The Role of Arena Virus Protein and Their Molar Ratio

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Abstract: *The current investigates the role of Arenavirus protein and their molar ratio. The arenavirus L protein has the characteristic sequence motifs conserved among the RdRp (L proteins) of NS RNA virus. The proposed polymerase module of L is located within domain 3 which contains highly conserved amino acids within motifs designated A and C. The L RNA segment encodes a high-molecular-mass protein (L; ca. 200 kDa) which has the characteristic motifs conserved in all the viral RNA dependent RNA polymerases and a small polypeptide Z (ca.11 kDa) which contains a RING finger motif and whose function is unknown (1, 19, 33) . The L RNA segment codes for the virus RNA-dependent RNA polymerase (L, ca 200 kDa) (19) and a small (11-kDa) RING finger protein (Z) (17).*

Key Words: *Role, Arenavirus, protein, molar ratio*

Introduction:

The genus arenavirus belongs to family Arenaviredae. This family currently comprises 22 viral species as recognized by the International Committee for Taxonomy of viruses (31). Newly discovered arena-like viruses such as Kadoka, Morogoro, Pinhal ,Chapare, Skinner Tank, Catarina and Dandenong virus, whose taxonomic status has not yet been determined by ICTV, represent putative new species. Arenavirus can be divided into two serogroups which differ genetically and by geographical distribution. It is assumed that humans usually become infected with arenavirus by inhalation of virus in aerosolized droplets of secretions or excretions from infected rodents .The family Arenaviredae is divided into old world and new world complexes. The New World serogroups can be subdivided into three clades, as shown in Fig. 1. All known arenaviruses are rodent-borne with the exception of Tacaribe virus, which was isolated from bats (10). Host species for arenaviruses are listed in Table 1.

Table 1. List of arenavirus species and newly discovered arenavirus not yet classified, and respective characteristics (adapted from (9)"

Virus	Acronym	Lineage	Country	Host	Path[5]
Allpahuayo	ALLV	NW-A[1]	Peru	*Oecomys bicolor, O. paricola*	
Amapari	AMAV	NW-B	Brazil	*Oryzomys goeldi, Neacomys guianae*	
Bear Canyon	BCNV	NW-Rec[2]	USA	*Peromyscus californicus, Neotoma macrotis*	
Catarina	NA[3]	NW-Rec	USA	*Neotoma micropus*	
Chapare	NA	NW-B	Bolvia	Unknown	Y
Cupixi	CPXV	NW-B	Brazil	*Oryzomys capito*	
Dandenong	NA	OW	Australia	Unknown	Y
Flexal	FLEV	NW-A	Brazil	*Oryzomys spp.*	
Guanarito	GTOV	NW-B	Venezuela	*Zygomtomys brevicauda, Sigmodon alstoni*	Y
Ippy	IPPYV	OW	Central African Republic	*Arvicanthus spp.*	
Junin	JUNV	NW-B	Argentina	*Callomys musculinus*	Y
Kodoko	NA	OW	Guinea	*Mus Nannomys minutoides*	
Lassa	LASV	OW	West Africa	*Mastomys natalensis*	Y
Latino	LATV	NW-C	Bolivia	*Callomys callosus*	
LCMV[4]	LCMV	OW	Ubiquitous	*Mus musculus, M. Domesticus*	Y
Lujo	LUJOV	OW	South Africa	Unknown	Y
Machupo	MACV	NW-B	Bolivia	*Callomys callosus*	Y
Mobala	MOBV	OW	Central	*Praomys spp.*	

			African Republic		
Mopeia	MOPV	OW	Mozambique, Zimbabwe	*Mastomys natalensis*	
Morogoro	NA	OW	Tanzania	*Mastomys sp.*	
Oliveros	OLVV	NW-C	Argentina	*Bolomys spp.*	
Pampa	NA	NW-C	Argentina	*Bolomys spp.*	
Parana	PARV	NW-A	Paraguay	*Oryzomys buccinatus*	
Pichinde	PICV	NW-A	Colombia	*Oryzomys albigularis*	
Pinhal	NA	NW-C	Brazil	*Calomys tener*	
Pirital	PIRV	NW-A	Venezuela	*Sigmodon alstoni*	
Sabia	SABV	NW-B	Brazil	Unknown	Y
Skinner Tank	NA	NW-Rec	USA	*Neotoma Mexicana*	
Tonto Creek	NA	NW-Rec	USA	*Neotoma spp.*	
Tacaribe	TCRV	NW-B	Trinidad	*Artibeus bat*	
Tamiami	TAMV	NW-Rec	USA	*Sigmodon hispidus*	
Whitewater Arroyo	WWAV	NW-Rec	USA	*Neotoma spp.*	?

