Diverse replication-associated protein encoding circular DNA viruses in guano samples of Central-Eastern European bats. Arch. Virol. 163, 671-678.
Kim, A.R., Chung, H.C., Kim, H.K., Kim, E.O., Nguyen, V.G., Choi, M.G., Yang, H.J., Kim, J.A., Park, B.K., 2014. Characterization of a complete genome of a circular single-stranded DNA virus from porcine stools in Korea. Virus Genes 48, 81-88.
Kim, H.K., Park, S.J., Nguyen, V.G., Song, D.S., Moon, H.J., Kang, B.K., Park, B.K., 2012. Identification of a novel single-stranded, circular DNA virus from bovine stool. J. Gen. Virol. 93, 635-639.
Kim, J., Kwak, H.-R., Kim, M., Seo, J.-K., Yang, J.W., Chung, M.-N., Kil, E.-J., Choi, H.-S., Lee, S., 2018. Phylogeographic analysis of the full genome of Sweepovirus to trace virus dispersal and introduction to Korea. PLoS One 13, e0202174.
Kim, K.-H., Bae, J.-W., 2011. Amplification Methods Bias Metagenomic Libraries of Uncultured Single-Stranded and Double-Stranded DNA Viruses. Appl. Environ. Microbiol. 77, 7663.
Kimura, K., Tomaru, Y., 2013. Isolation and characterization of a single-stranded DNA virus infecting the marine diatom Chaetoceros sp. strain SS628-11 isolated from western Japan. PLoS One 8, e82013.
Kimura, K., Tomaru, Y., 2015. Discovery of two novel viruses expands the diversity of single-stranded DNA and single-stranded RNA viruses infecting a cosmopolitan marine diatom. Appl. Environ. Microbiol. 81, 1120-1131.
Koonin, E.V., 1993. A common set of conserved motifs in a vast variety of putative nucleic acid-dependent ATPases including MCM proteins involved in the initiation of eukaryotic DNA replication. Nucleic Acids Res. 21, 2541-2547.
Koonin, E.V., Dolja, V.V., Krupovic, M., 2015. Origins and evolution of viruses of eukaryotes: The ultimate modularity. Virology 479-480, 2-25.
Koonin, E.V., Ilyina, T.V., 1993. Computer-assisted dissection of rolling circle DNA replication. BioSystems 30, 241-268.

Kraberger, S., Arguello-Astorga, G.R., Greenfield, L.G., Galilee, C., Law, D., Martin, D.P., Varsani, A., 2015a. Characterisation of a diverse range of circular replication-associated protein encoding DNA viruses recovered from a sewage treatment oxidation pond. Infect. Genet. Evol. 31, 73-86.

Kraberger, S., Farkas, K., Bernardo, P., Booker, C., Arguello-Astorga, G.R., Mesleard, F., Martin, D.P., Roumagnac, P., Varsani, A., 2015b. Identification of novel Bromus- and Trifolium-associated circular DNA viruses. Arch. Virol. 160, 1303-1311.

Kraberger, S., Geering, A.D.W., Walters, M., Martin, D.P., Varsani, A., 2017. Novel mastreviruses identified in Australian wild rice. Virus Res. 238, 193-197.

Kraberger, S., Kumari, S.G., Najar, A., Stainton, D., Martin, D.P., Varsani, A., 2018. Molecular characterization of faba bean necrotic yellows viruses in Tunisia. Arch. Virol. 163, 687-694.

Kraberger, S., Stainton, D., Dayaram, A., Zawar-Reza, P., Gomez, C., Harding, J.S., Varsani, A., 2013. Discovery of Sclerotinia sclerotiorum Hypovirulence-Associated Virus-1 in Urban River Sediments of Heathcote and Styx Rivers in Christchurch City, New Zealand. Genome Announc. 1, e00559-13.

Krenz, B., Thompson, J.R., Fuchs, M., Perry, K.L., 2012. Complete genome sequence of a new circular DNA virus from grapevine. J Virol. 86, 7715.

Krishnamurthy, S.R., Wang, D., 2017. Origins and challenges of viral dark matter. Virus Res. 239, 136-142.

Krupovic, M., 2013. Networks of evolutionary interactions underlying the polyphyletic origin of ssDNA viruses. Curr. Opin. Virol. 3, 578-586.

Krupovic, M., Forterre, P., 2015. Single-stranded DNA viruses employ a variety of mechanisms for integration into host genomes. Ann. N. Y. Acad. Sci. 1341, 41-53.

Krupovic, M., Ravantti, J.J., Bamford, D.H., 2009. Geminiviruses: a tale of a plasmid becoming a virus. BMC Evol. Biol. 9, 112.

Krupovic, M., Zhi, N., Li, J., Hu, G., Koonin, E.V., Wong, S., Shevchenko, S., Zhao, K., Young, N.S., 2015. Multiple layers of chimerism in a single-stranded DNA virus discovered by deep sequencing. Genome Biol. Evol. 7, 993-1001.

Kryukov, K., Ueda, M.T., Imanishi, T., Nakagawa, S., 2018. Systematic survey of non-retroviral virus-like elements in eukaryotic genomes. Virus Res.

Kumar, J., Kumar, J., Singh, S.P., Tuli, R., 2014. betaC1 is a pathogenicity determinant: not only for begomoviruses but also for a mastrevirus. Arch. Virol. 159, 3071-3076.

Kumari, S.G., Attar, N., Mustafayev, E., Akparov, Z., 2009. First Report of Faba bean necrotic yellows virus Affecting Legume Crops in Azerbaijan. Plant Dis. 93, 1220-1220.

Kundu, S., Faulkes, C.G., Greenwood, A.G., Jones, C.G., Kaiser, P., Lyne, O.D., Black, S.A., Chowrimootoo, A., Groombridge, J.J., 2012. Tracking Viral Evolution during a Disease Outbreak: the Rapid and Complete Selective Sweep of a Circovirus in the Endangered Echo Parakeet. J. Virol. 86, 5221.

Lamberto, I., Gunst, K., Muller, H., Zur Hausen, H., de Villiers, E.M., 2014. Mycovirus-like DNA virus sequences from cattle serum and human brain and serum samples from multiple sclerosis patients. Genome Announc. 2, e00848-14.

Lapidot, M., Gelbart, D., Gal-On, A., Sela, N., Anfoka, G., Haj Ahmed, F., Abou-Jawada, Y., Sobh, H., Mazyad, H., Aboul-Ata, A.-A.E., Kamal El-Attar, A., Ali-Shtayeh, M.S., Jamous, R.M.,

