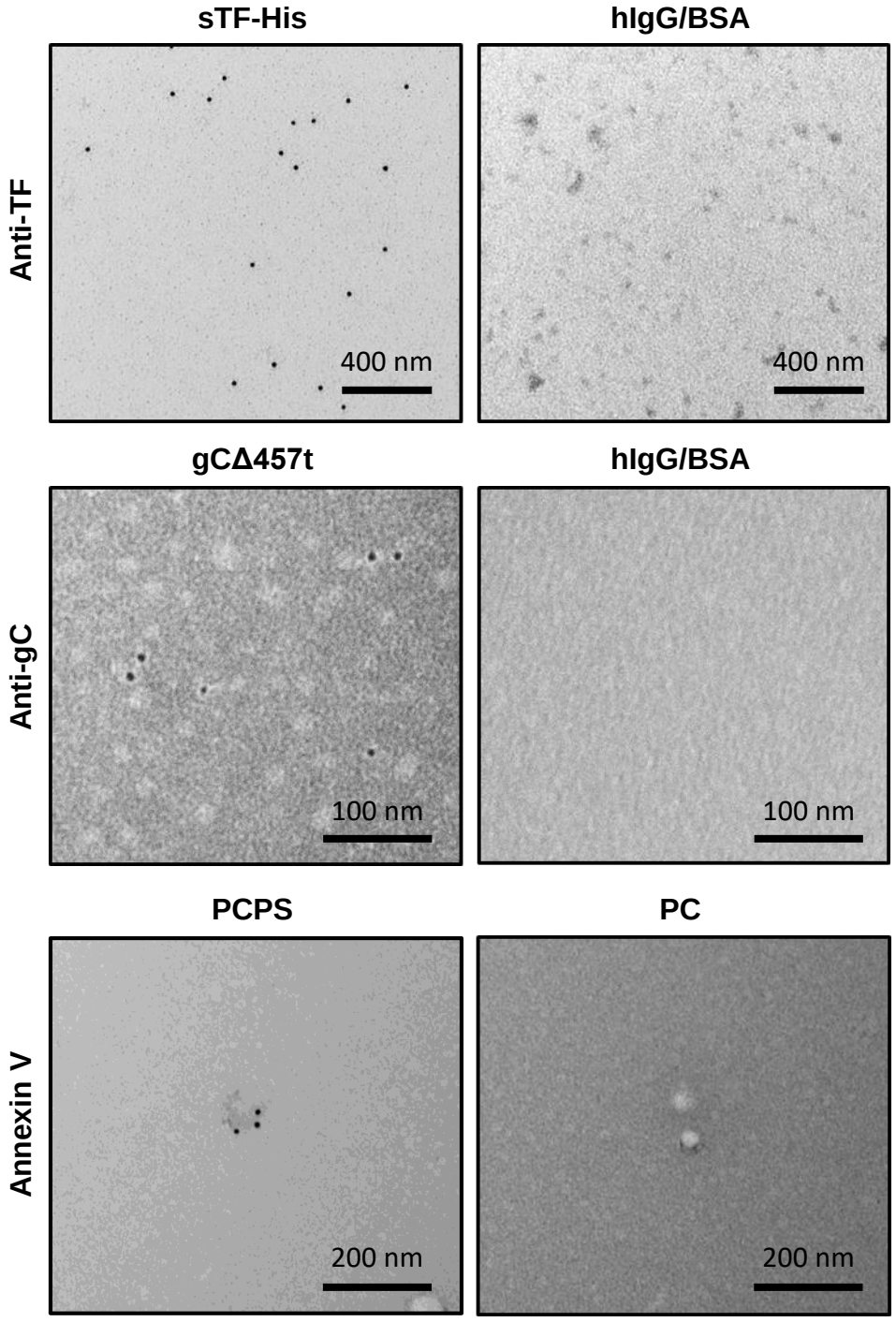

Fig. S1. Demonstration of specificity in immunogold EM.

