



A multiplex interactome of Ebola virus proteins reveals TM9SF2 as a cell-surface attachment factor that promotes viral entry

Limin Shang¹, Shouwen Du^{2,3}, Yuchen Liu¹, Letian Li⁴, Xi Wu⁵, Yanzhi Yuan¹,
Chaozhi Jin¹, Qingkun Mi¹, Yuhang Wang³, Xiaoshuang Shi⁴, Jiamin Wang^{2,4},
Guoqing Zhang⁴, Yidan Ma⁴, Weijin Huang⁵, Jigang Wang³, Jian Wang¹, Chang Li⁴

¹National Center for Protein Sciences (Beijing),

State Key Laboratory of Medical Proteomics, Beijing, China;

²Key Laboratory of Livestock Disease Prevention of Guangdong Province, Guangzhou, China;

³The First Affiliated Hospital of Southern University of Science and Technology
(Shenzhen People's Hospital), Shenzhen, China;

⁴Changchun Veterinary Research Institute,
Chinese Academy of Agricultural Sciences, Changchun, China;

⁵National Institutes for Food and Drug Control, Beijing, China



Limin Shang, Shouwen Du, Yuchen Liu, Letian Li, Xi Wu, Yanzhi Yuan, Chaozhi Jin, et al. 2026.

A multiplex interactome of Ebola virus proteins reveals TM9SF2 as a cell-surface attachment factor that promotes viral entry.

iMetaOmics 3: e70116. <https://doi.org/10.1002/imo2.70116>



Introduction

**Previous history
of Ebola
outbreaks in
Africa since 1976**

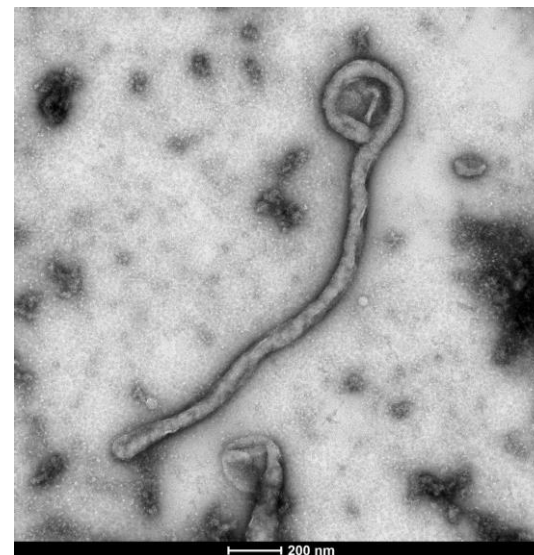
○ 1-10
○ 11-100
○ 101-1,000
○ 1,000+

● Previous Bundibugyo Ebola strain
● Other previous Ebola strains*



SOURCE © Mapcreator.io | © OpenStreetMaps, CDC; GRAPHIC Janet Loehrke/USA TODAY

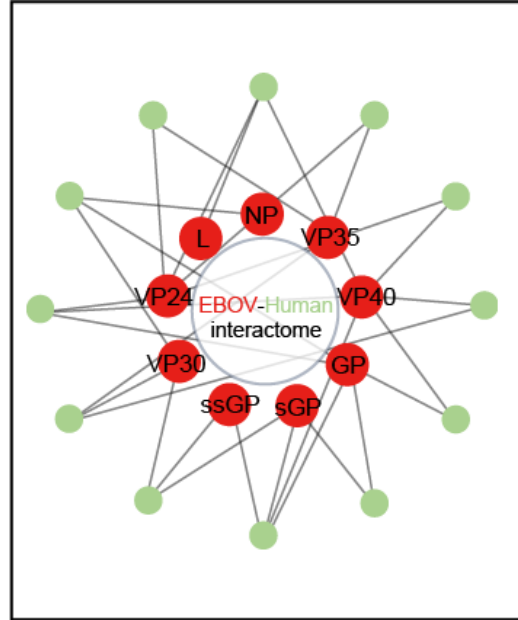
*NOTE Previous Ebola strains included: Ebola virus (species *Orthoebolavirus zairense*), Sudan virus (species *Orthoebolavirus sudanense*) and Taï Forest virus (species *Orthoebolavirus taiense*)