Polston, J.E., Duffy, S., 2014. Frequent migration of introduced cucurbit-infecting begomoviruses among Middle Eastern countries. Virol. J. 11, 181.
Lasken, R.S., Egholm, M., 2003. Whole genome amplification: abundant supplies of DNA from precious samples or clinical specimens. Trends Biotechnol. 21, 531-535.
Laufs, J., Traut, W., Heyraud, F., Matzeit, V., Rogers, S.G., Schell, J., Gronenborn, B., 1995. In vitro cleavage and joining at the viral origin of replication by the replication initiator protein of tomato yellow leaf curl virus. Proc. Natl. Acad. Sci. U.S.A. 92, 3879-3883.
Le, V.T., de Jong, M.D., Nguyen, V.K., Nguyen, V.T., Taylor, W., Wertheim, H.F., van der Ende, A., van der Hoek, L., Canuti, M., Crusat, M., Sona, S., Nguyen, H.U., Giri, A., Nguyen, T.T., Ho, D.T., Farrar, J., Bryant, J.E., Tran, T.H., Nguyen, V.V., van Doorn, H.R., 2014. Limited geographic distribution of the novel cyclovirus CyCV-VN. Sci. Rep. 4, 3967.
Lefeuvre, P., Harkins, G.W., Lett, J.-M., Briddon, R.W., Chase, M.W., Moury, B., Martin, D.P., 2011. Evolutionary Time-Scale of the Begomoviruses: Evidence from Integrated Sequences in the Nicotiana Genome. PLoS One 6, e19193.
Lefeuvre, P., Lett, J.-M., Reynaud, B., Martin, D.P., 2007. Avoidance of Protein Fold Disruption in Natural Virus Recombinants. PLoS Pathog. 3, e181.
Lefeuvre, P., Lett, J.M., Varsani, A., Martin, D.P., 2009. Widely conserved recombination patterns among single-stranded DNA viruses. J. Virol. 83, 2697-2707.
Lefeuvre, P., Martin, D.P., Harkins, G., Lemey, P., Gray, A.J., Meredith, S., Lakay, F., Monjane, A., Lett, J.M., Varsani, A., Heydarnejad, J., 2010. The spread of tomato yellow leaf curl virus from the Middle East to the world. PLoS Pathog. 6, e1001164.
Lefeuvre, P., Moriones, E., 2015. Recombination as a motor of host switches and virus emergence: geminiviruses as case studies. Curr. Opin. Virol. 10, 14-19.
Legg, J.P., Lava Kumar, P., Makeshkumar, T., Tripathi, L., Ferguson, M., Kanju, E., Ntawuruhunga, P., Cuellar, W., 2015. Cassava virus diseases: biology, epidemiology, and management. Adv Virus Res. 91, 85-142.
Li, L., Giannitti, F., Low, J., Keyes, C., Ullmann, L.S., Deng, X., Aleman, M., Pesavento, P.A., Pusterla, N., Delwart, E., 2015a. Exploring the virome of diseased horses. J. Gen. Virol. 96, 2721-2733.
Li, L., Kapoor, A., Slikas, B., Bamidele, O.S., Wang, C., Shaukat, S., Masroor, M.A., Wilson, M.L., Ndjango, J.B., Peeters, M., Gross-Camp, N.D., Muller, M.N., Hahn, B.H., Wolfe, N.D., Triki, H., Bartkus, J., Zaidi, S.Z., Delwart, E., 2010a. Multiple diverse circoviruses infect farm animals and are commonly found in human and chimpanzee feces. J. Virol. 84, 1674-1682.
Li, L., Shan, T., Soji, O.B., Alam, M.M., Kunz, T.H., Zaidi, S.Z., Delwart, E., 2011. Possible cross-species transmission of circoviruses and cycloviruses among farm animals. J. Gen. Virol. 92, 768-772.
Li, L., Victoria, J.G., Wang, C., Jones, M., Fellers, G.M., Kunz, T.H., Delwart, E., 2010b. Bat guano virome: predominance of dietary viruses from insects and plants plus novel mammalian viruses. J. Virol. 84, 6955-6965.
Li, W., Gu, Y., Shen, Q., Yang, S., Wang, X., Wan, Y., Zhang, W., 2015b. A novel gemycircularvirus from experimental rats. Virus Genes 51, 302-305.
Li, Y., Khalafalla, A.I., Paden, C.R., Yusof, M.F., Eltahir, Y.M., Al Hammadi, Z.M., Tao, Y., Queen, K., Hosani, F.A., Gerber, S.I., Hall, A.J., Al Muhairi, S., Tong, S., 2017. Identification of diverse

viruses in upper respiratory samples in dromedary camels from United Arab Emirates. PLoS One 12, e0184718.
Lian, H., Liu, Y., Li, N., Wang, Y., Zhang, S., Hu, R., 2014. Novel circovirus from mink, China. Emerg. Infect. Dis. 20, 1548-1550.
Lima, A.T.M., Silva, J.C.F., Silva, F.N., Castillo-Urquiza, G.P., Silva, F.F., Seah, Y.M., Mizubuti, E.S.G., Duffy, S., Zerbini, F.M., 2017a. The diversification of begomovirus populations is predominantly driven by mutational dynamics. Virus Evol. 3, vex005.
Lima, D.A., Cibulski, S.P., Finkler, F., Teixeira, T.F., Varela, A.P.M., Cerva, C., Loiko, M.R., Scheffer, C.M., dos Santos, H.F., Mayer, F.Q., Roehe, P.M., 2017b. Faecal virome of healthy chickens reveals a large diversity of the eukaryote viral community, including novel circular ssDNA viruses. J. Gen. Virol. 98, 690-703.
Lima, F.E.D., Cibulski, S.P., dos Santos, H.F., Teixeira, T.F., Varela, A.P.M., Roehe, P.M., Delwart, E., Franco, A.C., 2015. Genomic Characterization of Novel Circular ssDNA Viruses from Insectivorous Bats in Southern Brazil. PLoS One 10, 11.
Liu, H.Q., Fu, Y.P., Li, B., Yu, X., Xie, J.T., Cheng, J.S., Ghabrial, S.A., Li, G.Q., Yi, X.H., Jiang, D.H., 2011. Widespread Horizontal Gene Transfer from Circular Single-stranded DNA Viruses to Eukaryotic Genomes. BMC Evol. Biol. 11, 15.
Loconsole, G., Saldarelli, P., Doddapaneni, H., Savino, V., Martelli, G.P., Saponari, M., 2012. Identification of a single-stranded DNA virus associated with citrus chlorotic dwarf disease, a new member in the family Geminiviridae. Virology 432, 162-172.
Lozano, G., Trenado, H.P., Fiallo-Olive, E., Chirinos, D., Geraud-Pouey, F., Briddon, R.W., Navas-Castillo, J., 2016. Characterization of Non-coding DNA Satellites Associated with Sweepoviruses (Genus Begomovirus, Geminiviridae) - Definition of a Distinct Class of Begomovirus-Associated Satellites. Front. Microbiol. 7, 162.
Lu, Q.Y., Wu, Z.J., Xia, Z.S., Xie, L.H., 2015. Complete genome sequence of a novel monopartite geminivirus identified in mulberry (Morus alba L.). Arch. Virol. 160, 2135-2138.
Ma, Y., Navarro, B., Zhang, Z., Lu, M., Zhou, X., Chi, S., Di Serio, F., Li, S., 2015. Identification and molecular characterization of a novel monopartite geminivirus associated with mulberry mosaic dwarf disease. J. Gen. Virol. 96, 2421-2434.
Mabvakure, B., Martin, D.P., Kraberger, S., Cloete, L., van Brunschot, S., Geering, A.D.W., Thomas, J.E., Bananej, K., Lett, J.M., Lefeuvre, P., Varsani, A., Harkins, G.W., 2016. Ongoing geographical spread of Tomato yellow leaf curl virus. Virology 498, 257-264.
Macera, L., Focosi, D., Vatteroni, M.L., Manzin, A., Antonelli, G., Pistello, M., Maggi, F., 2016. Cyclovirus Vietnam DNA in immunodeficient patients. J. Clin. Virol. 81, 12-15.
Magar, R., Larochelle, R., Thibault, S., Lamontagne, L., 2000. Experimental transmission of porcine circovirus type 2 (PCV2) in weaned pigs: a sequential study. J. Comp. Pathol. 123, 258-269.
Magee, C.J., 1927. Investigation on the bunchy top disease of the banana. Bull. Counc. Sci. Ind. Res. Aust. 30, 1-64.
Makkouk, K.M., Kumari, S.G., 2009. Epidemiology and integrated management of persistently transmitted aphid-borne viruses of legume and cereal crops in West Asia and North Africa. Virus Res. 141, 209-218.

