OXCT1 driven succinylation of PSMG3 stabilizes the proteasome to facilitate picornavirus replication

Huisheng Liu[1#], Qiao Xue[1#], Pengfei Liu[1#]
Zhihua Dong[1], Weijun Cao[1], Weijun Cao[1], Yingming Zhu[1]
Lei Deng[2*], Zixiang Zhu[1*], Haixue Zheng[1*]

[1]Lanzhou Veterinary Research Institute, Chinese Academy of Agricultural Sciences
[2]Shanghai Veterinary Research Institute, Chinese Academy of Agricultural Sciences



Huisheng Liu, Qiao Xue, Pengfei Liu, Zhihua Dong, Weijun Cao, Fan Yang, Yingming Zhu, et al. 2026. OXCT1 driven succinylation of PSMG3 stabilizes the proteasome to facilitate picornavirus replication. ***iMetaOmics*** 3: e70151. https://doi.org/10.1002/imo2.70151

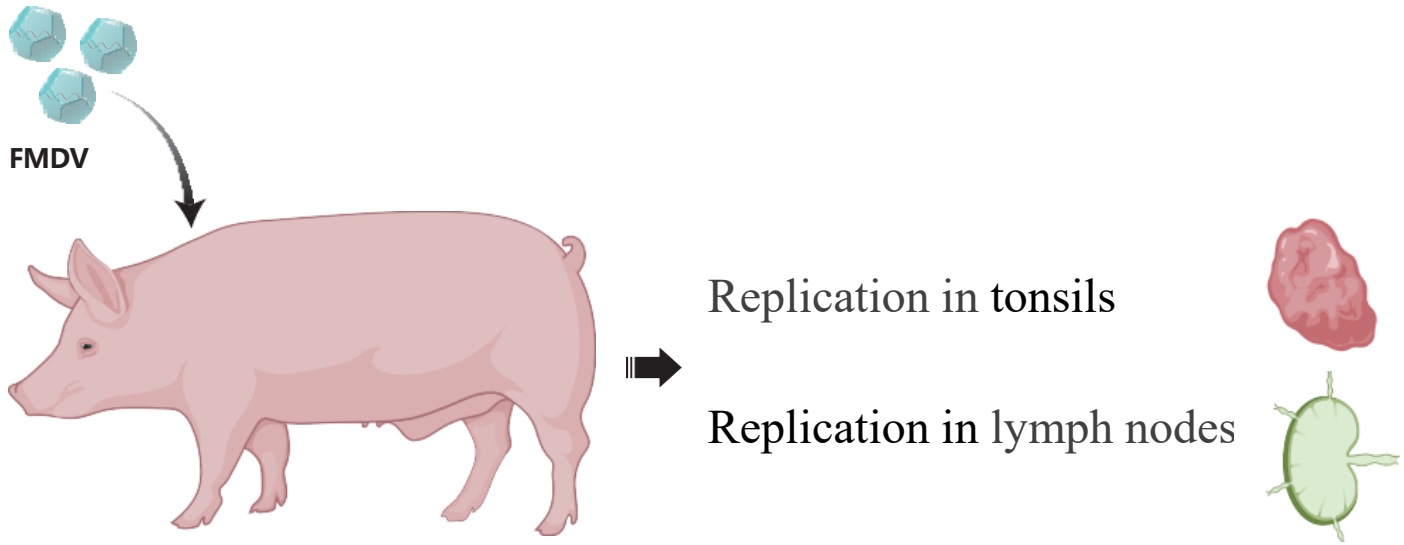
Introduction

Picornavirus include foot-and-mouth disease virus (FMDV), enterovirus 71 (EV71), and Seneca Valley virus (SVV).

Foot-and-mouth disease is a severe worldwide infectious disease caused by FMDV infection in cloven-hoofed animals such as pigs, cattle, and sheep.