[1]New World (NW) virus clades A-C and Old World arenaviruses
[2]Recent New World arenavirus isolate
[3]Not available
[4]Lymphocytic Choriomeningitis Virus
[5]Significant human pathogens are marked "Y"

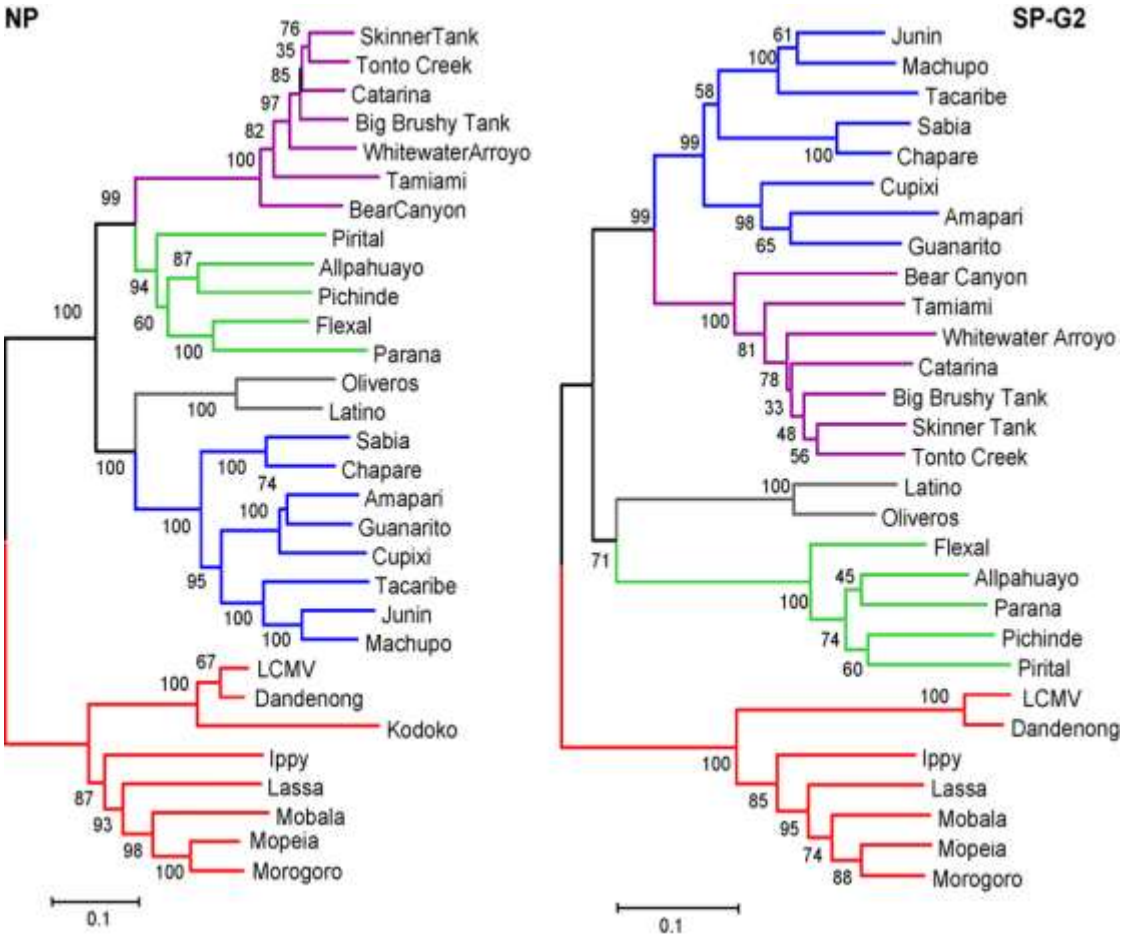

Figure1. Phylogenetic relationships between arena viruses within evolutionary lineages from (9). Red, Old world viruses; Green, lineage A new world viruses, Blue, lineage B new world viruses; Grey, lineage C new world viruses; Purple, recombinant new world viruses. Left panel, phylogram based on nucleoprotein amino acid sequences, right panel, and phylogram based on concatenated signal peptide and glycoprotein two amino acid sequences. The neighbor-joining, poisson and bootstrapping (200 pseudo replications) algorithms were computed by MEGA 2 software package.

Arenavirus particles are spherical and have an average diameter of 110-130nm. All are enveloped in a lipid bilayer. Arenaviruses are enveloped and have a bisegmented negative-strand (NS) RNA genome. Each RNA segment has an ambisense coding strategy, encoding two proteins in opposite orientations, separated by an antigenic region (2, 3, 38). The two genomic RNA segments are designated L and S and have approximate sizes of 7.2 and 3.4 kb, respectively (28, 29, 32).

All *cis*-acting signals required for encapsidation and polymerase entry of negative-strand RNA viruses appeared to be located within the 59- and 39-terminal untranslated regions(UTRs)(11). The 3" terminus of genomic RNAs in highly conserved among other members of the family *Arenaviredae*, suggesting that these 19 terminal nt may contain *cis* acting signals for the replication and transcription. The IGRs in both L and S segments have the potential to form stable stem-loop (hairpin) structures (1, 33, 38). Arenavirus transcribe subgenomic messager RNA for each of the five viral protein. The viral 3" ends of the mRNAs, which are nonpolyadenylated and heterologous, have been mapped to the base of the hairpin on the distal sides (15, 22) , suggesting a possible transcriptional regulatory role of the IGR.