Maldonado, J., Segales, J., Martinez-Puig, D., Calsamiglia, M., Riera, P., Domingo, M., Artigas, C., 2005. Identification of viral pathogens in aborted fetuses and stillborn piglets from cases of swine reproductive failure in Spain. Vet. J. 169, 454-456.

Male, M.F., Kami, V., Kraberger, S., Varsani, A., 2015. Genome Sequences of Poaceae-Associated Gemycircularviruses from the Pacific Ocean Island of Tonga. Genome Announc. 3.

Male, M.F., Kraberger, S., Stainton, D., Kami, V., Varsani, A., 2016. Cycloviruses, gemycircularviruses and other novel replication-associated protein encoding circular viruses in Pacific flying fox (Pteropus tonganus) faeces. Infect. Genet. Evol. 39, 279-292.

Malik, H.S., Katzourakis, A., Gifford, R.J., 2010. Endogenous Viral Elements in Animal Genomes. PLoS Genet. 6.

Martin, D.P., Biagini, P., Lefeuvre, P., Golden, M., Roumagnac, P., Varsani, A., 2011. Recombination in Eukaryotic Single Stranded DNA Viruses. Viruses 3, 1699-1738.

Marzano, S.L., Domier, L.L., 2016. Novel mycoviruses discovered from metatranscriptomics survey of soybean phyllosphere phytobiomes. Virus Res. 213, 332-342.

McDaniel, L.D., Rosario, K., Breitbart, M., Paul, J.H., 2014. Comparative metagenomics: natural populations of induced prophages demonstrate highly unique, lower diversity viral sequences. Environ. Microbiol. 16, 570-585.

Medina, C.G.V., Teppa, E., Bornancini, V.A., Flores, C.R., Marino-Buslje, C., Lambertini, P.M.L., 2018. Tomato Apical Leaf Curl Virus: A Novel, Monopartite Geminivirus Detected in Tomatoes in Argentina. Front. Microbiol. 8.

Meng, X.J., 2013. Porcine circovirus type 2 (PCV2): pathogenesis and interaction with the immune system. Annu. Rev. Anim. Biosci. 1, 43-64.

Mi, S., Lee, X., Li, X.-p., Veldman, G.M., Finnerty, H., Racie, L., LaVallie, E., Tang, X.-Y., Edouard, P., Howes, S., Keith Jr, J.C., McCoy, J.M., 2000. Syncytin is a captive retroviral envelope protein involved in human placental morphogenesis. Nature 403, 785.

Mu, F., Xie, J., Cheng, S., You, M.P., Barbetti, M.J., Jia, J., Wang, Q., Cheng, J., Fu, Y., Chen, T., Jiang, D., 2017. Virome Characterization of a Collection of S. sclerotiorum from Australia. Front. Microbiol. 8, 2540.

Muñoz-Martín, A., Collin, S., Herreros, E., Mullineaux, P.M., Fernández-Lobato, M., Fenoll, C., 2003. Regulation of MSV and WDV virion-sense promoters by WDV nonstructural proteins: a role for their retinoblastoma protein-binding motifs. Virology 306, 313-323.

Murphy, F.A., Fauquet, C.M., Bishop, D.H.L., Ghabrial, S.A., Jarvis, A.W., Martelli, G., P. Mayo, M.A., Summers, M.D., 1995. Virus Taxonomy. Sixth report of the International Committee on Taxonomy of Viruses. Arch. Virol. Suppl. 10, 590.

Naccache, S.N., Greninger, A.L., Lee, D., Coffey, L.L., Phan, T., Rein-Weston, A., Aronsohn, A., Hackett, J., Delwart, E.L., Chiu, C.Y., 2013. The Perils of Pathogen Discovery: Origin of a Novel Parvovirus-Like Hybrid Genome Traced to Nucleic Acid Extraction Spin Columns. J. Virol. 87, 11966.

Nagasaki, K., Tomaru, Y., Takao, Y., Nishida, K., Shirai, Y., Suzuki, H., Nagumo, T., 2005. Previously unknown virus infects marine diatom. Appl. Environ. Microbiol. 71, 3528-3535.

Nagy, G.N., Suardiaz, R., Lopata, A., Ozohanics, O., Vekey, K., Brooks, B.R., Leveles, I., Toth, J., Vertessy, B.G., Rosta, E., 2016. Structural Characterization of Arginine Fingers: Identification

of an Arginine Finger for the Pyrophosphatase dUTPases. J. Am. Chem. Soc. 138, 15035-15045.
Nakasu, E.Y.T., Melo, F.L., Michereff, M., Nagata, T., Ribeiro, B.M., Ribeiro, S.G., Lacorte, C., Inoue-Nagata, A.K., 2017. Discovery of two small circular ssDNA viruses associated with the whitefly Bemisia tabaci. Arch. Virol. 162, 2835-2838.
Nawaz-ul-Rehman, M.S., Fauquet, C.M., 2009. Evolution of geminiviruses and their satellites. FEBS Lett. 583, 1825-1832.
Nawaz-ul-Rehman, M.S., Nahid, N., Mansoor, S., Briddon, R.W., Fauquet, C.M., 2010. Post-transcriptional gene silencing suppressor activity of two non-pathogenic alphasatellites associated with a begomovirus. Virology 405, 300-308.
Nayar, G.P., Hamel, A., Lin, L., 1997. Detection and characterization of porcine circovirus associated with postweaning multisystemic wasting syndrome in pigs. Can. Vet. J. 38, 385-386.
Ng, T.F., Chen, L.F., Zhou, Y., Shapiro, B., Stiller, M., Heintzman, P.D., Varsani, A., Kondov, N.O., Wong, W., Deng, X., Andrews, T.D., Moorman, B.J., Meulendyk, T., MacKay, G., Gilbertson, R.L., Delwart, E., 2014. Preservation of viral genomes in 700-y-old caribou feces from a subarctic ice patch. Proc. Natl. Acad. Sci. USA 111, 16842-16847.
Ng, T.F., Duffy, S., Polston, J.E., Bixby, E., Vallad, G.E., Breitbart, M., 2011a. Exploring the diversity of plant DNA viruses and their satellites using vector-enabled metagenomics on whiteflies. PLoS One 6, e19050.
Ng, T.F., Willner, D.L., Lim, Y.W., Schmieder, R., Chau, B., Nilsson, C., Anthony, S., Ruan, Y., Rohwer, F., Breitbart, M., 2011b. Broad surveys of DNA viral diversity obtained through viral metagenomics of mosquitoes. PLoS One 6, e20579.
Ng, T.F.F., Alavandi, S., Varsani, A., Burghart, S., Breitbart, M., 2013. Metagenomic identification of a nodavirus and a circular ssDNA virus in semi-purified viral nucleic acids from the hepatopancreas of healthy Farfantepenaeus duorarum shrimp. Dis. Aquat. Org. 105, 237-242.
Ng, T.F.F., Zhang, W., Sachsenröder, J., Kondov, N.O., da Costa, A.C., Vega, E., Holtz, L.R., Wu, G., Wang, D., Stine, C.O., Antonio, M., Mulvaney, U.S., Muench, M.O., Deng, X., Ambert-Balay, K., Pothier, P., Vinjé, J., Delwart, E., 2015. A diverse group of small circular ssDNA viral genomes in human and non-human primate stools. Virus Evol. 1, vev017.
Nguyen, T.T., Robertsen, E.M., Landfald, B., 2017. Viral assemblage variation in an Arctic shelf seafloor. Aquat. Microb. Ecol. 78, 135-145.
Oba, M., Katayama, Y., Naoi, Y., Tsuchiaka, S., Omatsu, T., Okumura, A., Nagai, M., Mizutani, T., 2017. Discovery of fur seal feces-associated circular DNA virus in swine feces in Japan. J. Vet. Med. Sci. 79, 1664-1666.
Opriessnig, T., Meng, X.-J., Halbur, P.G., 2007. Porcine Circovirus Type 2–Associated Disease: Update on Current Terminology, Clinical Manifestations, Pathogenesis, Diagnosis, and Intervention Strategies. J. Vet. Diagn. Invest. 19, 591-615.
Opriessnig, T., Xiao, C.-T., Halbur, P.G., Gerber, P.F., Matzinger, S.R., Meng, X.-J., 2017. A commercial porcine circovirus (PCV) type 2a-based vaccine reduces PCV2d viremia and shedding and prevents PCV2d transmission to naïve pigs under experimental conditions. Vaccine 35, 248-254.

