Hantaviruses are distributed worldwide and can cause a hemorrhagic fever or a cardiopulmonary syndrome in humans. Mature virions consist of RNA genome, nucleocapsid protein, RNA polymerase, and two transmembrane glycoproteins, G1 and G2. The ectodomain of G1 is surface-exposed; however, it has a 142-residue C-terminal cytoplasmic tail that plays important roles in viral assembly and host-pathogen interaction. Here we show by NMR, circular dichroism spectroscopy, and mutagenesis that a highly conserved cysteine/histidine-rich region in the G1 tail of hantaviruses forms two CCHC-type classical zinc fingers. Unlike classical zinc fingers, however, the two G1 zinc fingers are intimately joined together, forming a compact domain with a unique fold. We discuss the implication of the hantaviral G1 zinc fingers in viral assembly and host-pathogen interaction.

Many viruses in the family Bunyaviridae, which consists of five genera (Hantavirus, Orthobunyavirus, Nairovirus, Phlebovirus, and Tospovirus), cause emerging zoonotic infections in humans (1). Examples are the La Crosse encephalitis orthobunyavirus, Rift Valley fever phlebovirus, and the Crimean-Congo hemorrhagic fever nairovirus (tospoviruses are plant pathogens). Hantaviruses use rodents as their primary reservoir, and humans (e.g. Prospect Hill virus) are nonpathogenic to humans, others (e.g. Andes virus) can cause either the hantaviral cardiopulmonary syndrome or the hemorrhagic fever with renal syndrome in humans (1). Annually, over 150,000 cases of hantaviral infections are reported worldwide (2) with mortality rates reaching as high as 40% (3).

Bunyaviridae viruses are enveloped and have three genomic RNA molecules: the small (S), medium (M), and large (L) segments, and four viral proteins: the RNA polymerase, the nucleocapsid (N) protein, and the membrane glycoproteins, G1 and G2 (1). The ectodomains of G1 and G2 are glycosylated, form a heterodimer on the viral surface, and function as the viral spike proteins (1). In G1 and G2, the N termini form the ectodomains, followed by single pass transmembrane helices, then the C termini or cytoplasmic tails project within the virions. Bunyaviridae viruses lack a matrix protein (4), which link the membrane to the ribonucleoprotein among enveloped viruses (5). Based on this observation, it was suggested that the cytoplasmic tails of the viral glycoproteins might bind the viral ribonucleoprotein (6). Indeed, recent results have shown that the G1 tail binds the viral ribonucleoprotein in phlebovirus (7) and is required for packaging the genome in orthobunyavirus (8). These data suggest that the G1 tail plays a critical role in viral assembly.

Other reports suggest that among hantaviruses, the G1 tail is important in host-pathogen interaction. The G1 tail of human pathogenic hantaviruses inhibits the cellular interferon response (9, 10) against viral infection by disrupting protein-protein interactions (10). In nonpathogenic hantaviruses, by contrast, the interferon response is activated (9, 11). The G1 tail contains conserved immunoreceptor tyrosine-based activation motifs, which are involved in protein-protein interactions in the cellular immune response to viral infection (12). Further, the G1 tail of pathogenic hantaviruses is ubiquitinated and proteasomally degraded (13), which is thought to regulate the activity of the G1 tail (13), whereas the nonpathogenic hantavirus G1 tail is stable.

The G1 tail varies in length from 78 residues in orthobunyaviruses to 142 residues among hantaviruses. Sequence alignment shows a region of conserved cysteine and histidine residues in the G1 tail of Bunyaviridae. Further, this region was predicted to form a RING finger motif in the G1 tail of hantavirus (14). Here, we show by NMR that the conserved cysteine/histidine region in the G1 tail of hantaviruses forms two classical ββα-fold zinc fingers (15–18) and not a RING finger structure as suggested earlier (14). We also discuss the implication of our structural findings of the hantavirus G1 tail in the context of viral assembly and host pathogen interaction.
Hantavirus G1 Zinc Finger Domain

The cells were centrifuged, resuspended in buffer A (20 mM Tris-HCl, pH 8.0, 20 mM NaCl, 1 mM DTT, 0.1 mM ZnSO4), and lyzed against TEV digestion buffer (50 mM Tris-HCl, pH 8.0, 8 M urea, 1 mM DTT, 0.1 mM ZnSO4, and 0.1 mM phenylmethanesulfonyl fluoride). Solubilized protein was dialyzed into buffer (20 mM Tris-HCl, pH 8.0, 0.5 mM NaCl, 1 mM DTT, 1 mM ZnSO4). TEV digestion was carried out at 25 °C for 16 h with 0.16 mg of recombinant TEV protease (20) per 10 ml of fusion protein. The His6-tagged GB1 domain was removed by passing the digest through a 1-ml nickel affinity column (GE Healthcare), and bound protein was eluted with a 100 ml linear gradient of buffer B (20 mM Tris-HCl, pH 8.0, 0.5 mM NaCl, 1 mM DTT, 1 mM ZnSO4).