Antigen specificity of antibodies and probes used in immunogold EM were tested by coating grids with purified sTF-His (100 ng) for anti-TF, purified gCΔ457t (100 ng) for anti-gC, or aPL-containing PCPS liposomes (200 nmol) for Annexin V. Human IgG (5 µg/mL) with 5% BSA and PC only liposomes were used as negative controls.

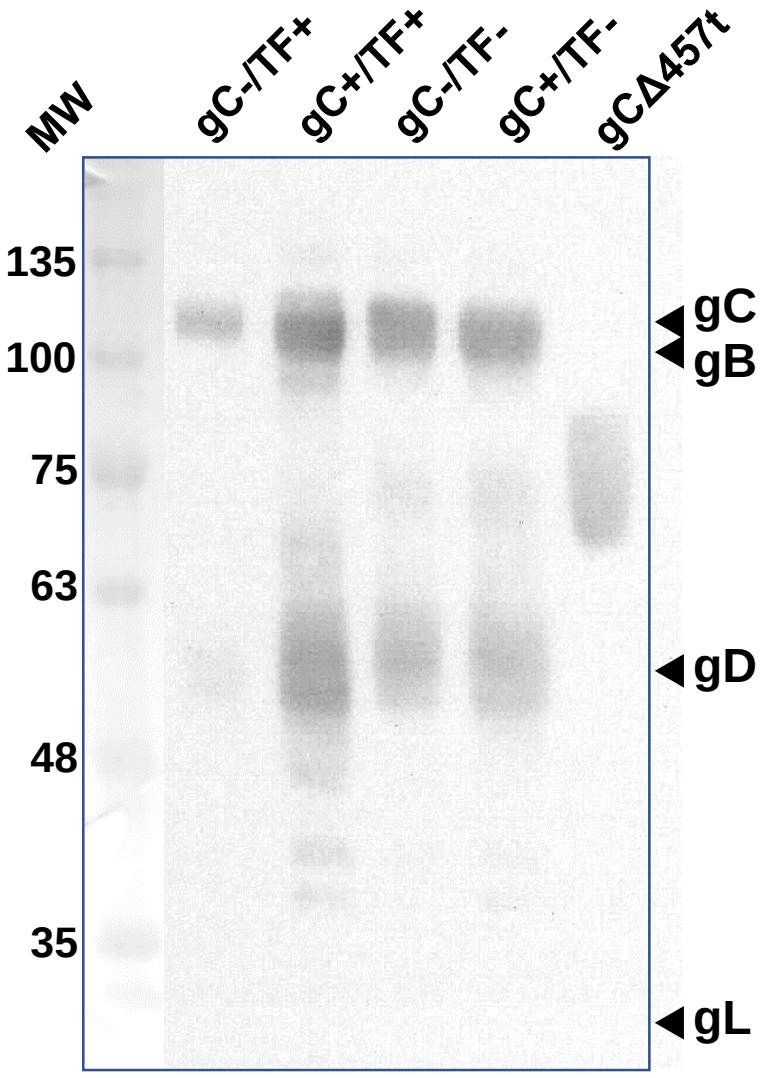

Fig. S2. Demonstration of viral antibodies in patient plasma.

Human IgG purified from normal pooled human plasma by Protein G agarose chromatography was used as a primary antibody to detect virus proteins from different forms of HSV1 (HSV1/TF+/gC+, HSV1/TF+/gC-, HSV1/TF-/gC+, and HSV1/TF-/gC-) that were separated by SDS-PAGE (1 x 10^{10} virus particles). gC is highly antigenic in plasma and gCΔ457t was detected as a purified positive control protein. (100 ng). MW; molecular weight markers