Padilla-Rodriguez, M., Rosario, K., Breitbart, M., 2013. Novel cyclovirus discovered in the Florida woods cockroach Eurycotis floridana (Walker). Arch. Virol. 158, 1389-1392.
Pass, D.A., Perry, R.A., 1984. The pathology of psittacine beak and feather disease. Aust. Vet. J. 61, 69-74.
Pearson, V.M., Caudle, S.B., Rokyta, D.R., 2016. Viral recombination blurs taxonomic lines: examination of single-stranded DNA viruses in a wastewater treatment plant. PeerJ 4, 18.
Phan, T.G., da Costa, A.C., Mendoza, J.D., Bucardo-Rivera, F., Nordgren, J., O'Ryan, M., Deng, X.T., Delwart, E., 2016. The fecal virome of South and Central American children with diarrhea includes small circular DNA viral genomes of unknown origin. Arch. Virol. 161, 959-966.
Phan, T.G., Kapusinszky, B., Wang, C., Rose, R.K., Lipton, H.L., Delwart, E.L., 2011. The Fecal Viral Flora of Wild Rodents. PLOS Pathog. 7, e1002218.
Phan, T.G., Luchsinger, V., Avendano, L.F., Deng, X.T., Delwart, E., 2014. Cyclovirus in nasopharyngeal aspirates of Chilean children with respiratory infections. J. Gen. Virol. 95, 922-927.
Phan, T.G., Mori, D., Deng, X.T., Rajindrajith, S., Ranawaka, U., Ng, T.F.F., Bucardo-Rivera, F., Orlandi, P., Ahmed, K., Delwart, E., 2015. Small circular single stranded DNA viral genomes in unexplained cases of human encephalitis, diarrhea, and in untreated sewage. Virology 482, 98-104.
Piewbang, C., Jo, W.K., Puff, C., van der Vries, E., Kesdangsakonwut, S., Rungsipipat, A., Kruppa, J., Jung, K., Baumgartner, W., Techangamsuwan, S., Ludlow, M., Osterhaus, A., 2018. Novel canine circovirus strains from Thailand: Evidence for genetic recombination. Sci. Rep. 8, 7524.
Quaiser, A., Krupovic, M., Dufresne, A., Francez, A.J., Roux, S., 2016. Diversity and comparative genomics of chimeric viruses in Sphagnum-dominated peatlands. Virus Evol. 2, vew025.
Rahaus, M., Desloges, N., Probst, S., Loebbert, B., Lantermann, W., Wolff, M.H., 2008. Detection of beak and feather disease virus DNA in embryonated eggs of psittacine birds. Vet. Med. (Praha) 53, 53-58.
Raidal, S.R., Sarker, S., Peters, A., 2015. Review of psittacine beak and feather disease and its effect on Australian endangered species. Aust. Vet. J. 93, 466-470.
Reavy, B., Swanson, M.M., Cock, P.J.A., Dawson, L., Freitag, T.E., Singh, B.K., Torrance, L., Mushegian, A.R., Taliansky, M., 2015. Distinct Circular Single-Stranded DNA Viruses Exist in Different Soil Types. Appl. Environ. Microbiol. 81, 3934-3945.
Regenmortel, M.H.V.v., Fauquet, C.M., Bishop, D.H.L., Carstens, E.B., Estes, M.K., Lemon, S.M., Maniloff, J., Mayo, M.A., McGeoch, D.J., Pringle, C.R., Wickner, R.B., 2000. Virus taxonomy: classification and nomenclature of viruses. Seventh report of the International Committee on Taxonomy of Viruses. Academic Press, San Diego.
Regnard, G.L., Rybicki, E.P., Hitzeroth, II, 2017. Recombinant expression of beak and feather disease virus capsid protein and assembly of virus-like particles in Nicotiana benthamiana. Virol. J. 14, 174.
Reuter, G., Boros, A., Delwart, E., Pankovics, P., 2014. Novel circular single-stranded DNA virus from turkey faeces. Arch. Virol. 159, 2161-2164.
Rey, M.E.C., Ndunguru, J., Berrie, L.C., Paximadis, M., Berry, S., Cossa, N., Nuaila, V.N., Mabasa, K.G., Abraham, N., Rybicki, E.P., Martin, D., Pietersen, G., Esterhuizen, L.L., 2012. Diversity of