Fractions containing the fusion protein were pooled and dialyzed against TEV digestion buffer (50 mM Tris-HCl, pH 8.0, 20 mM NaCl, 1 mM DTT, 1 mM ZnSO4). TEV digestion was carried out at 25 °C for 16 h with 0.16 mg of recombinant TEV protease (20) per 10 ml of fusion protein. The His6-tagged GB1 domain was removed by passing the digest through a 1-ml nickel affinity column (GE Healthcare), and bound protein was eluted with a 100 ml linear gradient of buffer B (20 mM Tris-HCl, pH 8.0, 0.5 mM NaCl, 1 mM DTT, 1 mM ZnSO4).

Site-directed mutagenesis was performed using the QuikChange kit (Stratagene). In total, 7 cysteine and 5 histidine residues (4 native His residues and the cloning artifact, His542) were mutated individually to serine or phenylalanine, respectively, and confirmed by DNA sequencing. Mutants H542F, H553F, H552F, H590F, and C594S were expressed as soluble proteins and were purified by nickel affinity chromatography as previously described (21). Mutants C548S, C551S, C555S, H564F, C568S, C573S, and C576S were expressed as inclusion bodies (despite the presence of the GB1 solubility tag) and were purified as follows. Inclusion bodies were resuspended at room temperature in buffer (50 mM Tris-HCl, pH 8.0, 100 mM NaCl, 8 mM urea, 1 mM DTT, 0.1 mM ZnSO4, and 0.1 mM phenylmethanesulfonyl fluoride). Solubilized protein was dialyzed into buffer (20 mM Tris-HCl, pH 8.0, 0.5 mM NaCl, 6 mM urea, 1 mM DTT, and 0.1 mM ZnSO4), loaded into a 5-ml nickel affinity column, and eluted with buffer (20 mM Tris-HCl, pH 8.0, 20 mM NaCl, 6 mM urea, 1 mM DTT, 0.1 mM ZnSO4, 1 mM imidazole). Eluted protein was refolded using stepwise dialysis to remove urea. None of the mutant fusion proteins was cleaved. The two-dimensional 1H-15N HSQC of GB1 in the fusion protein was used as a marker to determine the refolding of the fusion protein.

RNA Binding Assay—Andes virus (strain 23) was used to inoculate a T175 flask of confluent monolayer of Vero E6 cells at a multiplicity of infection of 0.1 plaque-forming unit/cell and incubated for 14 days in a Biosafety Level 3 environment. The cells were harvested, and total RNA was extracted using TRIzol (15596-018; Invitrogen), ethanol-precipitated, and resuspended in water to a final concentration of 300 ng/μl. The presence of viral and cellular RNA was confirmed by reverse transcription-PCR. Total cellular and viral RNA was incubated at room temperature for 15 min with increasing amounts of Andes G1 zinc finger protein and a known RNA-binding protein, PACT (22) (a gift from Dr. Gaya Amarasinghe, Iowa State University) in binding buffer (10 mM NaPO4, 10 mM NaCl, pH 7.6). Samples were mixed with an equal volume 50% glycerol and loaded in a 0.7% agarose Tris-borate gel for electrophoretic mobility shift assay. The gel was run at 70 V for 50 min in Tris-borate buffer, pH 8.3. The gel was visualized by staining with SYBR Green II RNA specific dye (Invitrogen).

CD Spectroscopy—The GB1 tag was removed in all samples for CD spectroscopy. Each sample contained 5–10 μg protein in buffer (10 mM NaPO4, pH 7.0, 10 mM NaCl, 1 mM DTT, 0.1 mM ZnSO4). CD spectra were acquired in triplicate using a JASCO J-815 Spectropolarimeter at 25 °C and 50 nm/min scan rate. Titration with EDTA and ZnSO4 were applied to the same sample.