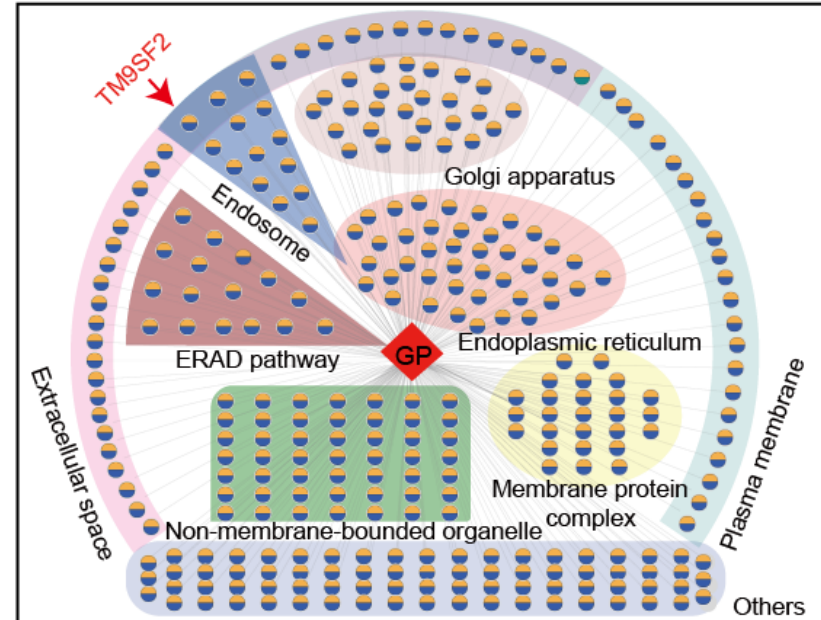
- Ebola virus
- ✓ Severe symptoms
- ✓ Highly contagious
- ✓ High lethality