Dicotyledenous-Infecting Geminiviruses and Their Associated DNA Molecules in Southern Africa, Including the South-West Indian Ocean Islands. Viruses 4, 1753-1791.
Ribeiro, S.G., Ambrozevicius, L.P., Avila, A.C., Bezerra, I.C., Calegario, R.F., Fernandes, J.J., Lima, M.F., de Mello, R.N., Rocha, H., Zerbini, F.M., 2003. Distribution and genetic diversity of tomato-infecting begomoviruses in Brazil. Arch. Virol. 148, 281-295.
Ritchie, B.W., Niagro, F.D., Lukert, P.D., Steffens, W.L., Latimer, K.S., 1989. Characterization of a new virus from cockatoos with psittacine beak and feather disease. Virology 171, 83-88.
Ritchie, P.A., Anderson, I.L., Lambert, D.M., 2003a. Evidence for specificity of psittacine beak and feather disease viruses among avian hosts. Virology 306, 109-115.
Ritchie, P.A., Anderson, I.L., Lambert, D.M., 2003b. Evidence for specificity of psittacine beak and feather disease viruses among avian hosts. Virology 306, 109-115.
Robino, P., Grego, E., Rossi, G., Bert, E., Tramuta, C., Stella, M.C., Bertoni, P., Nebbia, P., 2014. Molecular analysis and associated pathology of beak and feather disease virus isolated in Italy from young Congo African grey parrots (Psittacus erithacus) with an "atypical peracute form" of the disease. Avian Pathol. 43, 333-344.
Roossinck, M.J., 2011. The good viruses: viral mutualistic symbioses. Nat. Rev. Microbiol. 9, 99-108.
Roossinck, M.J., Saha, P., Wiley, G.B., Quan, J., White, J.D., Lai, H., Chavarria, F., Shen, G., Roe, B.A., 2010. Ecogenomics: using massively parallel pyrosequencing to understand virus ecology. Mol. Ecol. 19 Suppl 1, 81-88.
Rosario, K., Breitbart, M., Harrach, B., Segales, J., Delwart, E., Biagini, P., Varsani, A., 2017. Revisiting the taxonomy of the family Circoviridae: establishment of the genus Cyclovirus and removal of the genus Gyrovirus. Arch. Virol. 162, 1447-1463.
Rosario, K., Dayaram, A., Marinov, M., Ware, J., Kraberger, S., Stainton, D., Breitbart, M., Varsani, A., 2012a. Diverse circular ssDNA viruses discovered in dragonflies (Odonata: Epiprocta). J. Gen. Virol. 93, 2668-2681.
Rosario, K., Duffy, S., Breitbart, M., 2009. Diverse circovirus-like genome architectures revealed by environmental metagenomics. J. Gen. Virol. 90, 2418-2424.
Rosario, K., Duffy, S., Breitbart, M., 2012b. A field guide to eukaryotic circular single-stranded DNA viruses: insights gained from metagenomics. Arch. Virol. 157, 1851-1871.
Rosario, K., Marinov, M., Stainton, D., Kraberger, S., Wiltshire, E.J., Collings, D.A., Walters, M., Martin, D.P., Breitbart, M., Varsani, A., 2011. Dragonfly cyclovirus, a novel single-stranded DNA virus discovered in dragonflies (Odonata: Anisoptera). J. Gen. Virol. 92, 1302-1308.
Rosario, K., Marr, C., Varsani, A., Kraberger, S., Stainton, D., Moriones, E., Polston, J.E., Breitbart, M., 2016. Begomovirus-Associated Satellite DNA Diversity Captured Through Vector-Enabled Metagenomic (VEM) Surveys Using Whiteflies (Aleyrodidae). Viruses 8, 36.
Rosario, K., Mettel, K.A., Benner, B.E., Johnson, R., Scott, C., Yusseff-Vanegas, S.Z., Baker, C.C.M., Cassill, D.L., Storer, C., Varsani, A., Breitbart, M., 2018. Virus discovery in all three major lineages of terrestrial arthropods highlights the diversity of single-stranded DNA viruses associated with invertebrates. PeerJ Preprints 6, e27093v27091.
Rosario, K., Padilla-Rodriguez, M., Kraberger, S., Stainton, D., Martin, D.P., Breitbart, M., Varsani, A., 2013. Discovery of a novel mastrevirus and alphasatellite-like circular DNA in dragonflies (Epiprocta) from Puerto Rico. Virus Res. 171, 231-237.

Rosario, K., Schenck, R.O., Harbeitner, R.C., Lawler, S.N., Breitbart, M., 2015a. Novel circular single-stranded DNA viruses identified in marine invertebrates reveal high sequence diversity and consistent predicted intrinsic disorder patterns within putative structural proteins. Front. Microbiol. 6, 13.

Rosario, K., Seah, Y., Marr, C., Varsani, A., Kraberger, S., Stainton, D., Moriones, E., Polston, J., Duffy, S., Breitbart, M., 2015b. Vector-Enabled Metagenomic (VEM) Surveys Using Whiteflies (Aleyrodidae) Reveal Novel Begomovirus Species in the New and Old Worlds. Viruses 7, 2895.

Rose, N., Opriessnig, T., Grasland, B., Jestin, A., 2012. Epidemiology and transmission of porcine circovirus type 2 (PCV2). Virus Res. 164, 78-89.

Roux, S., Enault, F., Bronner, G., Vaulot, D., Forterre, P., Krupovic, M., 2013. Chimeric viruses blur the borders between the major groups of eukaryotic single-stranded DNA viruses. Nat. Commun. 4, 2700.

Roux, S., Enault, F., Robin, A., Ravet, V., Personnic, S., Theil, S., Colombet, J., Sime-Ngando, T., Debroas, D., 2012. Assessing the Diversity and Specificity of Two Freshwater Viral Communities through Metagenomics. PLoS One 7.

Roux, S., Solonenko, N.E., Dang, V.T., Poulos, B.T., Schwenk, S.M., Goldsmith, D.B., Coleman, M.L., Breitbare, M., Sullivan, M.B., 2016. Towards quantitative viromics for both double-stranded and single-stranded DNA viruses. PeerJ 4, 17.

Rwahnih, M.A., Dave, A., Anderson, M.M., Rowhani, A., Uyemoto, J.K., Sudarshana, M.R., 2013. Association of a DNA Virus with Grapevines Affected by Red Blotch Disease in California. Phytopathology 103, 1069-1076.

Rybicki, E.P., 1994. A phylogenetic and evolutionary justification for three genera of Geminiviridae. Arch. Virol. 139, 49-77.

Sachsenroder, J., Braun, A., Machnowska, P., Ng, T.F.F., Deng, X.T., Guenther, S., Bernstein, S., Ulrich, R.G., Delwart, E., Johne, R., 2014. Metagenomic identification of novel enteric viruses in urban wild rats and genome characterization of a group A rotavirus. J. Gen. Virol. 95, 2734-2747.

Sachsenroder, J., Twardziok, S., Hammerl, J.A., Janczyk, P., Wrede, P., Hertwig, S., Johne, R., 2012. Simultaneous Identification of DNA and RNA Viruses Present in Pig Faeces Using Process-Controlled Deep Sequencing. PLoS One 7, 11.

Salter, S.J., Cox, M.J., Turek, E.M., Calus, S.T., Cookson, W.O., Moffatt, M.F., Turner, P., Parkhill, J., Loman, N.J., Walker, A.W., 2014. Reagent and laboratory contamination can critically impact sequence-based microbiome analyses. BMC Biology 12, 87.

Sanchez, R., Nauwynch, G., Pensaert, M., 2001. Serological survey of PCV-2 antibodies in domestic and feral pig populations in Belgium. Proc. ssDNA viruses of plants, birds, pigs and primates. St. Malo, France, p. 122.

Sánchez-Campos, S., Domínguez-Huerta, G., Díaz-Martínez, L., Tomás, D.M., Navas-Castillo, J., Moriones, E., Grande-Pérez, A., 2018. Differential Shape of Geminivirus Mutant Spectra Across Cultivated and Wild Hosts With Invariant Viral Consensus Sequences. Front. Plant Sci. 9, 932.

Sanjuán, R., Nebot, M.R., Chirico, N., Mansky, L.M., Belshaw, R., 2010. Viral Mutation Rates. J. Virol. 84, 9733.

Sarker, S., Forwood, J.K., Ghorashi, S.A., Peters, A., Raidal, S.R., 2015a. Beak and feather disease virus genotypes in Australian parrots reveal flexible host-switching. Aust. Vet. J. 93, 471-475.

