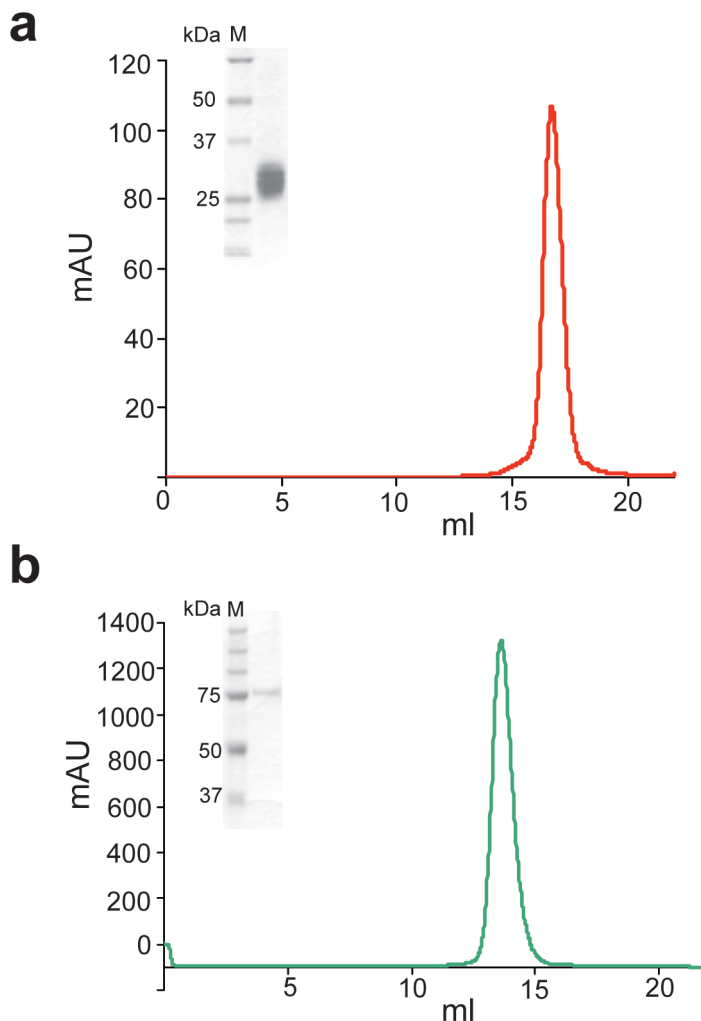


Supplementary Information

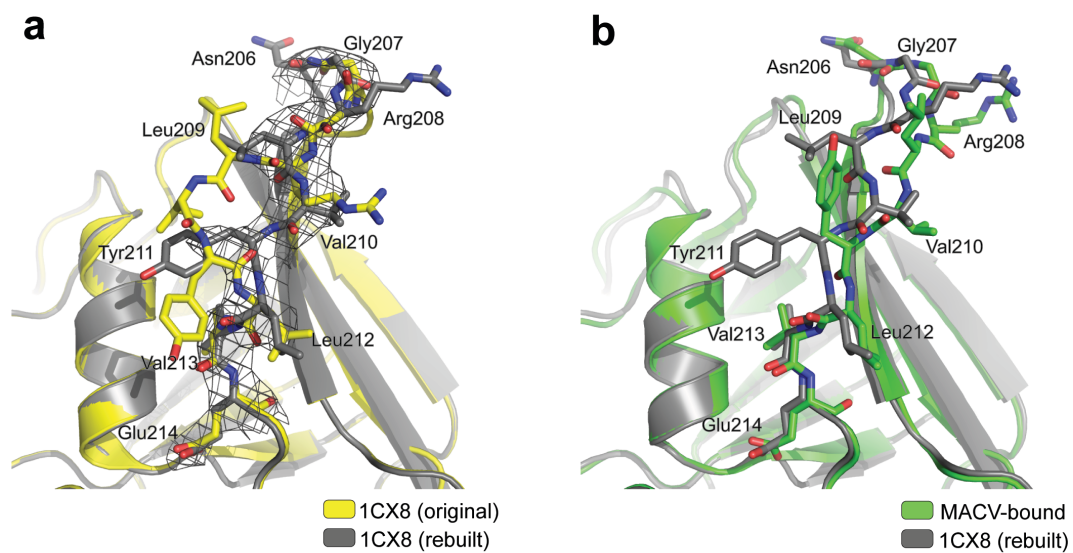
Structural basis for receptor recognition by New World hemorrhagic fever arenaviruses

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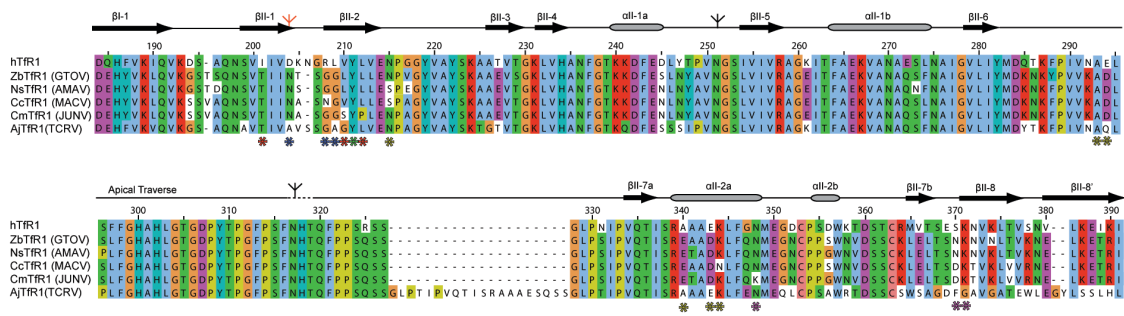
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Supplementary Figure 1 Purification of MACV GP1 and human TfR1. **(a)** MACV GP1 (residues 79-258) with the addition of a His₆-tag at the C-terminus, was expressed in insect cells and purified by nickel affinity chromatography. The purified protein, when passed over a size exclusion column (Superdex 200, GE Healthcare Life Sciences), elutes as a sharp peak at 17.3 ml (trace shown here). Inset is a SDS-PAGE gel of the protein under reducing conditions. MACV GP1-His₆ appears as a diffuse band because of extensive glycosylation. **(b)** The soluble ectodomain of hTfR1 (residues 117-760) was expressed in CHO cells and purified by affinity chromatography as previously described¹. The protein, when passed over a size exclusion column (Superdex 200), elutes as a sharp peak at 14 ml, consistent with the molecular weight of the TfR1 dimer (trace shown here). Inset is a SDS-PAGE gel of TfR1 under reducing conditions. M indicates molecular weight marker lane.