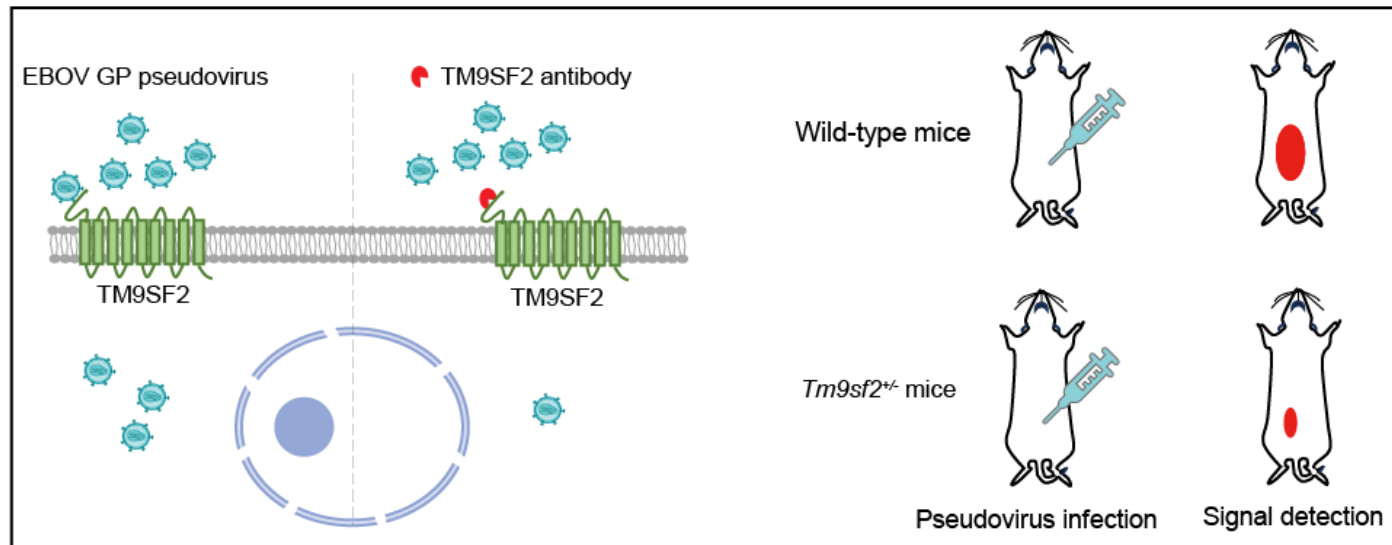
Highlights



EBOV-Human protein-protein interactome



EBOV GP interacts with TM9SF2



TM9SF2 promotes pseudoviral infection both *in vitro* and *in vivo*

Construction of a comprehensive EBOV-human interactome network

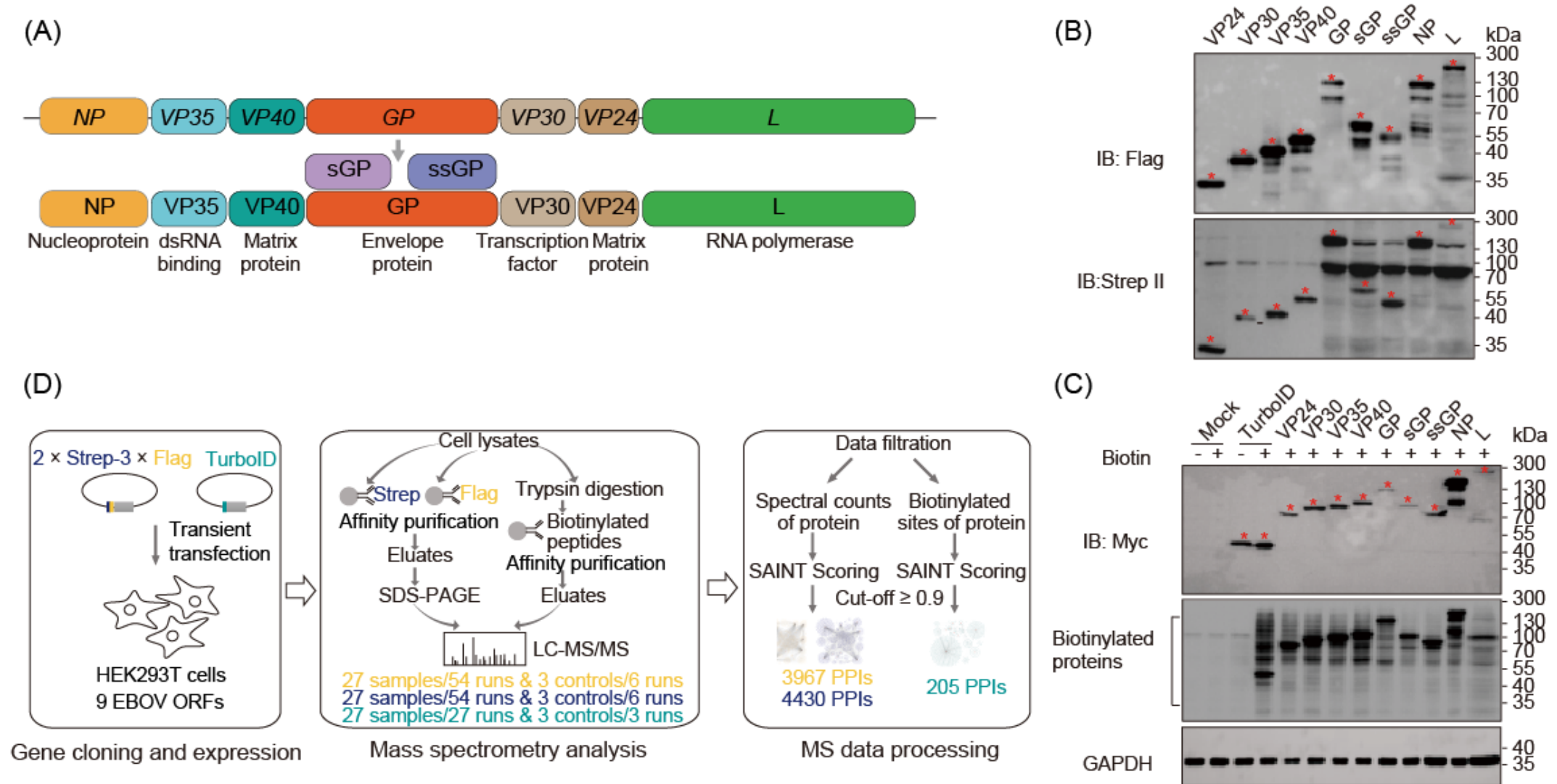


Figure 1. Screening strategies used for constructing the EBOV-human interactome.