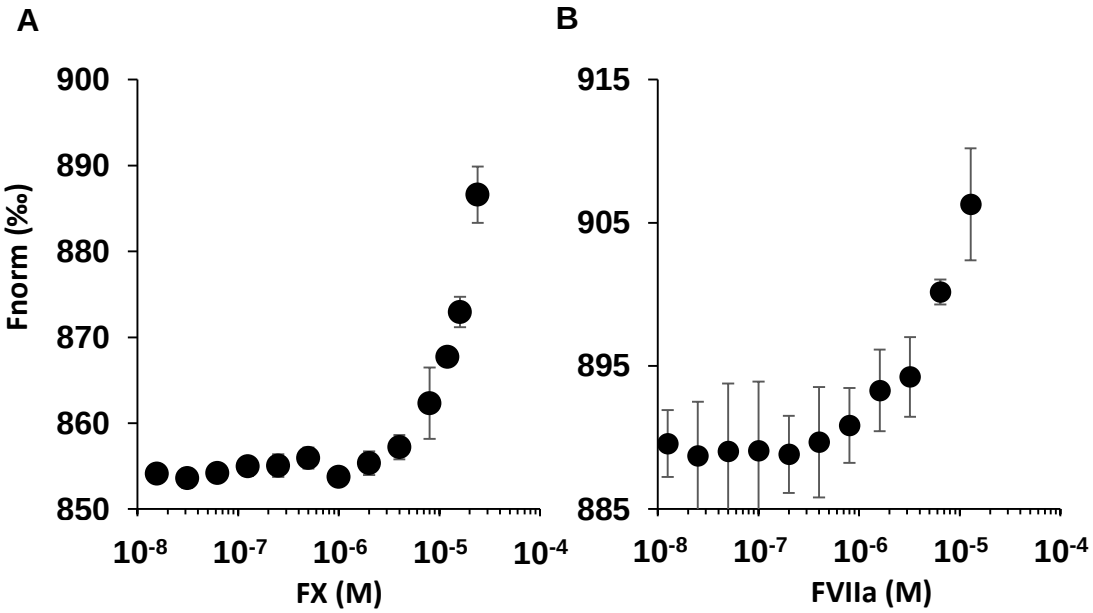

Fig. S3. MST traces demonstrating weak associations of FX and FVIIa with gCΔ457t in the absence of membrane associations.

MST was used to follow the interaction between gCΔ457t and (A) FX or (B) FVIIa. gCΔ457t (200 nM) was mixed with the RED-tris-NTA fluorescent probe (3.5 nM) for 30 minutes at room temperature before the addition of FX or FVIIa in HBS/0.05% BSA/0.05% Tween-20/5 mM Ca2+. MST power was set at medium with 10% excitation power. Samples were equilibrated at 25 °C prior to instrument reading. n = 3; Error bars: SEM.

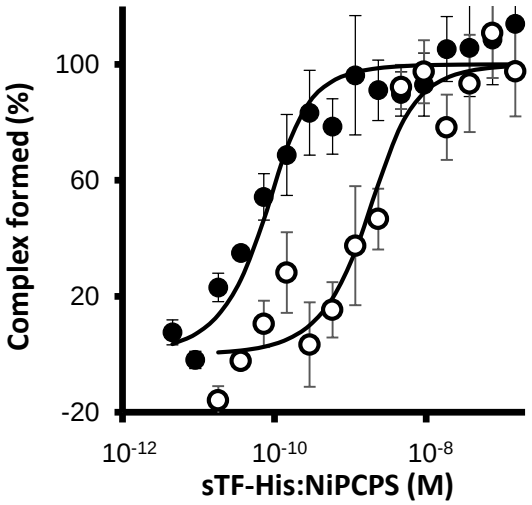

Fig. S4. sTF-His binding to FVIIa-R is enhanced by FX.

MST was used to follow the interaction between FVIIa-R (2 nM) and sTF-His on NiPCPS membranes (50 µM) with calcium (5 mM) and benzamidine (2 mM) in the absence or presence of 30 nM FX (○ and ●, respectively). n = 3; Error bars: SEM.