NMR Spectroscopy—NMR data were acquired at 25 °C using a Bruker Avance 800 MHz spectrometer equipped with a cryo-probe, processed with NMRPipe (23) and analyzed with NMR-View (24). For NMR structure determination, the G1 zinc-binding domain of the Andes virus was used. Typical NMR samples contained 1 mM 15N- or 15N,13C-labeled protein in buffer (10 mM NaPO4, pH 7.0, 10 mM NaCl, 1 mM DTT, 0.1 mM ZnSO4) dissolved in 10% D2O or 100% D2O. Backbone assignments were obtained from two-dimensional 1H-15N HSQC (25) and three-dimensional HNCA (26), CBCA(CO)NH (26), HNCACB (27), and HCNO (28). Secondary structures were identified from the Cα, Cβ, C′, and Hα chemical shifts (29). Side chain assignments were obtained from two-dimensional 1H-13C HMQC (30), three-dimensional HBHA(CO)NH (31), and three-dimensional 13C-edited HMQC-NOESY (32) (mixing time (t mix) = 120 ms). The tautomeric ring assignments of Zn2+-coordinated histidines were identified by 15N HMQC (33). NOE cross-peaks were identified from three-dimensional 15N-edited NOESY-HSQC (34) (t mix = 120 ms) and three-dimensional 13C-edited HMQC-NOESY (32) (t mix = 120 ms).

Structure Calculation—NOE distance restraints were classified into upper bounds of 2.7, 3.5, 4.5, and 5.5 Å and a lower bound of 1.8 Å based on peak volumes. Backbone dihedral angles in the α-helical regions were restrained to ϕ (−60 ± 20°) and ψ (−40 ± 20°). Initial structures were generated by torsion angle dynamics in CYANA (35), followed by molecular dynamics and simulated annealing in AMBER7 (52), first in vacuo and then with the generalized Born potential to account for the effect of solvent during structure calculation. Tight distance restraints that imposed tetrahedral Zn2+ coordination to Cys and His residues were used in the CYANA calculations (36). Structural calculations were also done without Zn2+ restraints to confirm that the domain could fold from NOE-derived restraints only. CYANA and AMBER structure calculation protocols have been described elsewhere (37). Iterative cycles of AMBER calculations followed by refinement of NMR-derived...
Hantavirus G1 Zinc Finger Domain

RESULTS

Protein Expression—Sequence analysis of the G1 cytoplasmic tail of hantaviruses revealed two highly conserved CX3CX12−13HX3C (where X is any amino acid) motifs, which suggested the presence of two CCHC-type zinc fingers (Fig. 1). Expression of the Andes virus G1 zinc fingers (residues 543–599) in E. coli resulted in cell death, with cell density reaching only ~0.9 after induction at A600 of ~0.8, suggesting that the zinc finger was toxic to E. coli. Thus, the zinc finger domain was expressed as a GB1 fusion protein. The GB1 tag contained His6 for nickel affinity purification and a TEV protease cleavage site to recover the native G1 zinc finger domain. The fusion protein was overexpressed in soluble form in E. coli, purified under native conditions, and digested with TEV protease to obtain the G1 zinc finger domain.

Zn2+ Is Required for Proper Folding—CD spectrum of the Andes virus G1 zinc finger showed a folded α-helical domain with local minima at 209 and 222 nm (Fig. 2). Titration of EDTA to a final concentration of 1.25 mM caused a spectral shift to 205 nm, indicating a partial loss of secondary structure. However, the minimum at 222 nm remained despite EDTA treatment, suggesting that although the global fold is disrupted by removal of zinc ion, some residual helical structure remained. Subsequently, titrating ZnSO4 back into the solution resulted in increased α-helical content, suggesting restoration of the global fold.

NMR data were also used to confirm the requirement for Zn2+ coordination on the proper folding of the zinc finger domain. The Andes virus and the Prospect Hill virus zinc-binding domains purified under native conditions showed well dispersed and sharp peaks in their two-dimensional 1H-15N HSQC spectra (supplemental Fig. S1). After treatment with excess EDTA, peaks in the HSQC of the Andes virus zinc-binding domains purified under native conditions showed well dispersed and sharp peaks in their two-dimensional 1H-15N HSQC spectra (Fig. 3). Nearly complete backbone assignments were obtained from three-dimensional HNCA, CBCA(CO)NH, HNCACB, and 15N-edited NOESY-HSQC. Analysis of the Cα, Hα, Cβ, and C′ secondary chemical shifts (supplemental Fig. S2) supported the presence of two short α-helices and two random coil regions flanking the central domain (29). Side chain assignments were completed using two-dimensional 1H-13C HMOC, three-dimensional HBHA-COHN, and three-dimensional 13C-edited HMOC-NOESY. There were four conserved histidines (at positions 552, 553, 564, and 590) that could potentially coordinate Zn2+ ion; how-

restraints were performed until the structures converged with low restraint violations and good statistics in the Ramachandran plot. A family of 20 lowest energy structures was analyzed using PROCHECK (38), and the graphics were generated using PyMol (39).

