# ICTV Virus Taxonomy Profile: Redondoviridae 

Arwa Abbas ${ }^{1} \dagger$, Louis J. Taylor${ }^{2} \dagger$, Ronald G. Collman ${ }^{2,3}$, Frederic D. Bushman²,* and ICTV Report Consortium


#### Abstract

Viruses in the family Redondoviridae have a circular genome of 3.0 kb with three open reading frames. The packaged genome is inferred to be single-stranded DNA by analogy to related viruses. Redondoviruses were discovered through metagenomic sequencing methods in samples from human subjects and are inferred to replicate in humans. Evidence of redondovirus infection is associated with periodontitis and critical illness, but redondoviruses have not been shown to be the causative agent of any diseases. This is a summary of the International Committee on Taxonomy of Viruses (ICTV) Report on the family Redondoviridae, which is available at ictv.global/report/redondoviridae.


Table 1. Characteristics of members of the family Redondoviridae

| Example: | human respiratory-associated brisavirus, isolate LC (KY052047), species Brisavirus, genus Torbevirus |
| :--- | :--- |
| Virion | Unknown |
| Genome | Circular 3.0 kb, inferred to be single-stranded DNA |
| Replication | Presumed to be by a rolling-circle mechanism |
| Translation | Unknown |
| Host range | Human <br> Taxonomy <br> two species |

## VIRION

The physical structure and properties of redondovirus particles are unknown. The capsid protein likely derives from the largest open reading frame (ORF). The number and orientation of capsomer units is unknown.

## GENOME

The genome is circular and inferred to be ssDNA (Table 1) [1]. The genome has three ORFs, with the two largest ORFs in opposite orientations. One ORF ( $C p$ ) encodes the putative capsid and one ( Rep ) encodes the replicationassociated protein (Rep). A third ORF, which overlaps $C p$, encodes a protein with no homology to any known protein,
but is conserved amongst all genome isolates. A stem-loop structure with a conserved nonanucleotide motif is found before the beginning of the Rep coding sequence (Fig. 1) [1] and is a likely candidate for the origin of replication, as in related circoviruses [2].

## REPLICATION

Since redondoviruses do not encode a DNA polymerase, the replication cycle is presumed to be similar to the rolling-circle mechanism used by other circular DNA elements such as ssDNA viruses and bacterial plasmids. In this model, upon entry of a host cell and uncoating of the virion, the viral ssDNA genome is converted to dsDNA by

[^0]

Fig. 1. Redondovirus genome structure. Three ORFs (coloured arrows) flank a hairpin loop that contains the conserved nonanucleotide sequence shown.
host polymerases. The viral Rep protein binds in a sequencespecific manner to the stem-loop structure and nicks the dsDNA, creating a free $3^{\prime}$-hydroxyl end from which viral DNA synthesis can begin. The Rep protein, meanwhile, remains covalently bonded to the $5^{\prime}$-phosphate end. After one round of genome synthesis, the Rep protein releases one ssDNA genome, and the dsDNA template is regenerated for additional rounds of rolling-circle replication. Other details are unknown.

## PATHOGENICITY

Redondovirus nucleic acid sequences have been detected in both healthy humans and those with various diseases. The first reported genome was discovered in the respiratory tract of a febrile patient [3] who tested negative for a limited panel of other pathogens. Subsequently, full-length genomes were found in bronchoalveolar lavage from organ transplant donor lungs, lung transplant recipients and patients with sarcoidosis [4-6]. A large screen of metagenomic samples from humans, animals and the environment revealed that redondoviral genome sequences were only detected with reasonable certainty in human samples, primarily from the oro-respiratory tract, but also in the gut [1]. Detection by qPCR also revealed that redondovirus nucleic acid was present at relatively high levels in
the upper and lower respiratory tract of patients in intensive care units, compared to healthy humans. Analysis of sequences [1] from two metagenomic studies of the oral cavity [7, 8] showed that the presence and abundance of redondoviral genome sequence was associated with periodontitis. Redondoviruses were also detected in sputum from a patient with respiratory symptoms in the absence of any identified respiratory pathogen [9].