Sarker, S., Moylan, K.G., Ghorashi, S.A., Forwood, J.K., Peters, A., Raidal, S.R., 2015b. Evidence of a deep viral host switch event with beak and feather disease virus infection in rainbow bee-eaters (Merops ornatus). Sci. Rep. 5, 14511.

Sarker, S., Patterson, E.I., Peters, A., Baker, G.B., Forwood, J.K., Ghorashi, S.A., Holdsworth, M., Baker, R., Murray, N., Raidal, S.R., 2014. Mutability Dynamics of an Emergent Single Stranded DNA Virus in a Naïve Host. PLoS One 9, e85370.

Sasaki, M., Orba, Y., Ueno, K., Ishii, A., Moonga, L., Hang'ombe, B.M., Mweene, A.S., Ito, K., Sawa, H., 2015. Metagenomic analysis of the shrew enteric virome reveals novel viruses related to human stool-associated viruses. J. Gen. Virol. 96, 440-452.

Sato, G., Kawashima, T., Kiuchi, M., Tohya, Y., 2015. Novel cyclovirus detected in the intestinal contents of Taiwan squirrels (Callosciurus erythraeus thaiwanensis). Virus Genes 51, 148-151.

Sattar, M.N., Kvarnheden, A., Saeed, M., Briddon, R.W., 2013. Cotton leaf curl disease - an emerging threat to cotton production worldwide. J. Gen. Virol. 94, 695-710.

Saunders, K., Bedford, I.D., Yahara, T., Stanley, J., 2003. The earliest recorded plant virus disease. Nature 422, 831.

Schoemaker, N.J., Dorrestein, G.M., Latimer, K.S., Lumeij, J.T., Kik, M.J., van der Hage, M.H., Campagnoli, R.P., 2000. Severe leukopenia and liver necrosis in young African grey parrots (Psittacus erithacus erithacus) infected with psittacine circovirus. Avian Dis. 44, 470-478.

Seal, S.E., Jeger, M.J., Van den Bosch, F., 2006a. Begomovirus Evolution and Disease Management. Ad. Vir. Res. 67, 297-316.

Seal, S.E., vandenBosch, F., Jeger, M.J., 2006b. Factors Influencing Begomovirus Evolution and Their Increasing Global Significance: Implications for Sustainable Control. Crit. Rev. Plant Sci. 25, 23-46.

Sertic, V., Bulgakov, N., 1935. Classification et identification des typhiphage. C R Soc. Biol. Paris 119, 1270-1272.

Shan, T., Li, L., Simmonds, P., Wang, C., Moeser, A., Delwart, E., 2011. The fecal virome of pigs on a high-density farm. J. Virol. 85, 11697-11708.

Sharman, M., Thomas, J.E., Skabo, S., Holton, T.A., 2008. Abaca bunchy top virus, a new member of the genus Babuvirus (family Nanoviridae). Arch. Virol. 153, 135-147.

Shen, H., Wang, C., Madson, D.M., Opriessnig, T., 2010. High prevalence of porcine circovirus viremia in newborn piglets in five clinically normal swine breeding herds in North America. Prev. Vet. Med. 97, 228-236.

Sicard, A., Yvon, M., Timchenko, T., Gronenborn, B., Michalakis, Y., Gutierrez, S., Blanc, S., 2013. Gene copy number is differentially regulated in a multipartite virus. Nat. Commun. 4, 2248.

Sikorski, A., Arguello-Astorga, G.R., Dayaram, A., Dobson, R.C.J., Varsani, A., 2013a. Discovery of a novel circular single-stranded DNA virus from porcine faeces. Arch. Virol. 158, 283-289.

Sikorski, A., Kearvell, J., Elkington, S., Dayaram, A., Arguello-Astorga, G.R., Varsani, A., 2013b. Novel ssDNA viruses discovered in yellow-crowned parakeet (Cyanoramphus auriceps) nesting material. Arch. Virol. 158, 1603-1607.

Sikorski, A., Massaro, M., Kraberger, S., Young, L.M., Smalley, D., Martin, D.P., Varsani, A., 2013c. Novel myco-like DNA viruses discovered in the faecal matter of various animals. Virus Res. 177, 209-216.

Simmonds, P., Adams, M.J., Benko, M., Breitbart, M., Brister, J.R., Carstens, E.B., Davison, A.J., Delwart, E., Gorbalenya, A.E., Harrach, B., Hull, R., King, A.M., Koonin, E.V., Krupovic, M., Kuhn, J.H., Lefkowitz, E.J., Nibert, M.L., Orton, R., Roossinck, M.J., Sabanadzovic, S., Sullivan, M.B., Suttle, C.A., Tesh, R.B., van der Vlugt, R.A., Varsani, A., Zerbini, F.M., 2017. Consensus statement: Virus taxonomy in the age of metagenomics. Nat. Rev. Microbiol. 15, 161-168.

Smits, S.L., Zijlstra, E.E., van Hellemond, J.J., Schapendonk, C.M., Bodewes, R., Schurch, A.C., Haagmans, B.L., Osterhaus, A.D., 2013. Novel cyclovirus in human cerebrospinal fluid, Malawi, 2010-2011. Emerg. Infect. Dis. 19, 1511-1513.

Soffer, N., Brandt, M.E., Correa, A.M.S., Smith, T.B., Thurber, R.V., 2014. Potential role of viruses in white plague coral disease. ISME J. 8, 271-283.

Stainton, D., Martin, D.P., Muhire, B.M., Lolohea, S., Halafihi, M.i., Lepoint, P., Blomme, G., Crew, K.S., Sharman, M., Kraberger, S., Dayaram, A., Walters, M., Collings, D.A., Mabvakure, B., Lemey, P., Harkins, G.W., Thomas, J.E., Varsani, A., 2015. The global distribution of Banana bunchy top virus reveals little evidence for frequent recent, human-mediated long distance dispersal events. Virus Evol. 1, vev009-vev009.

Stedman, K.M., 2015. Deep Recombination: RNA and ssDNA Virus Genes in DNA Virus and Host Genomes. Ann. Rev. Virol. 2, 203-217.

Steel, O., Kraberger, S., Sikorski, A., Young, L.M., Catchpole, R.J., Stevens, A.J., Ladley, J.J., Coray, D.S., Stainton, D., Dayarama, A., Julian, L., van Bysterveldt, K., Varsani, A., 2016. Circular replication-associated protein encoding DNA viruses identified in the faecal matter of various animals in New Zealand. Infect. Genet. Evol. 43, 151-164.

Steinfeldt, T., Finsterbusch, T., Mankertz, A., 2006. Demonstration of nicking/joining activity at the origin of DNA replication associated with the rep and rep' proteins of porcine circovirus type 1. J. Virol. 80, 6225-6234.

Stenzel, T., Piasecki, T., Chrzastek, K., Julian, L., Muhire, B.M., Golden, M., Martin, D.P., Varsani, A., 2014. Pigeon circoviruses display patterns of recombination, genomic secondary structure and selection similar to those of beak and feather disease viruses. J. Gen. Virol. 95, 1338-1351.

Stover, R.H., 1972. Banana, plantain, and abaca diseases. Commonwealth Mycological Institute, Kew, England.