FIGURE 1. The G1 tail of Hantaviruses, Nairoviruses, and Orthobunyaviruses (genera of Bunyaviridae) contains a cysteine/histidine-rich region with two CCHC arrays. Structure determination of the Andes virus dual CCHC-region revealed a novel zinc finger domain. Shown are the secondary structures ( α-helices and β-strands), zinc-coordinating residues (boxed), the two CCHC motifs (boxed), conserved residues (gray), and residue numbers for the Andes virus G1 sequence. Sequence alignment was generated using CLUSTALW and formatted with ESPript 2.2 (53).

FIGURE 2. CD spectroscopy and titration with EDTA and ZnSO4 of recombinant Andes virus G1 tail CCHC-region (residues 543–599), which was expressed and purified under native conditions, showed that Zn2+ binding is required for the proper folding of this domain. Native G1 tail zinc finger domain showed a folded CD spectrum (open squares). Titration with an excess of EDTA resulted to an unfolded peak (at 204 nm) and reduced the helical peak (at 222 nm) (closed squares). The addition of 2.5 and 5 mM ZnSO4 yielded folded CD spectra (triangles and circles).

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ever, long distance NOEs (between Cys\textsuperscript{548}, His\textsuperscript{564} and Cys\textsuperscript{573}, His\textsuperscript{590}) indicated that His\textsuperscript{564} and His\textsuperscript{590} were involved in Zn\textsuperscript{2+} coordination. A two-dimensional \textsuperscript{15}N HMQC (33) spectrum showed Zn\textsuperscript{2+} coordination through the His\textsuperscript{564} N\textsuperscript{ε1} and His\textsuperscript{590} N\textsuperscript{ε2} atoms (supplemental Fig. S3). Manual analysis of three-dimensional \textsuperscript{15}N- and \textsuperscript{13}C-edited NOESY spectra identified 859 unambiguous interproton distance restraints. The NOE restraints together with 24 and 15 ψ dihedral angle restraints and zinc coordination restraints (Table 1) were used in structure calculation and refinement with CYANA and AMBER. The 20 lowest energy NMR structures converged into a family of structures (Fig. 4A) with low restraint violations and good Ramachandran plot statistics (Table 1).

Structure of Individual Zinc Finger—Each G1 zinc finger folded similarly to the ββα fold of classical zinc fingers. In the first CCHC array (ZF1), residues Met\textsuperscript{546}–Cys\textsuperscript{551} formed a β-hairpin that encompassed the first two coordinating cysteines (Cys\textsuperscript{548} and Cys\textsuperscript{551}; Fig. 4B). Asp\textsuperscript{549} and Val\textsuperscript{550} formed the loop apex with the coordinating cysteines on either side of the β-hairpin. The structured region terminated at Lys\textsuperscript{559} where helix α\textsubscript{1} began and folded back toward the β-hairpin and allowed the completion of ZF1 with His\textsuperscript{564} and Cys\textsuperscript{568} on the interior face of helix α\textsubscript{1}.

In ZF2, the β-hairpin (Glu\textsuperscript{571}–Thr\textsuperscript{580}) contained the first two coordinating cysteines (Cys\textsuperscript{573} and Cys\textsuperscript{576}; Fig. 4, B and C). The coordination site on the loop was partly formed by the positioning of Pro\textsuperscript{574} between the two. Strong Cys\textsuperscript{573} H\textsuperscript{α} to Pro\textsuperscript{574} H\textsuperscript{α} NOEs indicated that Pro\textsuperscript{574} was in the trans configuration. A structured loop followed the β-hairpin and terminated at Glu\textsuperscript{584}, where helix α\textsubscript{2} began, and folded back toward the β-hairpin to complete ZF2 by coordinating His\textsuperscript{590} and Cys\textsuperscript{594} to the Zn\textsuperscript{2+} ion.