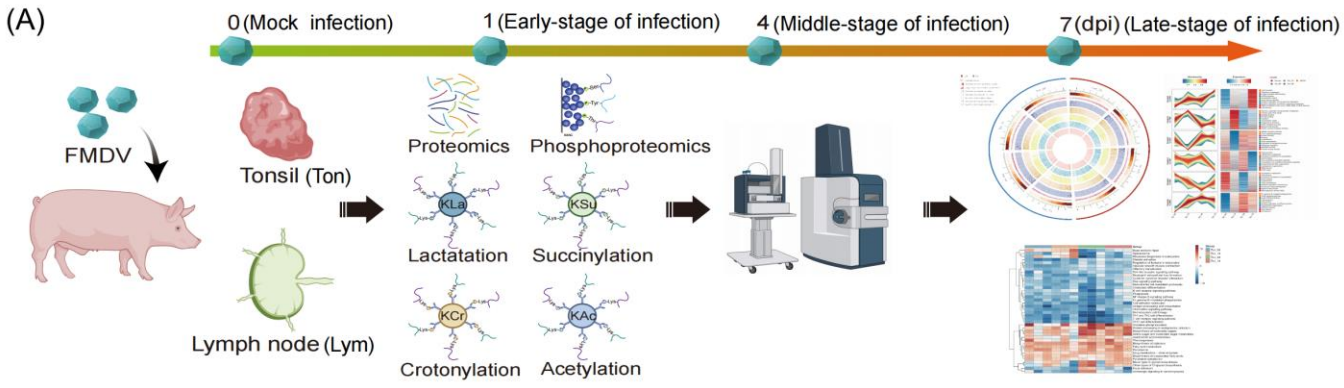
It is listed as a notifiable disease by WOAH and as a Class I animal disease in China.

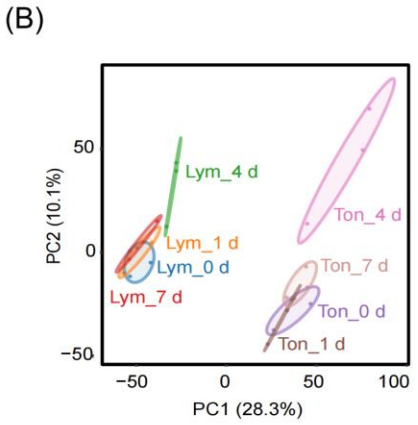
This study integrates proteomic and post-translational modifications (PTMs) data to investigate the mechanism underlying rapid FMDV replication in pigs.

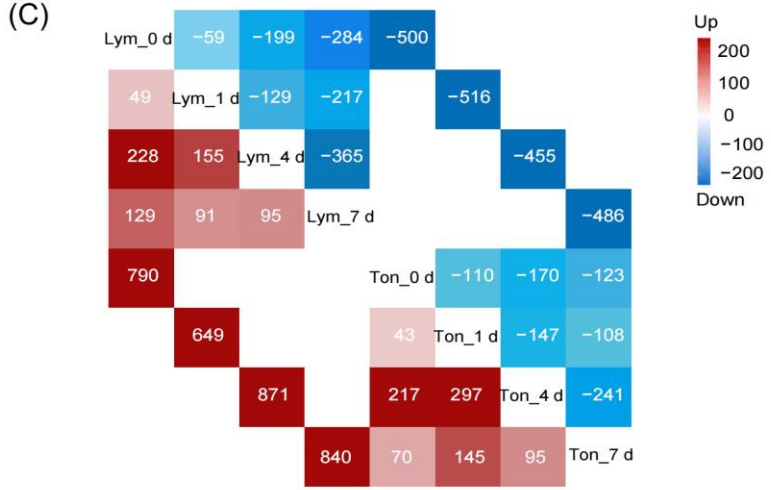


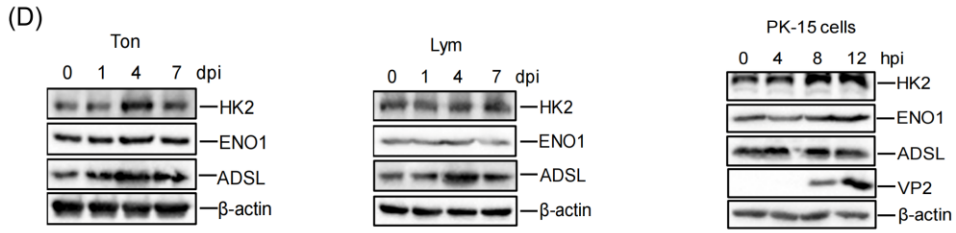
Scientific question: How does FMDV replicate in the tonsils and lymph nodes of pigs