## TAXONOMY

Current taxonomy: ictv.global/taxonomy. The genus Torbevirus includes the species Brisavirus and Vientovirus.

## RESOURCES

Current ICTV Report on the family Redondoviridae: ictv. global/report/redondoviridae

## Funding information

Production of this summary, the online chapter and associated resources was funded by a grant from the Wellcome Trust (WT108418AIA). Further support includes NIH grants R61-HL137063, R01-HL113252, and T32-AI-007324 and NSF grant DGE-1321851.

## Acknowledgements

Members of the ICTV Report Consortium are Stuart G. Siddell, Andrew J. Davison, Elliot J. Lefkowitz, Sead Sabanadzovic, Peter Simmonds, Donald B. Smith, Richard J. Orton and Balázs Harrach.

Conflicts of interest
The authors declare that there are no conflicts of interest.

## References

1. Abbas AA, Taylor LJ, Dothard MI, Leiby JS, Fitzgerald AS et al. Redondoviridae, a family of small, circular DNA viruses of the human oro-respiratory tract associated with periodontitis and critical illness. Cell Host Microbe 2019;25:719-729.
2. Mankertz A, Persson F, Mankertz J, Blaess G, Buhk HJ. Mapping and characterization of the origin of DNA replication of porcine circovirus. J Virol 1997;71:2562-2566.
3. Cui L, Wu B, Zhu X, Guo X, Ge Y et al. Identification and genetic characterization of a novel circular single-stranded DNA virus in a human upper respiratory tract sample. Arch Virol 2017;162:3305-3312.
4. Abbas AA, Diamond JM, Chehoud C, Chang B, Kotzin JJ et al. The perioperative lung transplant virome: torque teno viruses are elevated in donor lungs and show divergent dynamics in primary graft dysfunction. Am J Transplant 2017;17:1313-1324.
5. Abbas AA, Young JC, Clarke EL, Diamond JM, Imai I et al. Bidirectional transfer of Anelloviridae lineages between graft and host during lung transplantation. Am J Transplant 2019;19:1086-1097.
6. Clarke EL, Lauder AP, Hofstaedter CE, Hwang Y, Fitzgerald AS et al. Microbial lineages in sarcoidosis. A metagenomic analysis tailored for low-microbial content samples. Am J Respir Crit Care Med 2018;197:225-234.
7. Shi B, Chang M, Martin J, Mitreva M, Lux R et al. Dynamic changes in the subgingival microbiome and their potential for diagnosis and prognosis of periodontitis. mBio 2015;6:e01926-14.
8. Califf KJ, Schwarzberg-Lipson K, Garg N, Gibbons SM, Caporaso JG et al. Multi-Omics analysis of periodontal pocket microbial communities pre- and posttreatment. mSystems 2017;2:e:00016-17.
9. Lázaro-Perona F, Dahdouh E, Román-Soto S, Jiménez-Rodríguez S, Rodríguez-Antolín C et al. Metagenomic detection of two vientoviruses in a human sputum sample. Viruses 2020;12:327.

[^0]:    Received 29 October 2020; Accepted 02 November 2020; Published 01 December 2020
    Author affiliations: ${ }^{1}$ Department of Pathology and Laboratory Medicine, Children's Hospital of Philadelphia, Philadelphia, PA, USA; ${ }^{2}$ Department of Microbiology, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA; ${ }^{3}$ Department of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA.
    *Correspondence: Frederic D. Bushman, bushman@pennmedicine.upenn.edu
    Keywords: Redondoviridae; ICTV Report; taxonomy; torbevirus; CRESS DNA virus.
    Abbreviations: Cp, capsid; qPCR, quantitative polymerase chain reaction; Rep, replication-associated protein.
    $\dagger$ These authors contributed equally to this work
    001526 © 2021

