



# ICTV Virus Taxonomy Profile: *Inoviridae*

Petar Knezevic<sup>1,\*</sup>, Evelien M. Adriaenssens<sup>2</sup> and ICTV Report Consortium

## Abstract

Members of the family *Inoviridae* are non-enveloped flexible filamentous bacteriophages (600–2500×6–10 nm) with supercoiled, circular, positive-sense, single-stranded DNA genomes of 5.5–10.6 kb, encoding 7–15 proteins. They absorb to the pili of Gram-negative bacteria and replicate their DNA by a rolling-circle mechanism with progeny released from cells by extrusion without killing the host. Phage DNA can persist extra-chromosomally or integrate into the bacterial genome. This is a summary of the International Committee on Taxonomy of Viruses (ICTV) Report on the family *Inoviridae*, which is available at [ictv.global/report/inoviridae](https://www.ictv.global/report/inoviridae).

**Table 1.** Characteristics of members of the family *Inoviridae*

<b>Example:</b>	<b><i>Escherichia</i> phage M13 (V00604), species <i>Escherichia virus M13</i>, genus <i>Inovirus</i></b>
Virion	Non-enveloped flexible filaments; 6–10 nm in diameter, 600–2500 nm in length
Genome	5.5–10.6 kb, supercoiled, circular, positive-sense, single-stranded DNA, encoding 7–15 proteins
Replication	Rolling-circle mechanism
Translation	From mRNAs
Host range	Gram-negative bacteria
Taxonomy	Realm <i>Monodnaviria</i> , kingdom <i>Loebvirae</i> , phylum <i>Hofneiviricota</i> , class <i>Faserviricetes</i> , order <i>Tubulavirales</i> ; >20 genera and >25 species

## VIRION

Virions are non-enveloped, with the major coat protein helically organized around circular, positive-sense, single-stranded DNA [(+) ssDNA], forming long, flexible filaments whose length depends on the genome length, varying from 600 to 2500 nm with a diameter of 6–10 nm (Table 1). Virions of *Escherichia* phage M13, a member of the species *Escherichia virus M13*, are built up from 2700 copies of the major coat protein (CoaB; p8), with 5 copies each of p7 and p9 forming a blunt end, and of p3 (CoaA) and p6 forming a rounded end (Fig. 1) (reviewed in [1]).

## GENOME

The circular (+) ssDNA genome of members of the family *Inoviridae* has 7–15 protein coding regions with minimal inter-genic regions; some genes overlap or are embedded

within larger genes. The genome is organized in modules (Fig. 2): a DNA replication module, a structural module and a morphogenesis (assembly/extrusion) module, while inter-genic regions contain the origin of replication, packaging signals and promoters. Phages that are able to integrate into the bacterial chromosome have genomes containing insertion sequences and encode proteins for latent stage regulation (repressor), while some phages encode integration proteins (integrase or transposase). The repressor genes of integrative phages are usually expressed from the complementary (–) strand. The G+C content is 40.5–60.7%.

## REPLICATION

For *Escherichia* phage M13, infection starts when p3 (adhesion protein, CoaA) interacts with pili on the bacterial

Received 13 May 2021; Accepted 14 May 2021; Published 06 July 2021

**Author affiliations:** <sup>1</sup>University of Novi Sad, Faculty of Sciences, Department of Biology and Ecology, Trg Dositeja Obradovica 3, 21000 Novi Sad, Vojvodina, Serbia; <sup>2</sup>Quadram Institute Bioscience, Norwich Research Park, Norwich NR4 7UQ, UK.

**\*Correspondence:** Petar Knezevic, petar.knezevic@dbe.uns.ac.rs

**Keywords:** ICTV Report; taxonomy; *Inoviridae*.

**Abbreviations:** RF, replicative form; (+) ssDNA, positive-sense, single-stranded DNA.

001614 © 2021



This is an open-access article distributed under the terms of the Creative Commons Attribution License.

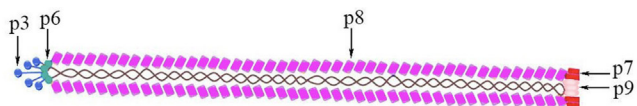


Fig. 1. Schematic drawing of Escherichia phage M13 virion.

cell surface (adhesion receptor) and TolQRA co-receptor (entry receptor) [2]. Phage (+) ssDNA is translocated into the bacterial cytoplasm and converted by bacterial polymerases into covalently bound dsDNA, the replicative form (RF) [3]. mRNAs are transcribed from the RF by host RNA polymerases and translated by the host machinery. Replication of DNA starts when p2, with endonuclease activity, nicks dsDNA at the origin site [4]. Host DNA polymerase synthesizes (+) ssDNA from the complementary strand of RF by a rolling-circle mechanism and these are converted back into RFs that serve as templates for transcription. At high concentrations of p5, its homodimers cover newly synthesized (+) ssDNA molecules, preventing further conversion of (+) ssDNA into RF and collapsing (+) ssDNA into filaments. A double-stranded packaging signal remains uncovered at the blunt end of the filament. The structural proteins integrate into the cytoplasmic membrane, together with p4, p1

