SUPPORTING INFORMATION

Extended interaction networks with HCV protease NS3-4A substrates explain the lack of adaptive capability against protease inhibitors

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SUPPLEMENTARY FIGURES

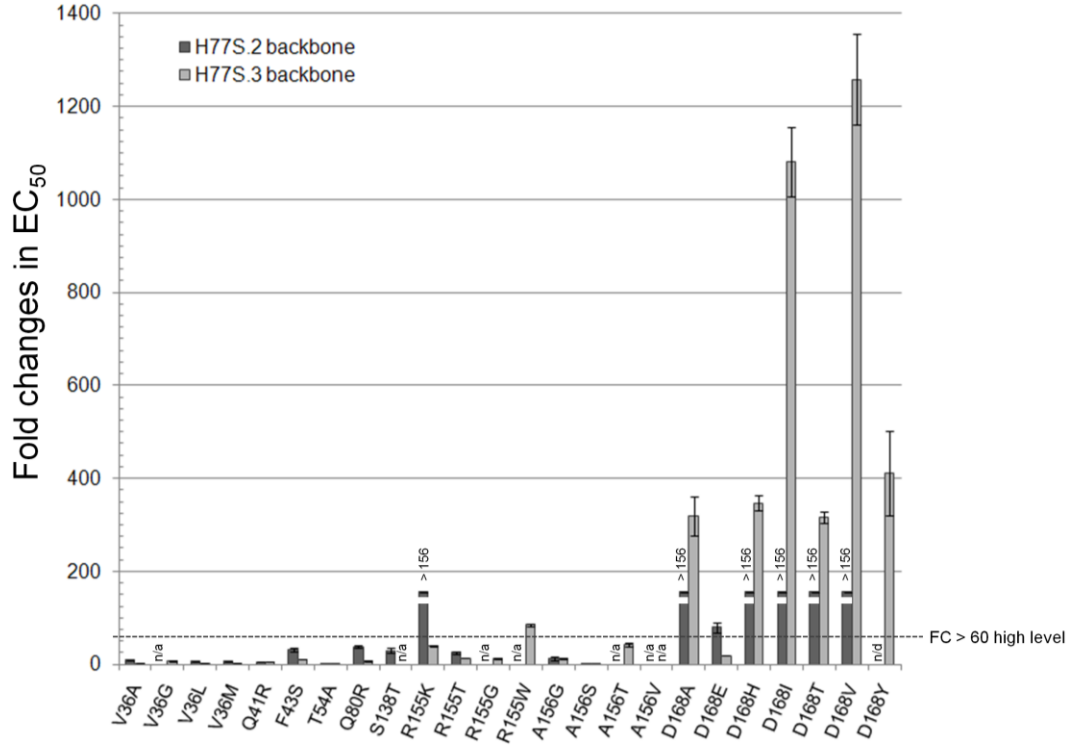

Figure S1.
Resistance level of simeprevir for PI-resistant variants. Resistance level expressed as fold change (FC) in EC_{50} values relative to H77S.2 (NS3-Q41R backbone) and H77S.3 (NS3-Q41 backbone). Data shown represent the mean ± S.D. from at least three independent experiments. n/a: not available; n/d: not done.