Analysis of the EBOV-human PPI network

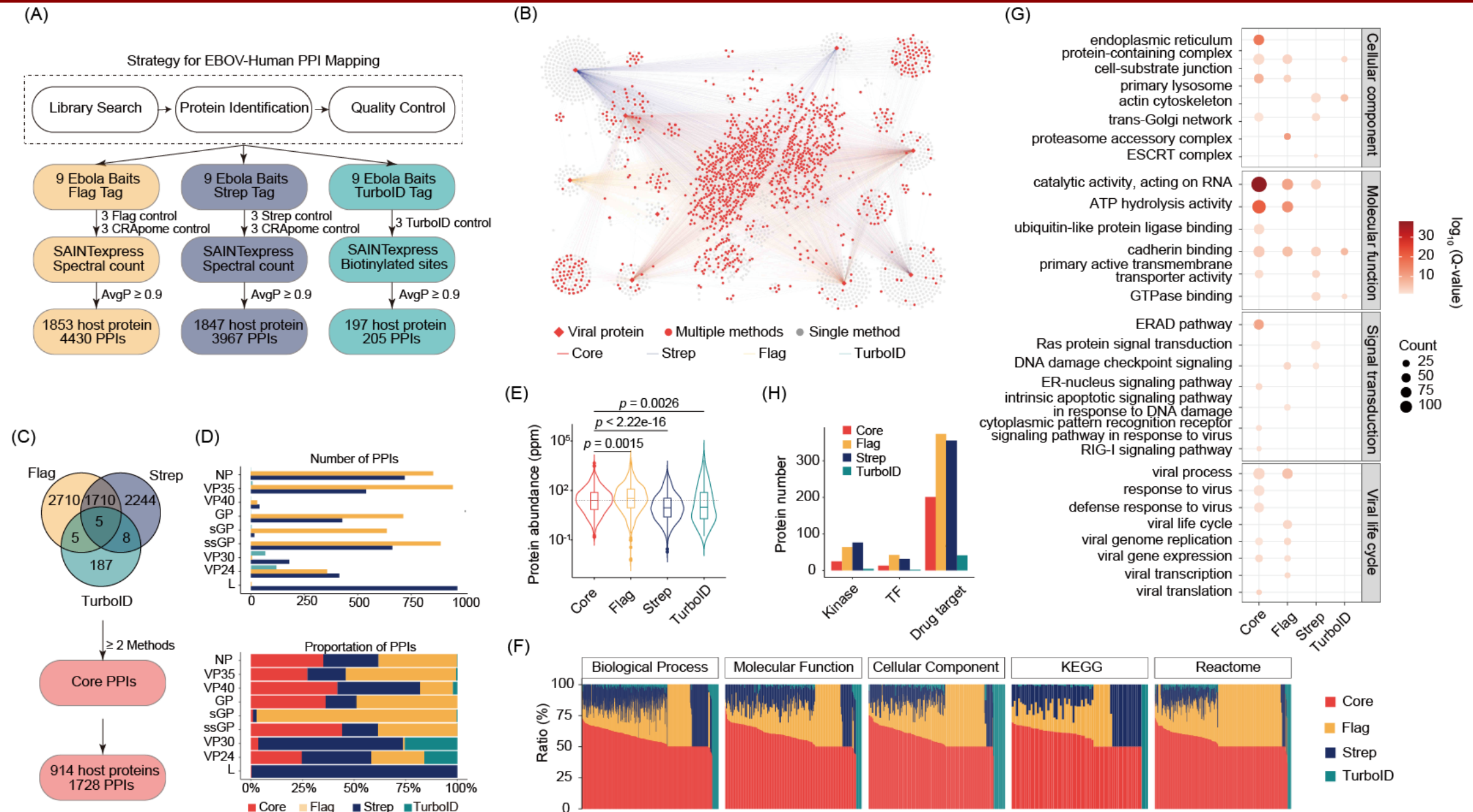


Figure 2. Bioinformatics analysis of the EBOV-human interactome.

TM9SF2 is a potential host factor for EBOV

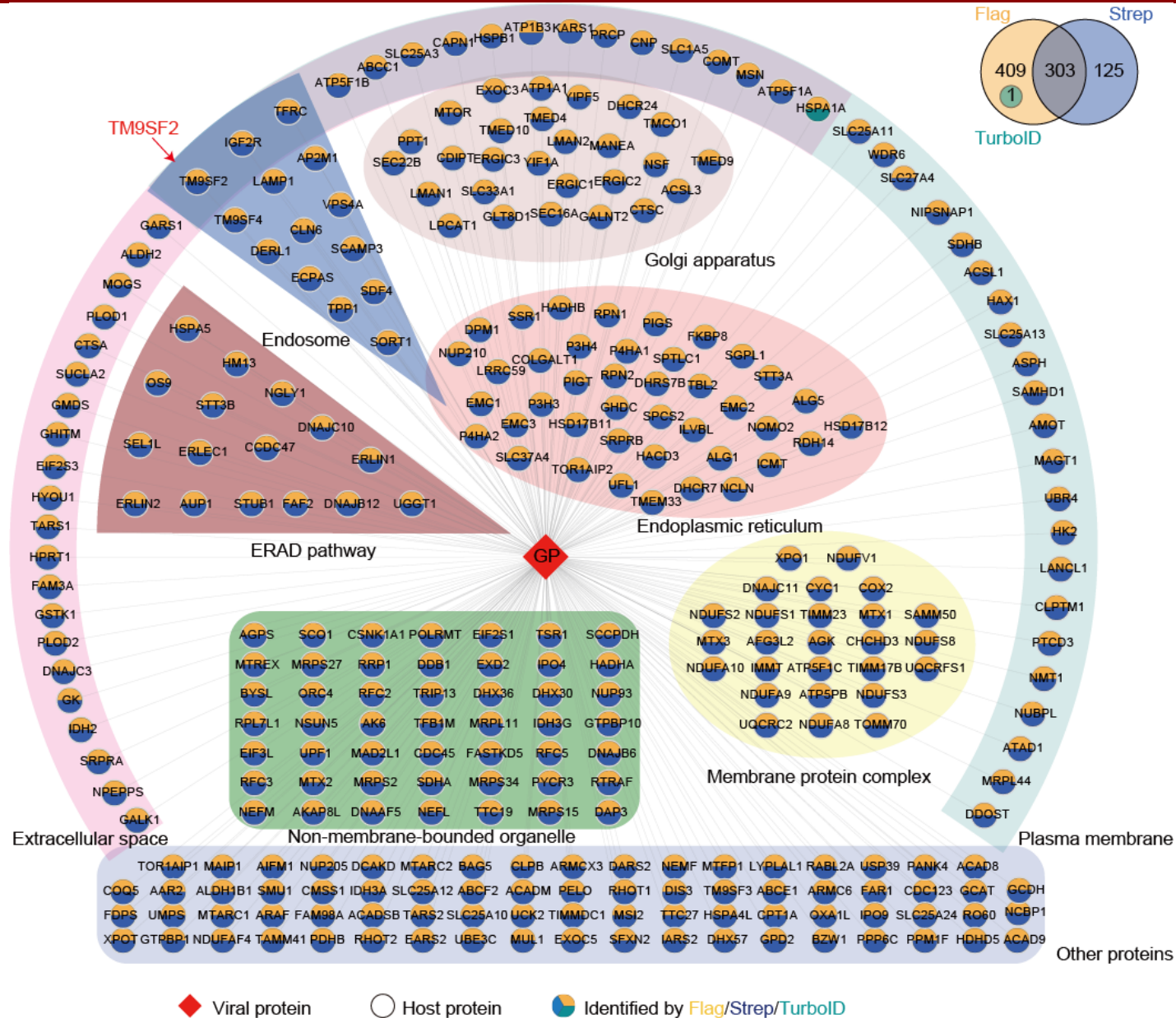


Figure 3. Core interaction network of EBOV glycoprotein.