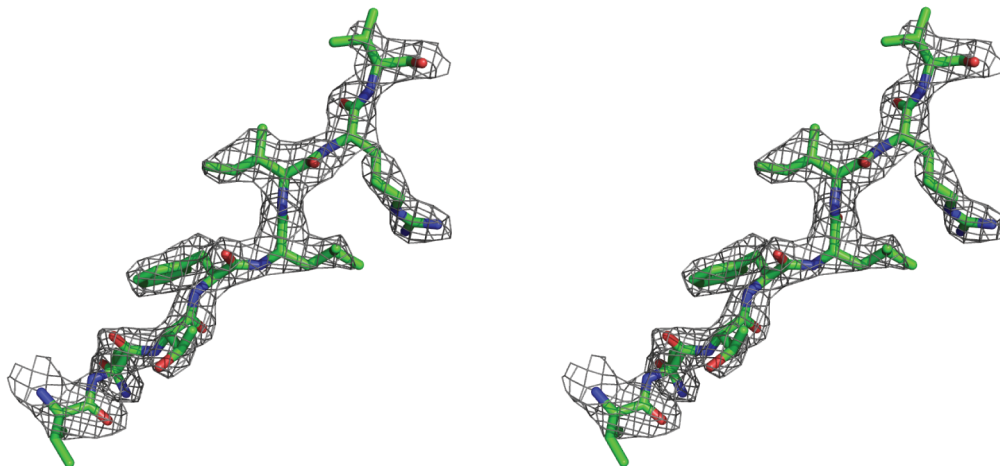
Supplementary Figure 2 Conformation of the unliganded human TfR1 apical domain. **(a)** Side-view ribbon diagram of the rebuilt unliganded hTfR1 apical domain (gray) overlaid with the same region of the originally-published TfR1 structure (yellow, PDB ID 1XC8)¹. The refined $2F_o - F_c$ density (at 1σ) is shown in gray. **(b)** Side-view of the rebuilt unliganded hTfR1 (gray) apical domain overlaid with the same region of hTfR1 in the MACV GP1-bound conformation (green). Residues 206-214 are labeled and shown as sticks.



Supplementary Figure 3 Sequence alignment of the apical domain of the human and NW clade B arenavirus host-species TfR1 orthologs. Human TfR1 (hTfR1, residues 184-391) were aligned with the corresponding sequences of the TfR1 orthologs of *Z. brevicauda* (ZbTfR1), *N. spinosus* (NsTfR1), *C. callosus* (CcTfR1), *C. musculinus* (CmTfR1), and *A. jamaicensis* (AjTfR1). The NW arenavirus that corresponds to the listed host-species receptor is indicated in parentheses. Secondary structure elements are shown for hTfR1. Tree diagrams indicate sites of N-linked glycosylation. The putative N-linked glycosylation site found in Zb, Ns, Cc, and CmTfR1 (human residue 204) is shown as a red tree. Residues are colored according to the ClustalX color scheme. TfR1 residues that interact with MACV GP1 are labeled with asterisks colored according to the scheme in Figures 2 and 4.

	MACV	SABV	Chapare
Motif 1	Arg111	S	A
	Ser113	T	L
	Ile115	V	M
	Val117	L	V
Motif 2	Asp114	D	D
	Ser116	T	S
Motif 3	Pro223	N*	N*
	Phe226	W	W
	Tyr228	-	-
Motif 4	Met119	M	L
	Tyr122	H	H
	Asp123	D	D
	Lys169	S	S
	Glu171	V	V
Motif 5	Ser97	S	T
	Phe98	T	L

Supplementary Figure 4 TfR1 predicted to function as a receptor for Chapare virus. List of MACV GP1 residues that contact TfR1, colored as in Figure 4. The residues found in analogous positions for the recently isolated NW hemorrhagic fever arenavirus Chapare are shown². SABV was included for reference, as Chapare and SABV are closely related (both are clade B3 viruses).



Supplemental Figure 5 Sample of electron density for MACV GP1. The volume, shown in stereoview, is from a $2F_o - F_c$ simulated-annealing composite all-omit electron density map, contoured at 1.5σ , in the region corresponding to MACV GP1 residues 105-112.

References

1. Lawrence, C.M. et al. Crystal structure of the ectodomain of human transferrin receptor. *Science* **286**, 779-82 (1999).
2. Delgado, S. et al. Chapare virus, a newly discovered arenavirus isolated from a fatal hemorrhagic fever case in Bolivia. *PLoS Pathog* **4**, e1000047 (2008).