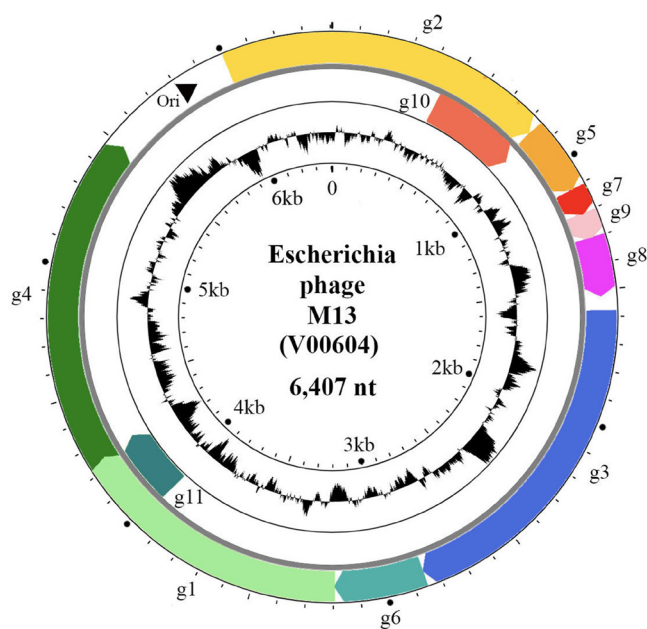


Fig. 2. Escherichia phage M13 (V00604) circular genome. Genes (coloured arrows) are organized in modules of replication genes (g2, g5 and g10), structural genes (g7, g9, g8, g3, g6) and morphogenesis genes (g1, g4 and g11). Inner circle indicates GC content.

and p11 that form the assembly machinery [5]. Virions are released by extrusion during the replacement of p5 with p8, the major coat protein (CoaB). Proteins p7 and p9 are the first to extrude, followed by numerous copies of p8, while p3 and p6 are added at the end of the process. New virions are released into the environment, without killing the host.

## TAXONOMY

Current taxonomy: [www.ictv.global/taxonomy](http://www.ictv.global/taxonomy). The family *Inoviridae* belongs to the order *Tubulavirales*, along with the families *Plectroviridae* and *Paulinoviridae*. More than 20 genera are included in the family, many of which only have a single species. Members of the same genus share considerable DNA sequence similarity (identity×query coverage), and also >50% amino acid sequence similarity for the morphogenesis (Zot; p1) and major coat (CoaB; p8) proteins. Phages belonging to the same species are ≥95% identical in DNA sequence over the entire genome length and have significant CoaA amino acid sequence similarity.

## RESOURCES

Full ICTV Report on the family *Inoviridae*: [www.ictv.global/report/inoviridae](http://www.ictv.global/report/inoviridae).

### Funding information

Production of this Profile, the ICTV Report, and associated resources was funded by a grant from the Wellcome Trust (WT108418A1A). E.M.A. gratefully acknowledges the support of the Biotechnology and Biological Sciences Research Council (BBSRC); this research was funded by the BBSRC Institute Strategic Programme Gut Microbes and Health BB/R012490/1 and its constituent project BBS/E/F/000PR10353, as well as the project PHANTER funded by Science Fund, Republic of Serbia.

### Acknowledgements

The authors would like to thank Nabil-Fareed Alikhan for bioinformatics support. Members of the ICTV Report Consortium are Stuart G. Siddell, Elliot J. Lefkowitz, Sead Sabanadzovic, Peter Simmonds, F. Murilo Zerbini, Donald B. Smith, Richard J. Orton and Evelien M. Adriaenssens.

### Conflicts of interest

The authors declare that there are no conflicts of interest.

### References

1. Rasched I, Oberer E. Ff coliphages: structural and functional relationships. *Microbiol Rev* 1986;50:401–427.
2. Click EM, Webster RE. The TolQRA proteins are required for membrane insertion of the major capsid protein of the filamentous phage f1 during infection. *J Bacteriol* 1998;180:1723–1728.
3. Geider K, Kornberg A. Conversion of the M13 viral single strand to the double-stranded replicative forms by purified proteins. *J Biol Chem* 1974;249:3999–4005.
4. Meyer TF, Geider K, Kurz C, Schaller H. Cleavage site of bacteriophage fd gene II-protein in the origin of viral strand replication. *Nature* 1979;278:365–367.
5. Feng JN, Model P, Russel M. A trans-envelope protein complex needed for filamentous phage assembly and export. *Mol Microbiol* 1999;34:745–755.