TM9SF2 facilitates EBOV GP-mediated infection

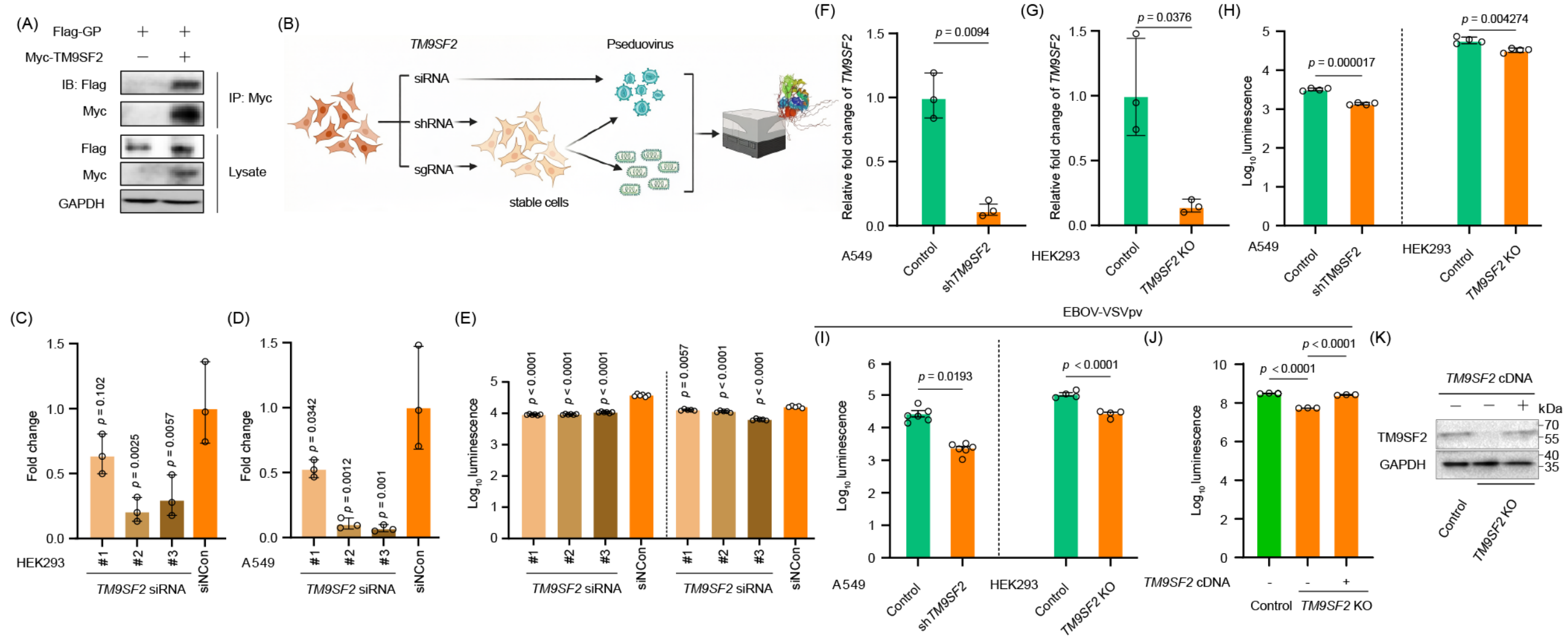


Figure 4. Suppression of TM9SF2 expression impairs EBOV GP-mediated viral infection.