Arenavirus protein coding strategy:

The S RNA directs synthesis of the three major structural proteins: the nucleoprotein, NP (ca. 63 kDa);and two mature virion glycoproteins, GP-1 (40 to 46 kDa) and GP-2 (35 kDa), that are derived by posttranslational cleavage of a precursor polypeptide, GP-C (75 kDa) (28, 34) . The Nucleoprotein (Mr 60-68 kDA) is the most abundant viral polypeptide both in infected cells and in virions (about 1530 NP molecules per virion particle). The NP and viral polymerase are complexed with the genomic viral RNA to form ribonucleoprotein (RNP) complexes, which are active in virus transcription and replication(18). The NP, the most abundant viral protein in virally infected cells, is associated with the viral RNA (vRNA) to form the nucleocapsid (NC) which is the template for the viral RNA polymerase (19) . The phosphorylated forms of the NP are usually detected at late stages of acute infection, and their abundance increases in persistently infected cells; however, the functional implications of these changes in the stage of NP phosphorylation have not been established (6).The NP is the main structural element of the viral nucleocapsid and associates with the genome RNA to form beadlike structures.

The virion contains four structural proteins Glycoprotein GP-C (cleaved into Stable Single Peptide (SSP), GP-1, GP-2), Matrix protein Z and Nucleoprotein(NP) (see table 2): (i) the large cleaved transmembrane glycoprotein (GP), which is similar in organization to type I membrane fusion proteins (20); (ii) a budding factor Z, which contains a metal-binding RING finger domain and regulates viral transcription and translation; (iii) the RNA binding nucleoprotein (NP), which is required for viral RNA polymerase activity; and (iv) a small, predominantly hydrophobic structural protein, organized similarly to the alphavirus 6K protein, that serves as a cleaved signal sequence for GP and is incorporated in the virion (13, 14, 16). In addition, the viral replicase protein is incorporated at a low copy number (see Fig 2)

Table 2. Arenavirus protein and their molar ratio.