A Novel Dual CCHC Zinc Finger—Unlike classical ββα zinc fingers, which fold independently of each other forming a “beads-on-a-string” configuration, the two G1 zinc fingers interacted with each other, forming a compact structure in which the two zinc atoms were located a mere 10 Å apart (Fig. 4). Two short, parallel helices of 8 and 9 residues in length were linked by a 15-residue β-hairpin extending between Cys\textsuperscript{546} of helix α\textsubscript{1} and Thr\textsuperscript{583} of helix α\textsubscript{2}. Another loop preceded helix 1 and an unstructured tail of 7 residues followed helix 2. Both zinc coordination sites were formed at the junction of a loop and the face of a proximal α-helix. Structural searches using DALI (40) and TM-align (41) returned no homologous structures; thus, the G1 zinc finger domain has a novel fold.

Mutations of Zn\textsuperscript{2+} -coordinating Residues—To confirm the Zn\textsuperscript{2+} coordination topology indicated by the NMR structure, we created point mutants in each of the cysteine and histidine residues within the Andes virus zinc finger domain. Of the 8 residues expected to coordinate zinc, only C594S and H590F expressed as soluble proteins, the rest (C548S, C551S, H564F, C573S, C576S, H590F, and C594S) all showed narrowly dispersed spectra consistent with an unfolded domain (supplemental Fig. S4). These results suggested that zinc coordination was necessary for stabilizing the overall fold of the zinc finger domain. For further analysis, all of the inclusion bodies were solubilized overnight in 8 M urea, purified by nickel affinity chromatography, and refolded by stepwise dialysis to remove urea. Refolding of the zinc finger domain was determined by the proper refolding of the attached GB1 tag using two-dimensional \textsuperscript{15}N HMQC, which served as a control to show that the refolding conditions would have properly refolded a native protein. The spectra of the mutated G1 zinc finger domain in the GB1 fusion proteins consisting of C548S, C551S, H564F, C573S, C576S, H590F, and C594S all showed narrowly dispersed spectra consistent with an unfolded domain (supplemental Fig. S4). These results suggested that the two zinc fingers did not fold independently of each other (supplemental Fig. S4). Of these eight positions, only C568S showed any peak dispersion at all (supplemental Fig. S4). In each instance, the peaks corresponding to the attached GB1 tag were well dispersed, thus indicating that the fusion protein was refolded properly (supplemental Fig. S4). These results suggested that, in the dual zinc finger domain, mutation of a Zn\textsuperscript{2+} -coordinating residue in either ZF1 or ZF2 lead to the unfolding of the entire domain.
Mutations of Non-Zn\textsuperscript{2+}/H11001-coordinating Residues—The domain contains three histidines (His\textsuperscript{552}, His\textsuperscript{553}, and His\textsuperscript{542}, the cloning artifact) and a cysteine (Cys\textsuperscript{555}) (Fig. 1) that are not involved in Zn\textsuperscript{2+}/H11001 coordination. To eliminate the possibility that Zn\textsuperscript{2+}/H11001 could coordinate these other cysteine and histidine residues, we generated four additional point mutants corresponding to H542F, H552F, H553F, and C555S. Three of the four mutants (H552F, H553F, and H542F) gave a dispersed spectrum consistent with a folded domain (supplemental Fig. S5). Only the C555S mutant gave an unfolded spectrum (supplemental Fig. S5). Analysis of the structure reveals that the side chain of Cys\textsuperscript{555} was oriented toward the interior of the structure and therefore played a role in stabilizing the hydrophobic core of the overall domain. These data hence confirmed that Zn\textsuperscript{2+}/H11001 was coordinated to the predicted zinc finger residues (Cys\textsuperscript{548}, Cys\textsuperscript{541}, Cys\textsuperscript{568}, Cys\textsuperscript{574}, Cys\textsuperscript{576}, and Cys\textsuperscript{594} and His\textsuperscript{564} and His\textsuperscript{590}).

Hantaviral G1 Zinc Fingers Does Not Bind RNA—Classical \(\beta\alpha\)-fold zinc fingers are well known nucleic acid-binding motifs (15–18). However, our attempts to verify the ability of the Andes virus G1 zinc finger domain to bind RNA by electrophoretic mobility shift assay revealed that under the conditions used, the G1 zinc finger domain did not bind RNA obtained from Andes virus-infected Vero E6 cells (supplemental Fig. S7). Although a known RNA-binding protein PACT (22) showed smearing of the RNA bands, which suggested nonspecific PACT-RNA interaction, increasing amounts of the Andes virus G1 zinc finger failed to demonstrate even nonspecific binding of RNA (supplemental Fig. S7).