TM9SF2 facilitates EBOV GP-mediated infection

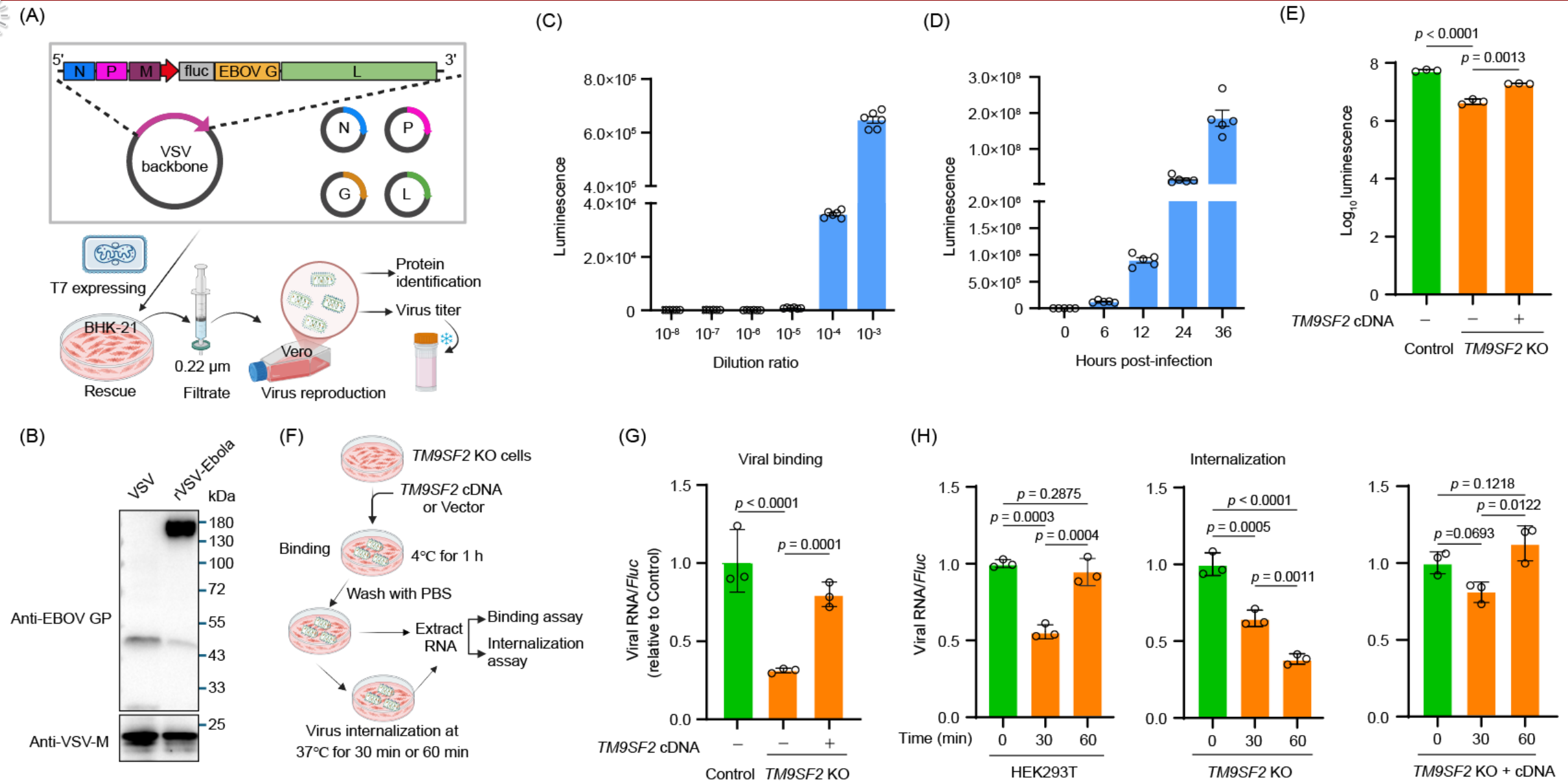


Figure 5. TM9SF2 functions as a host factor for EBOV GP-mediated infection.

