# ICTV Virus Taxonomy Profile: Arenaviridae 

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#### Abstract

Members of the family Arenaviridae produce enveloped virions containing genomes consisting of two or three single-stranded RNA segments totalling about 10.5 kb . Arenaviruses can infect mammals, including humans and other primates, snakes, and fish. This is a summary of the International Committee on Taxonomy of Viruses (ICTV) Report on the family Arenaviridae, which is available at www.ictv.global/report/arenaviridae.


Table 1. Characteristics of members of the family Arenaviridae

| Typical member: | lymphocytic choriomeningitis virus, Armstrong 53b (S segment: AY847350; L segment: AY847351), species <br> Lymphocytic choriomeningitis mammarenavirus, genus Mammarenavirus |
| :--- | :--- |
| Virion | Enveloped, pleomorphic virions $40-200 \mathrm{~nm}$ in diameter with trimeric surface spikes |
| Genome | Two or three single-stranded, usually ambisense, RNA molecules called small (S), medium (M) and large (L) |
| Replication | Ribonucleoprotein complexes containing anti-genomic RNA serve as templates for synthesis of genomic RNA |
| Translation | From capped and non-polyadenylated mRNAs. The 5'-cap structure is derived by polymerase slippage or cap- <br> snatching from cellular mRNAs |
| Taxonomy range | Fish (antennaviruses), mammals (mammarenaviruses) and reptiles (hartmaniviruses and reptarenaviruses), but <br> possibly also bats and ticks |
|  | Realm Riboviria, phylum Negarnaviricota, subphylum Polyploviricotina, class Ellioviricetes, order Bunyavirales. The <br> family includes several genera and $>40$ species |

## VIRION

Virions are spherical or pleomorphic in shape, $40-200 \mathrm{~nm}$ in diameter, with dense lipid envelopes (Table 1 and Fig. 1). The virion surface layer is covered with club-shaped projections with distinctive stalk and head regions. These projections
consist of trimeric spike structures of two virus-encoded membrane glycoprotein (GP) subunits (GP1 and GP2) and, in the case of some arenaviruses, a stable signal peptide (SSP). Isolated ribonucleoprotein (RNP) complexes appear as 'beads-on-a-string'-like structures [1-3].

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Fig. 1. (a) Electron micrograph of lymphocytic choriomeningitis virus particles, showing dark internal inclusion bodies, budding from an infected cell. (b) Schematic illustration of a (mammalian) arenavirus particle. Shown is the spherical and enveloped (grey) particle that is spiked with glycoproteins (GP, gold) around a layer of zinc finger matrix proteins (Z, brown; missing in hartmaniviruses). The small and large ribonucleoprotein (RNP) complexes inside the particle consist of nucleoprotein (NP, blue) and RNA-dependent RNA polymerase (L, green).


Fig. 2. Schematic representation of the bisegmented genome organization of the mammalian arenavirus lymphocytic choriomeningitis virus. The $5^{\prime}$ - and $3^{\prime}$-ends of both segments ( $S$ and $L$ ) are complementary at their termini, probably promoting the formation of circular RNP complexes within the virion. GPC, glycoprotein precursor; L, RNA-dependent RNA polymerase; NP, nucleoprotein; Z, zinc finger matrix protein. ORFs are separated by non-coding IGRs with predicted hairpin structures (not shown).

## GENOME

Arenavirus genomes consist of two or three single-stranded, typically ambisense RNA molecules, termed small (S), medium (M) and large (L). Some of these RNAs encode two proteins in non-overlapping ORFs of opposite polarities that are separated by non-coding intergenic regions (IGRs) (Fig. 2). The S RNA encodes nucleoprotein (NP) in the virus genome-complementary sequence, and, in many cases, the virus glycoprotein precursor (GPC) in the virus genome-sense sequence. The L RNA encodes the L protein in the virus genome-complementary sequence, and, in some cases, the zinc-finger matrix protein $(Z)$ in the virus genome-sense sequence [1-4].

## REPLICATION

Arenaviruses attach to cell-surface receptors and enter via the endosomal route. pH -dependent fusion with late endosomes releases the virion RNP complex into the cytoplasm. In some arenaviruses, this pH -dependent fusion event requires the previous participation of an intracellular receptor. The virus RNP directs both RNA genome replication and gene
transcription. During replication, L reads through the IGR transcription-termination signal and generates uncapped antigenomic and genomic RNAs. In ambisense coding arrangements, transcription of mRNAs encoding GPC and Z occurs only after the first round of virus replication, during which S and L antigenomes are produced.

Arenavirus proteins are synthesized from subgenomic mRNAs that lack $3^{\prime}$-terminal poly(A) and in which the $5^{\prime}$-cap is followed by several non-templated bases, possibly the result of cap-snatching.

Virion budding occurs from the cellular plasma membrane, thereby providing the virion envelope [1-3].

## TAXONOMY

Arenaviruses form a family in the order Bunyavirales. Within this order, arenaviruses are most closely related to members of the family Mypoviridae. Arenaviruses differ from most other bunyaviruses by having segmented genomes with an ambisense organization. The family includes several genera and $>40$ species. Some arenaviruses can cause severe and sometimes fatal diseases in humans (e.g. Lassa fever) [5]. Other arenaviruses cause disease in captive snakes [4, 6], and some arenaviruses can infect fish [4].

## Resources

Full ICTV Report on the family Arenaviridae: www.ictv.global/report/arenaviridae.

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## Conflicts of interest

The authors declare that there are no conflicts of interest.

## References

1. Buchmeier MJ, de la Torre JC, Peters CJ. Arenaviridae. In: Knipe DM and Howley PM (editors). Fields Virology, 6th ed. Philadelphia, USA: LippincottWilliams \&Wilkins; 2013. pp. 1283-1303.
2. Hallam SJ, Koma T, Maruyama J, Paessler S. Review of Mammarenavirus biology and replication. Front Microbiol 2018;9:1751.
3. Radoshitzky SR, Bào Y, Buchmeier MJ, Charrel RN, Clawson AN et al. Past, present, and future of arenavirus taxonomy. Arch Virol 2015;160:1851-1874.
4. Shi M, Lin X-D, Chen X, Tian J-H, Chen L-J et al. The evolutionary history of vertebrate RNA viruses. Nature 2018;556:197-202.
5. Radoshitzky SR, Kuhn JH, Jahrling PB, Bavari S. Hemorrhagic fever-causing mammarenaviruses. In: Bozue J, Cote CK and Glass PJ (editors). Medical Aspects of Biological Warfare. Fort Sam Houston, USA: Borden Institute, US Army Medical Department Center and School, Health Readiness Center of Excellence; 2018. pp. 517-545.
6. Pontremoli C, Forni D, Cagliani R, Sironi M. Analysis of Reptarenavirus genomes indicates different selective forces acting on the $S$ and $L$ segments and recent expansion of common genotypes. Infect, Genet Evol 2018;64:212-218.

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    Abbreviations: GP, glycoprotein; GPC, glycoprotein precursor; IGR, intergenic region; NP, nucleoprotein; RNP, ribonucleoprotein; SSP, stable signal peptide.
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