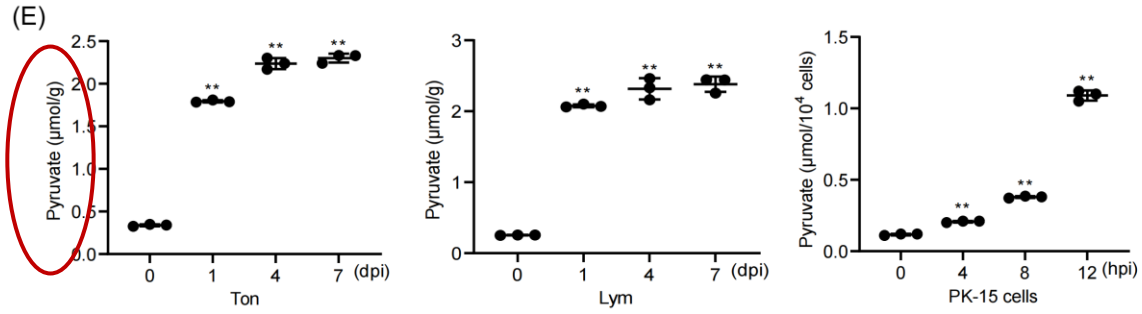
FMDV regulates host metabolism by modulating the metabolic enzymes

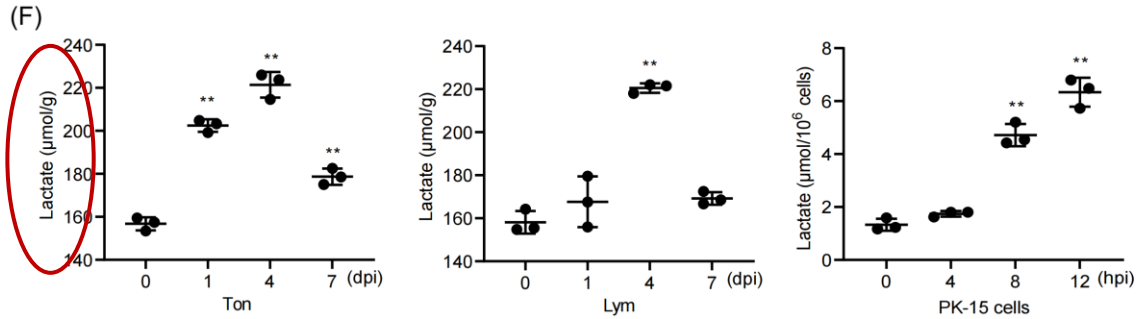


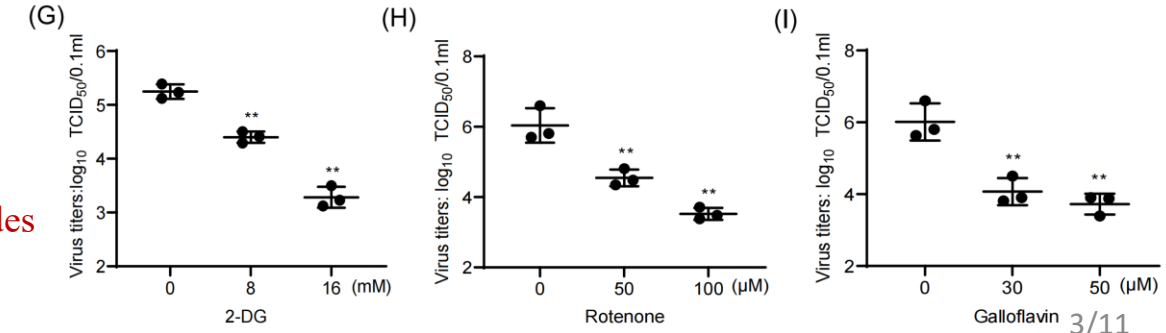












FMDV promotes the host innate immune responses while regulating the expression of numerous metabolic enzymes