TM9SF2 binds to the RBD of GP to promote viral attachment

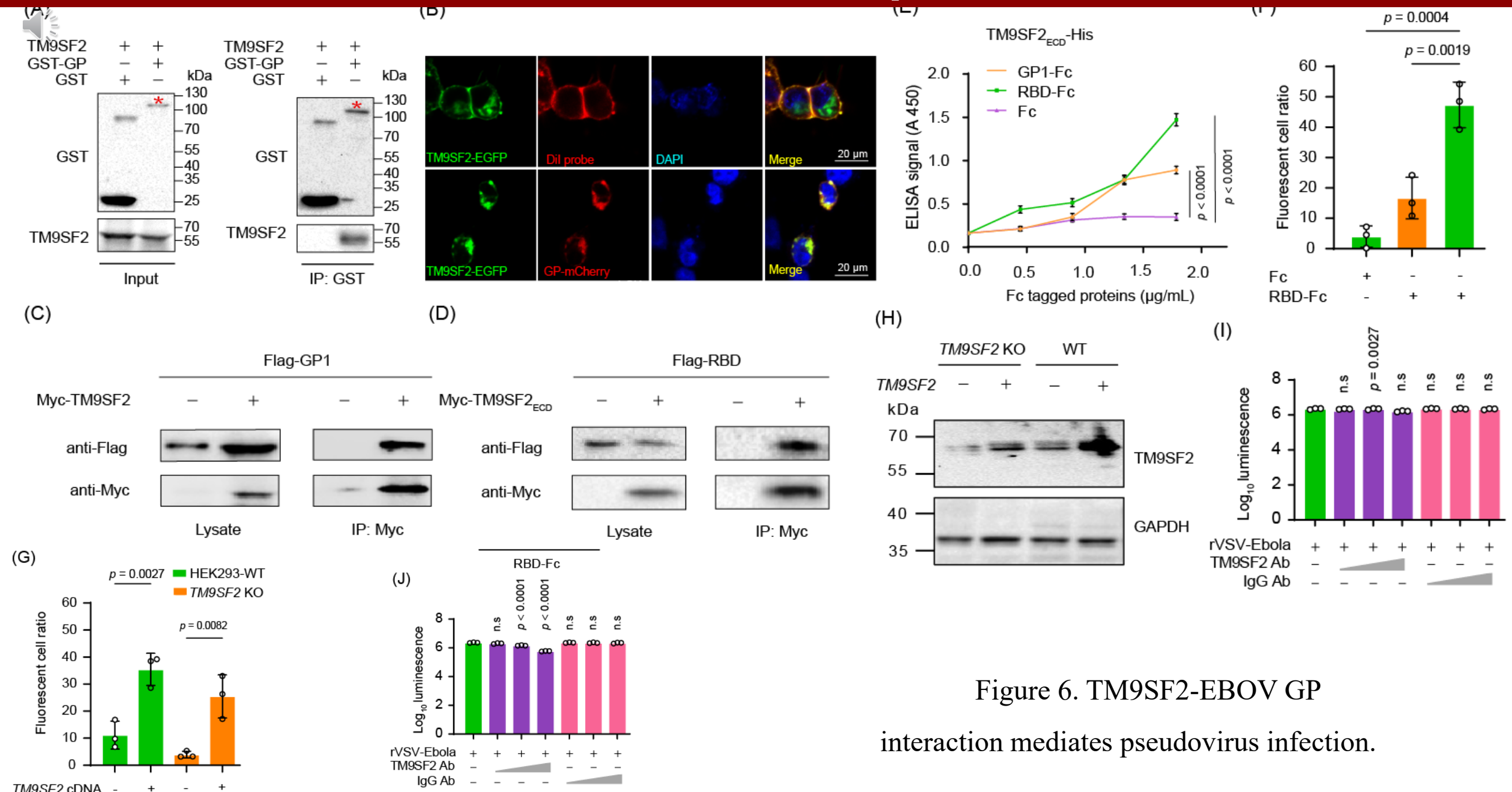
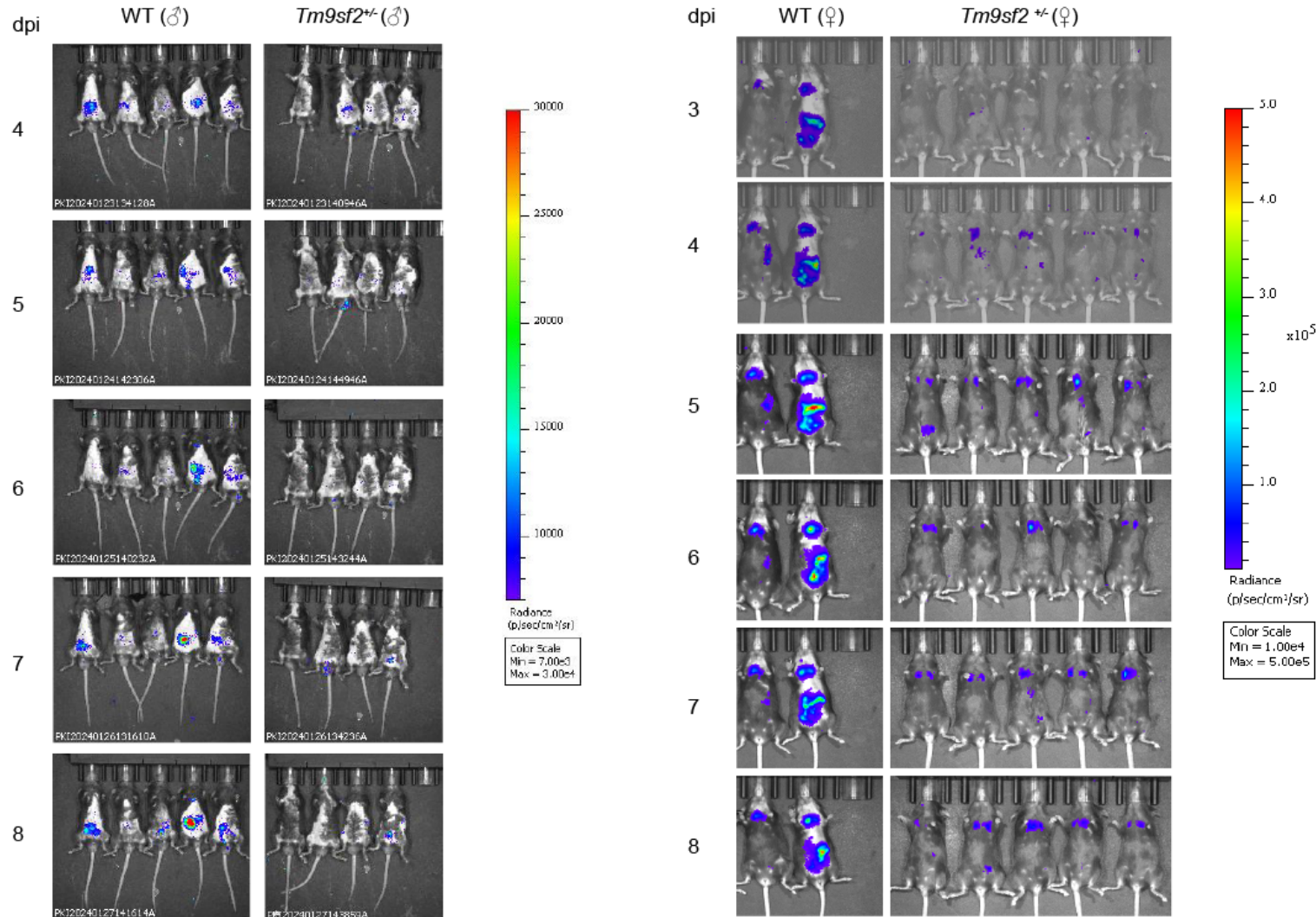