Tan, L.V., van Doorn, H.R., Nghia, H.D.T., Chau, T.T.H., Tu, L.T.P., de Vries, M., Canuti, M., Deijs, M., Jebbink, M.F., Baker, S., Bryant, J.E., Tham, N.T., Bkrong, N.T.T.C., Boni, M.F., Loi, T.Q., Phuong, L.T., Verhoeven, J.T.P., Crusat, M., Jeeninga, R.E., Schultsz, C., Chau, N.V.V., Hien, T.T., van der Hoek, L., Farrar, J., de Jong, M.D., 2013. Identification of a New Cyclovirus in Cerebrospinal Fluid of Patients with Acute Central Nervous System Infections. mBio 4, e00231-00213.

Thresh, J.M., Cooter, R.J., 2005. Strategies for controlling cassava mosaic virus disease in Africa. Plant Pathology 54, 587-614.

Tijssen, P., Penzes, J.J., Yu, Q., Pham, H.T., Bergoin, M., 2016. Diversity of small, single-stranded DNA viruses of invertebrates and their chaotic evolutionary past. J. Invertebr. Pathol. 140, 83-96.

Timchenko, T., de Kouchkovsky, F., Katul, L., David, C., Vetten, H.J., Gronenborn, B., 1999. A Single Rep Protein Initiates Replication of Multiple Genome Components of Faba Bean Necrotic Yellows Virus, a Single-Stranded DNA Virus of Plants. Journal of Virology 73, 10173-10182.

Timchenko, T., Katul, L., Sano, Y., de Kouchkovsky, F., Vetten, H.J., Gronenborn, B., 2000. The master Rep concept in nanovirus replication: Identification of missing genome components and potential for natural genetic reassortment. Virology 274, 189-195.

Tischer, I., Gelderblom, H., Vettermann, W., Koch, M.A., 1982. A very small porcine virus with circular single-stranded DNA. Nature 295, 64-66.

Tischer, I., Rasch, R., Tochtermann, G., 1974. Characterization of papovavirus-and picornavirus-like particles in permanent pig kidney cell lines. Zentralblatt fur Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene. Erste Abteilung Originale. Reihe A: Medizinische Mikrobiologie und Parasitologie 226, 153-167.

Todd, D., 2004. Avian circovirus diseases: lessons for the study of PMWS. Veterinary Microbiology 98, 169-174.

Tomaru, Y., Shirai, Y., Suzuki, H., Nagumo, T., Nagasaki, K., 2008. Isolation and characterization of a new single-stranded DNA virus infecting the cosmopolitan marine diatom *Chaetoceros dehilis*. Aquat. Microb. Ecol. 50, 103-112.

Tomaru, Y., Shirai, Y., Toyoda, K., Nagasaki, K., 2011a. Isolation and characterisation of a single-stranded DNA virus infecting the marine planktonic diatom *Chaetoceros tenuissimus*. Aquat. Microb. Ecol. 64, 175-184.

Tomaru, Y., Takao, Y., Suzuki, H., Nagumo, T., Koike, K., Nagasaki, K., 2011b. Isolation and Characterization of a Single-Stranded DNA Virus Infecting *Chaetoceros lorenzianus Grunow*. Appl. Environ. Microbiol. 77, 5285-5293.

Tomaru, Y., Toyoda, K., Kimura, K., Hata, N., Yoshida, M., Nagasaki, K., 2012. First evidence for the existence of pennate diatom viruses. ISME J. 6, 1445-1448.

Tomaru, Y., Toyoda, K., Suzuki, H., Nagumo, T., Kimura, K., Takao, Y., 2013. New single-stranded DNA virus with a unique genomic structure that infects marine diatom *Chaetoceros setoensi*s. Sci. Rep. 3, 8.

Toyoda, K., Kimura, K., Hata, N., Nakayama, N., Nagasaki, K., Tomaru, Y., 2012. Isolation and characterization of a single-stranded DNA virus infecting the marine planktonic diatom *Chaetoceros* sp. (strain TG07-C28). Plank. Benthos Res. 7, 20-28.

Tu, J., Guo, J., Li, J., Gao, S., Yao, B., Lu, Z., 2015. Systematic Characteristic Exploration of the Chimeras Generated in Multiple Displacement Amplification through Next Generation Sequencing Data Reanalysis. PLoS One 10, e0139857.

Uch, R., Fournier, P.E., Robert, C., Blanc-Tailleur, C., Galicher, V., Barre, R., Jordier, F., de Micco, P., Raoult, D., Biagini, P., 2015. Divergent Gemycircularvirus in HIV-Positive Blood, France. Emerg. Infect. Dis. 21, 2096-2098.

van den Brand, J.M., van Leeuwen, M., Schapendonk, C.M., Simon, J.H., Haagmans, B.L., Osterhaus, A.D., Smits, S.L., 2012. Metagenomic analysis of the viral flora of pine marten and European badger feces. J. Virol. 86, 2360-2365.

van der Walt, E., Martin, D.P., Varsani, A., Polston, J.E., Rybicki, E.P., 2008. Experimental observations of rapid Maize streak virus evolution reveal a strand-specific nucleotide substitution bias. Virol. J. 5, 104.

Varma, A., Mandal, B., Singh, M.K., 2011. Global Emergence and Spread of Whitefly (Bemisia tabaci) Transmitted Geminiviruses, in: Thompson, W.M.O. (Ed.), The Whitefly, Bemisia tabaci (Homoptera: Aleyrodidae) Interaction with Geminivirus-Infected Host Plants: Bemisia tabaci, Host Plants and Geminiviruses. Springer Netherlands, Dordrecht, pp. 205-292.

Varsani, A., Krupovic, M., 2017. Sequence-based taxonomic framework for the classification of uncultured single-stranded DNA viruses of the family Genomoviridae. Virus Evol. 3, vew037.

Varsani, A., Krupovic, M., 2018. Smacoviridae: a new family of animal-associated single-stranded DNA viruses. Arch. Virol. 163, 2005-2015.

Varsani, A., Monjane, A.L., Donaldson, L., Oluwafemi, S., Zinga, I., Komba, E.K., Plakoutene, D., Mandakombo, N., Mboukoulida, J., Semballa, S., Briddon, R.W., Markham, P.G., Lett, J.-M., Lefeuvre, P., Rybicki, E.P., Martin, D.P., 2009. Comparative analysis of Panicum streak virus and Maize streak virus diversity, recombination patterns and phylogeography. Virol. J. 6, 194.

Varsani, A., Navas-Castillo, J., Moriones, E., Hernández-Zepeda, C., Idris, A., Brown, J.K., Murilo Zerbini, F., Martin, D.P., 2014. Establishment of three new genera in the family Geminiviridae: Becurtovirus, Eragrovirus and Turncurtovirus. Arch. Virol. 159, 2193-2203.

Varsani, A., Roumagnac, P., Fuchs, M., Navas-Castillo, J., Moriones, E., Idris, A., Briddon, R.W., Rivera-Bustamante, R., Murilo Zerbini, F., Martin, D.P., 2017. Capulavirus and Grablovirus: two new genera in the family Geminiviridae. Arch. Virol. 162, 1819-1831.

Vega-Rocha, S., Byeon, I.J., Gronenborn, B., Gronenborn, A.M., Campos-Olivas, R., 2007a. Solution structure, divalent metal and DNA binding of the endonuclease domain from the replication initiation protein from porcine circovirus 2. J. Mol. Biol. 367, 473-487.