DISCUSSION

The G1 tail of \textit{Bunyaviridae} viruses is important in viral assembly (7, 8) and host-pathogen interaction (9–13). Our results showed that a conserved cysteine/histidine-rich region in the hantavirus G1 tail (Fig. 1) required Zn\textsuperscript{2+} binding to fold properly (Fig. 2). This region formed an independently folded domain that gave excellent NMR data (Fig. 3) and NMR structure determination revealed dual CCHC-type zinc fingers where Zn\textsuperscript{2+} ligands were sequential and nonoverlapping (Fig. 4). The folding of each G1 zinc finger is related to the classical \(\beta\alpha\) zinc finger fold (42), which are among the most abundant protein motifs in eukaryotic genomes (reviewed in Ref. 43).

Implication of the Zinc Finger Structure in the Biology of Hantavirus—It has been suggested that the conserved cysteine-histidine region in the G1 tail of hantaviruses forms a RING finger motif (14). This assumption is based on the following observations: (i) the G1 tail is ubiquitinated and proteasomally degraded as part of the host-pathogen interaction of hantaviruses (13), (ii) RING fingers are structural domains of ubiquitin ligases, which are part of the ubiquitin degradation pathway, and (iii) some viruses contain RING finger motifs that are involved in the ubiquitin degradation pathway as part of their host evasion mechanism (14).

Instead of forming a RING finger motif (14), however, our results showed that the conserved cysteine/histidine region in the G1 tail of hantaviruses formed a dual classical type \(\beta\alpha\)-fold zinc fingers. Classical zinc fingers are well known DNA- and RNA-binding domains (17, 18, 44). Recent reports indicate that proteins containing classical zinc fingers are also involved in protein-protein interaction (43, 45–47). Thus, instead of functioning as a domain of a ubiquitin ligase (as a RING finger), the classical \(\beta\alpha\)-fold of the hantaviral zinc fingers suggests nucleic acid binding...
and/or protein-protein interaction. This is consistent with the observations that the G1 tail is important in binding the ribonucleoprotein during viral assembly of Bunyaviridae (7, 8).

Thus, the ββα-fold implies that the hantaviral zinc fingers may interact with the RNA genome or the protein component of the ribonucleoprotein during viral assembly. Our electrophoretic mobility shift assay showed that the hantaviral zinc fingers did not interact with RNA (supplemental Fig. S7). Additionally, the hantaviral zinc domain has a theoretical pl of 5.8, which is too acidic to be a nucleic acid-binding motif. Further, the hantaviral zinc domain has a theoretical pi of 5.8, which is likely due to a short 4-residue linker between the two zinc fingers. Commonly, classical zinc fingers fold independently of each other, forming a beads-on-a-string configuration. However, multiple classical zinc fingers can interact with each other when bound to DNA (44) or RNA (17, 18). Another example of a dual classical ββα zinc finger that folds together as one unit is the yeast Zap1 transcription factor (49). Second, the folding of one hantaviral zinc finger affects the folding of the other zinc finger. For example, mutations in cysteine and histidine residues that disrupted the first or second zinc finger disrupted the folding of the entire dual zinc finger domain (supplemental Fig. S4). Because classical zinc fingers fold independently of each other, disrupting the folding of one zinc finger domain does not affect the folding of the other zinc fingers.

Other Viral Zinc Fingers—Among viruses, the CCHC zinc fingers of the nuleocapsid proteins of retroviruses (50) have been studied extensively because of their critical role in binding and packaging the RNA genomes. Examples of zinc fingers in viral glycoproteins, however, are scarce. Our structure presented here is the first atomic resolution structure of a zinc finger domain from a viral glycoprotein. The sequence homology of the hantaviral zinc finger region with other Bunyaviridae (Fig. 1) also suggests that that the G1 tail in nairoviruses and orbubunyaviruses will also form zinc finger motifs. Therefore, our results form the structural framework for future studies aimed at elucidating the precise role of the G1 tail in the viral assembly and immune evasion of Bunyaviridae.

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Hantavirus G1 Zinc Finger Domain

The Hantavirus Glycoprotein G1 Tail Contains Dual CCHC-type Classical Zinc Fingers
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