

2. THE VIRUSES

Hantaviruses are lipid-enveloped, spherical viruses of 80 to 110 nm in diameter. The RNA genome is tri-segmented, with the large (L) segment approximately 6,500 nucleotides long, the middle (M) segment approximately 3,600–3,800 nucleotides long, and the small (S) segment approximately 1,700–2,100 nucleotides long (4). The L segment encodes a viral polymerase, the M segment encodes G1 and G2 envelope glycoproteins, and the S segment encodes the N nucleocapsid protein.

Phylogenetic analysis of rodent-borne hantavirus genes has revealed three main lineages. While HFRS-causing viruses are linked to an Old World lineage, all HPS-associated viruses have a common New World lineage and are associated with members of a single rodent subfamily (*Sigmodontinae*) of the family *Muridae* (4, 5). Some of the sigmodontine-derived viruses are clearly independent species based on genetic evidence, serology, and/or reservoir-host association (Table 1); others are in the process of evaluation (Table 2), as are our criteria for defining a hantavirus species. At least 13 hantavirus species have been identified exclusively in the Americas,

and 6 have been shown to cause HPS (Table 1). The various HPS-causing hantaviruses generally differ by no more than 30% at the nucleotide level. Serum antibodies of HPS patients cross-react strongly with other New World viruses, but to varying degrees with Old World hantavirus antigens.

No evidence of genetic reassortment with previously recognized Old World hantaviruses was found in the initial characterization of Sin Nombre virus, and proven natural reassortment events have been restricted to different genotypes of SNV (6, 7). All known SNV strains share at least 90% nucleotide sequence homology and even higher amino acid sequence homologies. Natural reassortment may result in different nucleotide sequence homologies for one gene segment as compared to the other two, but this has not yet been related to differences in viral pathogenicity. Therefore, it is unlikely that genetic reassortment with other viruses accounts for the newly recognized pathogenicity of HPS-causing viruses. Rather, HPS and HPS-causing hantaviruses have likely existed in the Western Hemisphere for many years despite only recently having been detected.

TABLE 1. Viruses of the genus *Hantavirus*, family *Bunyaviridae*.

Virus	Abbr.	Original source	Location	Geographic distribution of rodent host ^a	Human disease	Isolated in cell culture
<i>Murinae</i> subfamily-associated viruses						
Hantaan	HTN	<i>Apodemus agrarius</i>	Korea	Asia, Europe	HFRS ^b	yes
Seoul	SEO	<i>Rattus norvegicus</i> , <i>R. rattus</i>	Korea	Asia, Europe, the Americas	HFRS	yes
Dobrava-Belgrade	DOB	<i>Apodemus flavicollis</i>	Slovenia	Europe, Middle East	HFRS	yes
Thai-749	THAI	<i>Bandicota indica</i>	Thailand	Asia	unknown	yes
<i>Arvicolinae</i> subfamily-associated viruses						
Puumala	PUU	<i>Clethrionomys glareolus</i>	Finland	Europe, Asia	HFRS	yes
Prospect Hill	PH	<i>Microtus pennsylvanicus</i>	Maryland	N. America	unknown	yes
Tula	TUL	<i>Microtus arvalis</i>	Russia	Europe	unknown	yes
Khabarovsk	KBR	<i>Microtus fortis</i>	Russia	Asia	unknown	yes
Topografov	TOP	<i>Lemmus sibiricus</i>	Siberia	Russia, Asia, N. America	unknown	yes
Isla Vista	ISLA	<i>Microtus californicus</i>	California	N. America	unknown	no
<i>Sigmodontinae</i> subfamily-associated viruses						
Sin Nombre	SN	<i>Peromyscus maniculatus</i>	New Mexico	N. America	HPS ^c	yes
New York	NY	<i>Peromyscus leucopus</i>	New York	N. America	HPS	yes
Black Creek Canal	BCC	<i>Sigmodon hispidus</i>	Florida	The Americas	HPS	yes
Bayou	BAY	<i>Oryzomys palustris</i>	Louisiana	Southeastern United States	HPS	yes
Caño Delgadito	CANO	<i>Sigmodon alstoni</i>	Venezuela	S. America	unknown	yes
Río Mamore	RM	<i>Oligoryzomys microtis</i>	Bolivia	S. America	unknown	yes
Laguna Negra	CHP	<i>Calomys laucha</i>	Paraguay	S. America	HPS	yes
Muleshoe	MULE	<i>Sigmodon hispidus</i>	Texas	The Americas	unknown	no
El Moro Canyon	ELMC	<i>Reithrodontomys megalotis</i>	California	N. America	unknown	no
Río Segundo	RIOS	<i>Reithrodontomys mexicanus</i>	Costa Rica	Mexico, Central America	unknown	no
Andes	AND	<i>Oligoryzomys longicaudatus</i>	Argentina	S. America	HPS	yes
Insectivore-associated virus						
Thottapalayam	TPM	<i>Suncus murinus</i>	India	Asia	unknown	yes

^aGiven as approximate distribution; many rodent species occur focally, many others have widespread distributions.

^bHFRS = hemorrhagic fever with renal syndrome.

^cHPS = hantavirus pulmonary syndrome.

TABLE 2. Genotypes of Sigmodontine-associated hantavirus under evaluation.

Virus	Original source	Location	Human disease
Monongahela	<i>Peromyscus maniculatus</i>	United States	HPS
Blue River	<i>Peromyscus leucopus</i>	United States	Unknown
Oran	<i>Oligoryzomys longicaudatus</i>	Argentina	HPS
Lechiguanas	<i>Oligoryzomys flavescens</i>	Argentina	HPS
Bermejo	<i>Oligoryzomys chacoensis</i>	Argentina	Unknown
Maciel	<i>Necomys benefactus</i>	Argentina	Unknown
Pergamino	<i>Akodon azarae</i>	Argentina	Unknown
Juquitiba	Unknown	Brazil	HPS
HU39694	Unknown	Argentina	HPS