Vega-Rocha, S., Gronenborn, B., Gronenborn, A.M., Campos-Olivas, R., 2007b. Solution Structure of the Endonuclease Domain from the Master Replication Initiator Protein of the Nanovirus Faba Bean Necrotic Yellows Virus and Comparison with the Corresponding Geminivirus and Circovirus Structures. Biochemistry 46, 6201-6212.

Vetten, H.J., 2008. Nanoviruses, in: Mahy, B.W.J., Regenmortel, M.V. (Eds.), Encyclopedia of Virology, 3rd edn ed. Elsevier, Oxford, pp. 385-391.

Vidigal, P.M.P., Mafra, C.L., Silva, F.M.F., Fietto, J.L.R., Silva Júnior, A., Almeida, M.R., 2012. Tripping over emerging pathogens around the world: A phylogeographical approach for determining the epidemiology of Porcine circovirus-2 (PCV-2), considering global trading. Virus Res. 163, 320-327.

Vincent, I.E., Carrasco, C.P., Herrmann, B., Meehan, B.M., Allan, G.M., Summerfield, A., McCullough, K.C., 2003. Dendritic cells harbor infectious porcine circovirus type 2 in the absence of apparent cell modulation or replication of the virus. J. Virol. 77, 13288-13300.

Waits, K., Edwards, M.J., Cobb, I.N., Fontenele, R.S., Varsani, A., 2018. Identification of an anellovirus and genomoviruses in ixodid ticks. Virus Genes 54, 155-159.

Walker, I.W., Konoby, C.A., Jewhurst, V.A., McNair, I., McNeilly, F., Meehan, B.M., Cottrell, T.S., Ellis, J.A., Allan, G.M., 2000. Development and Application of a Competitive Enzyme-Linked Immunosorbent Assay for the Detection of Serum Antibodies to Porcine Circovirus Type 2. J. Vet. Diagn. Invest. 12, 400-405.

Wang, H., Li, S.X., Mahmood, A., Yang, S.X., Wang, X.C., Shen, Q., Shan, T.L., Deng, X.T., Li, J.J., Hua, X.G., Cui, L., Delwart, E., Zhang, W., 2018. Plasma virome of cattle from forest region revealed diverse small circular ssDNA viral genomes. Virol. J. 15, 11.

Wege, C., Gotthardt, R.-D., Frischmuth, T., Jeske, H., 2000. Fulfilling Koch's postulates for Abutilon mosaic virus. Arch. Virol. 145, 2217-2225.
Whon, T.W., Kim, M.S., Roh, S.W., Shin, N.R., Lee, H.W., Bae, J.W., 2012. Metagenomic characterization of airborne viral DNA diversity in the near-surface atmosphere. J. Virol. 86, 8221-8231.
Woo, P.C., Lau, S.K., Teng, J.L., Tsang, A.K., Joseph, M., Wong, E.Y., Tang, Y., Sivakumar, S., Bai, R., Wernery, R., Wernery, U., Yuen, K.Y., 2014. Metagenomic analysis of viromes of dromedary camel fecal samples reveals large number and high diversity of circoviruses and picobirnaviruses. Virology 471-473, 117-125.
Wu, B., Melcher, U., Guo, X., Wang, X., Fan, L., Zhou, G., 2008. Assessment of codivergence of Mastreviruses with their plant hosts. BMC Evol. Biol. 8, 335.
Wu, Z., Yang, L., Ren, X., He, G., Zhang, J., Yang, J., Qian, Z., Dong, J., Sun, L., Zhu, Y., Du, J., Yang, F., Zhang, S., Jin, Q., 2016. Deciphering the bat virome catalog to better understand the ecological diversity of bat viruses and the bat origin of emerging infectious diseases. ISME J. 10, 609-620.
Wyant, P.S., Strohmeier, S., Schäfer, B., Krenz, B., Assunção, I.P., Lima, G.S.d.A., Jeske, H., 2012. Circular DNA genomics (circomics) exemplified for geminiviruses in bean crops and weeds of northeastern Brazil. Virology 427, 151-157.
Xia, H., Wang, Y., Shi, C., Atoni, E., Zhao, L., Yuan, Z., 2018. Comparative Metagenomic Profiling of Viromes Associated with Four Common Mosquito Species in China. Virol Sin 33, 59-66.
Yoon, H.S., Price, D.C., Stepanauskas, R., Rajah, V.D., Sieracki, M.E., Wilson, W.H., Yang, E.C., Duffy, S., Bhattacharya, D., 2011. Single-Cell Genomics Reveals Organismal Interactions in Uncultivated Marine Protists. Science 332, 714.
Yoshida, M., Takaki, Y., Eitoku, M., Nunoura, T., Takai, K., 2013. Metagenomic analysis of viral communities in (hado)pelagic sediments. PLoS One 8, e57271.
Yu, X., Li, B., Fu, Y., Xie, J., Cheng, J., Ghabrial, S.A., Li, G., Yi, X., Jiang, D., 2013. Extracellular transmission of a DNA mycovirus and its use as a natural fungicide. Proc. Natl. Acad. Sci. USA 110, 1452-1457.
Yu, X., Li, B., Fu, Y.P., Jiang, D.H., Ghabrial, S.A., Li, G.Q., Peng, Y.L., Xie, J.T., Cheng, J.S., Huang, J.B., Yi, X.H., 2010. A geminivirus-related DNA mycovirus that confers hypovirulence to a plant pathogenic fungus. Proc. Natl. Acad. Sci. USA 107, 8387-8392.
Zawar-Reza, P., Arguello-Astorga, G.R., Kraberger, S., Julian, L., Stainton, D., Broady, P.A., Varsani, A., 2014. Diverse small circular single-stranded DNA viruses identified in a freshwater pond on the McMurdo Ice Shelf (Antarctica). Infect. Genet. Evol. 26, 132-138.
Zerbini, F.M., Briddon, R.W., Idris, A., Martin, D.P., Moriones, E., Navas-Castillo, J., Rivera-Bustamante, R., Roumagnac, P., Varsani, A., Consortium, I.R., 2017. ICTV Virus Taxonomy Profile: Geminiviridae. J. Gen. Virol. 98, 131-133.
Zhang, W., Li, L., Deng, X., Kapusinszky, B., Pesavento, P.A., Delwart, E., 2014. Faecal virome of cats in an animal shelter. J. Gen. Virol. 95, 2553-2564.
Zhang, W., Yang, S., Shan, T., Hou, R., Liu, Z., Li, W., Guo, L., Wang, Y., Chen, P., Wang, X., Feng, F., Wang, H., Chen, C., Shen, Q., Zhou, C., Hua, X., Cui, L., Deng, X., Zhang, Z., Qi, D., Delwart, E., 2017. Virome comparisons in wild-diseased and healthy captive giant pandas. Microbiome 5, 90.

Zhou, X., 2013. Advances in understanding begomovirus satellites. Annu. Rev. Phytopathol. 51, 357-381.

Zhou, X., Liu, Y., Calvert, L., Munoz, C., Otim-Nape, G.W., Robinson, D.J., Harrison, B.D., 1997. Evidence that DNA-A of a geminivirus associated with severe cassava mosaic disease in Uganda has arisen by interspecific recombination. J. Gen. Virol. 78, 2101-2111.