	Transmembrane	Molar ratio
SSP	2	3
GP1	0	3
GP2	1	3
Z	Myristoylated	~1
NP	0	8

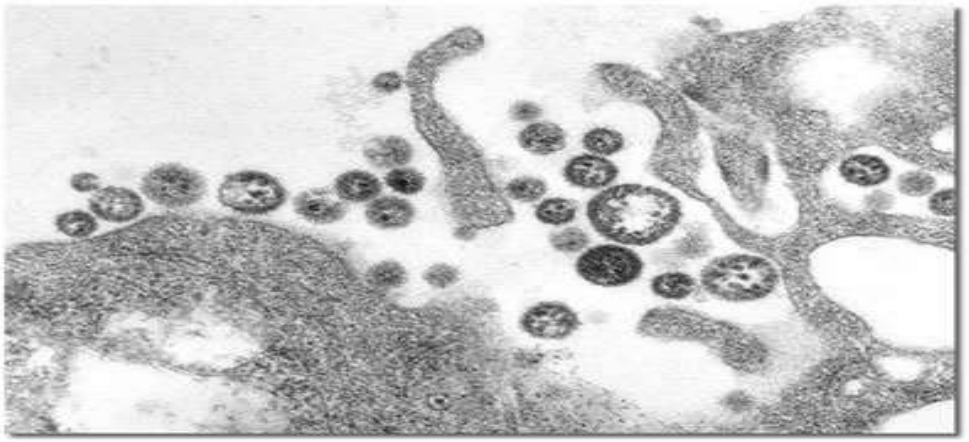

Figure 2. Arenavirus images showing protein inside of image.

Glycoprotein(GP):

Both GP-1 and GP-2, as well as NP, L, and Z, are structural proteins present in virions. GP-1 and GP-2 make up the spikes on the virion envelope and mediate virus interaction with host cell surface receptor (4, 5). Evidence indicated that GP-1 mediates virus interaction with host cell surface receptor, which has been recently identified as a-dystroglycan (5, 7). Tetramers of GP-1 and GP-2 make up the spikes on the virion envelope.

Z Matrix Protein:

Ring finger Z protein of LCMV is a matrix protein which is essential for particle budding. Results from in vitro transcription and immunodepletion studies have implicated Z in both genome replication and mRNA synthesis in Tacaribe virus (21), a member of the *Arenaviridae*. In addition, biochemical and immunological studies have suggested that Z might be the arenavirus counterpart of the matrix protein found in other negative-strand RNA viruses (33).

L Protein:

The L protein is thought to be the main viral component of the arenavirus polymerase (18). The arenavirus L protein has the characteristic sequence motifs conserved among the RdRp (L proteins) of NS RNA virus. The proposed polymerase module of L is located within domain 3 which contains highly conserved amino acids within motifs designated A and C. The L RNA segment encodes a high-molecular-mass protein (L; ca. 200 kDa) which has the characteristic motifs conserved in all the viral RNA dependent RNA polymerases and a small polypeptide Z (ca.11 kDa) which contains a RING finger motif and whose function is unknown (1, 19, 33) . The L RNA segment codes for the virus RNA-dependent RNA polymerase (L, ca 200 kDa) (19) and a small (11-kDa) RING finger protein (Z) (17).

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Nucleoprotein (NP):

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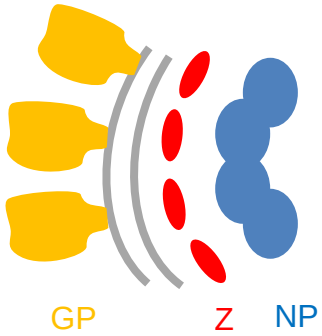

Figure 3. Model showing how the arenavirus structural proteins GP-C, Z and NP are arranged in virions. The viral envelope is shown in grey.

Conclusions

(18). The arenavirus L protein has the characteristic sequence motifs conserved among the RdRp (L proteins) of NS RNA virus. The proposed polymerase module of L is located within domain 3 which contains highly conserved amino acids within motifs designated A and C. The L RNA segment encodes a high-molecular-mass protein (L; ca. 200 kDa) which has the characteristic motifs conserved in all the viral RNA dependent RNA polymerases and a small polypeptide Z (ca.11 kDa) which contains a RING finger motif and whose function is unknown (1, 19, 33).

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