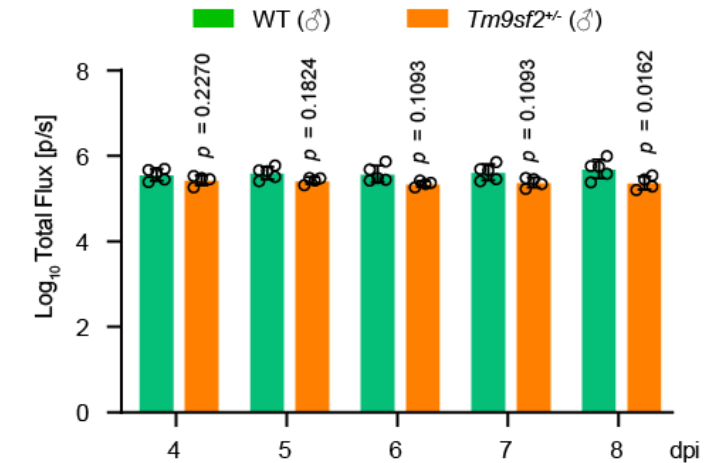
Figure 6. TM9SF2-EBOV GP interaction mediates pseudovirus infection.

Murine TM9SF2 facilitates EBOV pseudovirus infection *in vivo*

(A)



(B)



(C)

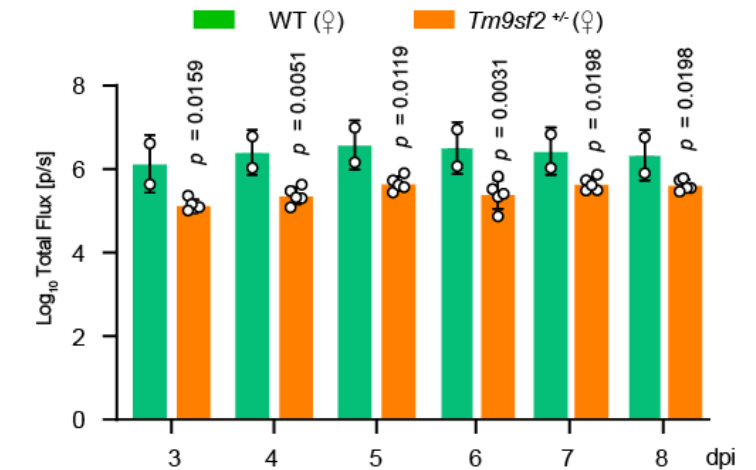


Figure 7. TM9SF2 promotes pseudoviral infection *in vivo*.



Summary

- ❑ This study provides a comprehensive analysis of the EBOV-human protein-protein interaction network.
- ❑ Identifies TM9SF2 as a critical host factor that promotes viral attachment and internalization during EBOV GP-mediated pseudovirus entry.
- ❑ Targeting TM9SF2 represents a promising therapeutic strategy for antiviral intervention.
- ❑ These findings advance our understanding of EBOV entry mechanisms and pave the way for developing host-targeted therapies against EBOV and other viral infections.

Limin Shang, Shouwen Du, Yuchen Liu, Letian Li, Xi Wu, Yanzhi Yuan, Chaozhi Jin, et al. 2026.

A multiplex interactome of Ebola virus proteins reveals TM9SF2 as a cell-surface attachment factor that promotes viral entry.

iMetaOmics 3: e70116. <https://doi.org/10.1002/imo2.70116>



“***iMeta***” launched in 2022 by iMeta Science Society, **impact factor (IF) 44.4**, **ranking top 47/22643 in the world**. It aims to publish innovative and high-quality papers with broad and diverse audiences. Its scope is similar to *Cell*, *Nature* and *Science*. Its unique features include video abstract, bilingual publication, and social media with 800,000 followers. Indexed by [SCIE/ESI](#), [PubMed](#), [Google Scholar](#) etc.

“***iMetaOmics***” launched in 2024, indexed by [ESCI](#), [PubMed](#), [Google Scholar](#), with a **target IF>15**, and its scope is similar to *Nature Communications*, *Science Advances*, *Advanced Science*, *Nucleic Acids Research*, etc.

“***iMetaMed***” launched in 2025, with a target IF>15, similar to *Med*, *Cell Reports Medicine*, *eBioMedicine*, *eClinicalMedicine* etc.



Society: <http://www.imeta.science>

Publisher: <https://wileyonlinelibrary.com/journal/imeta>

iMeta: <https://wiley.atyponrex.com/journal/IMT2>

Submission: iMetaOmics: <https://wiley.atyponrex.com/journal/IMO2>

iMetaMed: <https://wiley.atyponrex.com/journal/IMM3>



[iMetaScience](#)



[iMetaScience](#)



office@imeta.science
imetaomics@imeta.science



[Promotion Video](#)

Update
2026/6/17