		*Simplest binding model			
		No FX		With FX	
Ligand	Lipid	K_d (μM) (95% CI)	r^2	K_d (μM) (95% CI)	r^2
sgC-His	None	No fit	-	2.9 (1.5 – 4.2)	0.994
sgC-His	PCPS	No fit	-	2.2 (0.9 – 3.5)	0.822
sgC-His	NiPC	2.0 (1.3 – 2.8)	0.896	0.9 (0.7 – 1.0)	0.980
sgC-His	NiPCPS	1.3 (0.1 – 2.7)	0.935	0.6 (0.2 – 0.9)	0.963
sTF-His	NiPCPS	8.2×10^{-4} (8.6×10^{-5} – 1.5×10^{-3})	0.930	3.7×10^{-5} (3.2×10^{-7} – 7.4×10^{-5})	0.950

		Hill equation			
		No FX		With FX	
Ligand	Lipid	EC_{50} (μM) (95% CI)	r^2	EC_{50} (μM) (95% CI)	r^2
sgC-His	None	>12.0	-	2.9 (1.6 – 4.2)	0.994
sgC-His	PCPS	>13.0	-	2.7 (1.3 – 5.3)	0.812
sgC-His	NiPC	1.6 (0.7 – 3.7)	0.925	1.0 (0.8 – 1.1)	0.992
sgC-His	NiPCPS	0.8 (0.5 – 1.3)	0.943	0.4 (0.3 – 0.6)	0.974
sTF-His	NiPCPS	1.0×10^{-3} (4.3×10^{-4} – 2.4×10^{-3})	0.927	3.2×10^{-5} (1.8×10^{-5} – 5.6×10^{-5})	0.957

Table S1

*Data were analyzed using two equations

Simple binding curve: A single interaction between two molecules is characterized by $\mathrm{K_d} = ([\mathrm{A}] \cdot [\mathrm{T}])/[\mathrm{AT}]$, where A is the protein being monitored (i.e. fluorescent), T is the titrant, and AT is the resulting complex. Where A_0 and T_0 are the initial concentrations added and A and T are the free/unbound concentrations, the law of conservation of mass dictates $[\mathrm{A_0}] = [\mathrm{A}] + [\mathrm{AT}]$ and $[\mathrm{T_0}] = [\mathrm{T}] + [\mathrm{AT}]$. These are used to derive the quadratic equation:
$[\mathrm{AT}] = 1/2\ ([\mathrm{A_0}] + [\mathrm{T_0}] + \mathrm{Kd} \pm \sqrt{}(([\mathrm{A_0}] + [\mathrm{T_0}] + \mathrm{Kd}\ )^2 - 4 \cdot [\mathrm{A_0}] \cdot [\mathrm{T_0}]\ ))$.
To convert F_{norm} to [AT], the following equation was used:

$$\mathrm{F_{norm}} = \left(\frac{[\mathrm{A}]}{[\mathrm{A_0}]} \cdot \mathrm{F_{norm,A}}\right) + \left(\frac{[\mathrm{AT}]}{[\mathrm{A_0}]} \cdot \mathrm{F_{norm,AT}}\right)$$

$\mathrm{F_{norm,A}}$ is the normalized fluorescence signal when A is not bound to T. Conversely, $\mathrm{F_{norm,AT}}$ is the corresponding signal when A is bound to T.

Hill equation: A complex interaction where ligand binding shows cooperativity and may deviate from 1:1 binding,
$\mathrm{F_{norm}(c)} = \mathrm{Unbound} + \frac{\mathrm{Bound-Unbound}}{1+10^{\mathrm{Hill}\cdot\log(\mathrm{EC50}-\mathrm{c})}}$.
The concentration of titrant (c) was subject to $\log_{10}$ transformation. “Unbound” is the F_{norm} signal of the non-complexed protein whereas “Bound” is the F_{norm} signal of the complex. EC_{50} is the half-maximal effective concentration and “Hill” is the Hill coefficient of cooperativity.

Table S1 Footnote