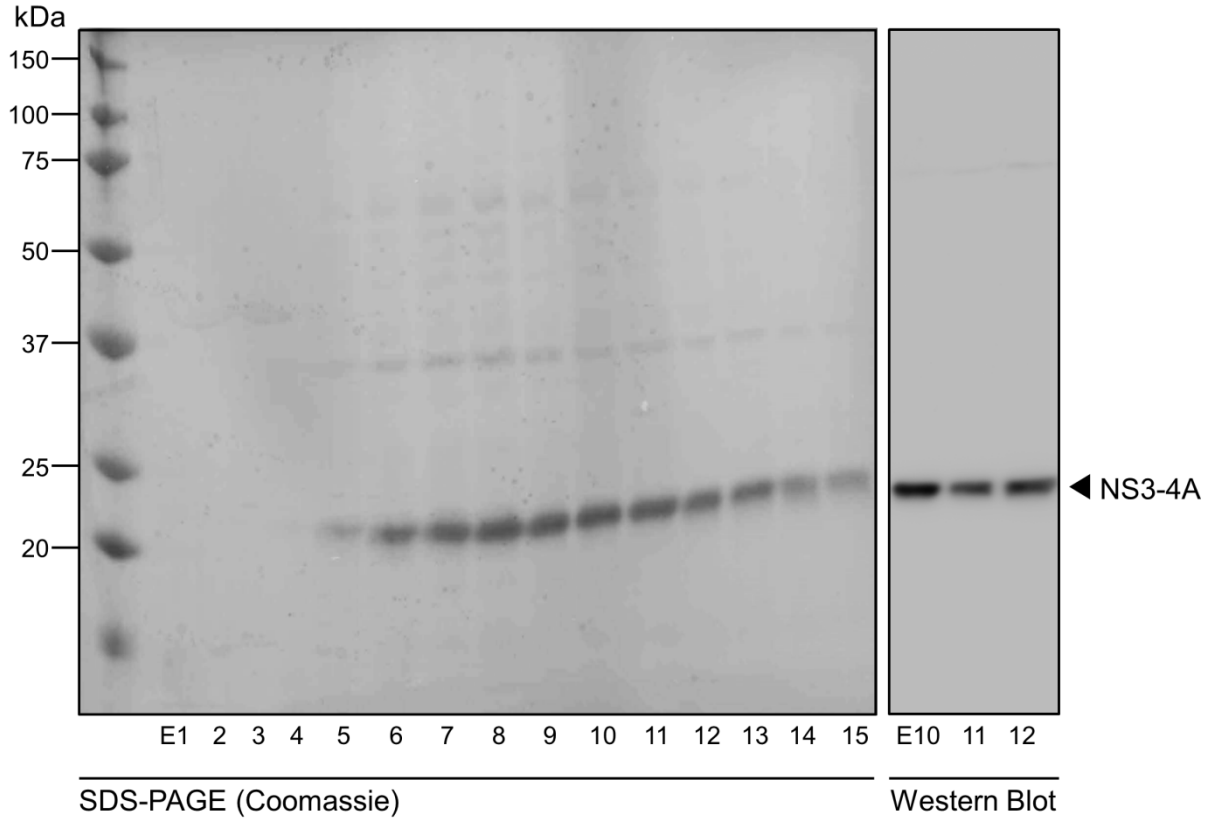

Figure S2.
Expression of purified NS3-4A protease. Purification results of the NS3-4A protease proteolytic domain expressed in Rosetta pLysS cells, purified by Ni-NTA agarose affinity chromatography (Coomassie stained SDS-PAGE). Length standard in line 1 and eluted fractions from the Ni-NTA in line E1 to E15; purified product identified by anti-NS3 Western blot in line E10 to E12.

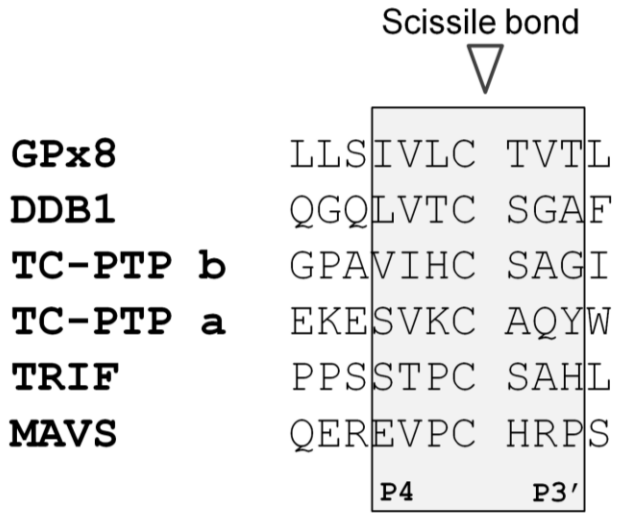

Figure S3.
Cellular targets of the NS3-4A protease. Alignment of NS3-4A cleavage sites within two adaptor proteins in viral RNA sensing and innate immunity, MAVS and TRIF, a membrane-associated glutathione peroxidase (GPx8), the E3 ubiquitin ligase component UV-damaged DNA-binding protein 1 (DDB1) and the T-cell protein tyrosine phosphatase (TC-PTP), cleavage site *a* and *b* (52-55). Residues surrounding a cleavage site are designated from the amino- to carboxyl-terminus, that is, P7-P1 and P1'-P4', with the scissile bond between P1 and P1' (51).

SUPPLEMENTARY REFERENCES

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55. Kang, X., Chen, X., He, Y., Guo, D., Guo, L., Zhong, J., and Shu, H.B. (2013) DDB1 is a cellular substrate of NS3/4A protease and required for hepatitis C virus replication. *Virology*. **435**, 385-394.