Ton: tonsils

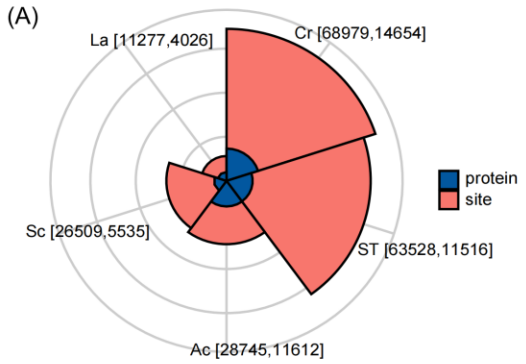
Lym: lymph nodes

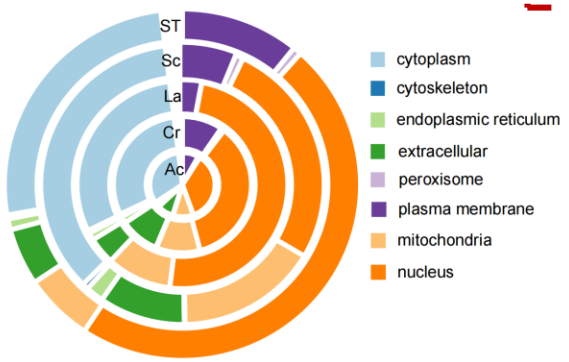
Glycolysis inhibitor

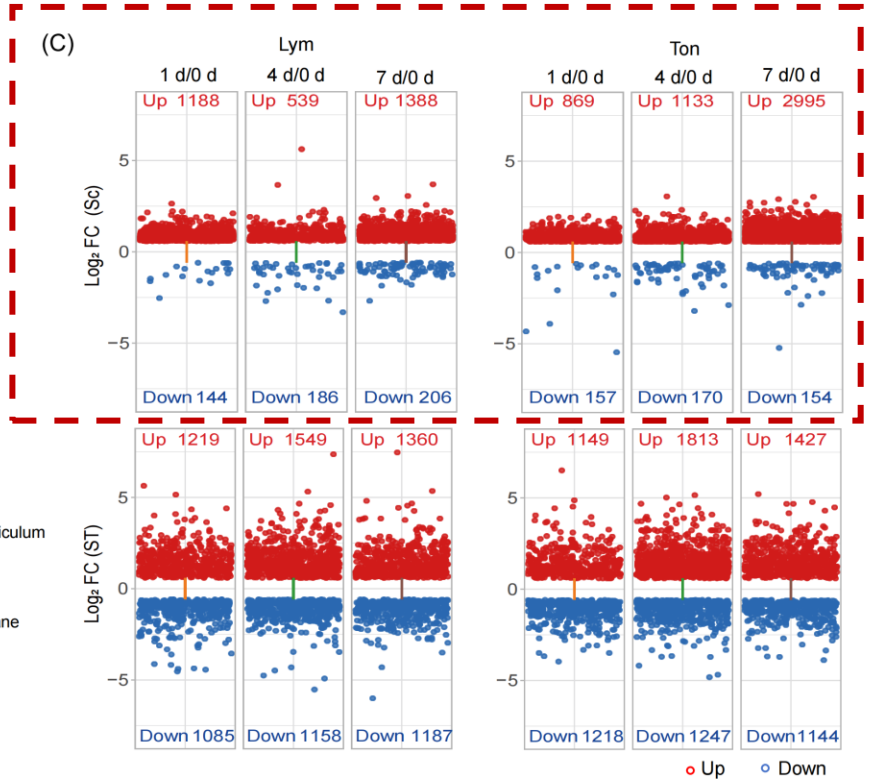
TCA cycle inhibitor

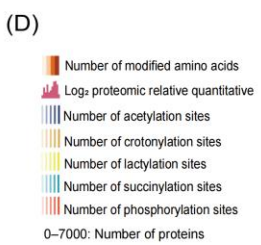
Lactate inhibitor

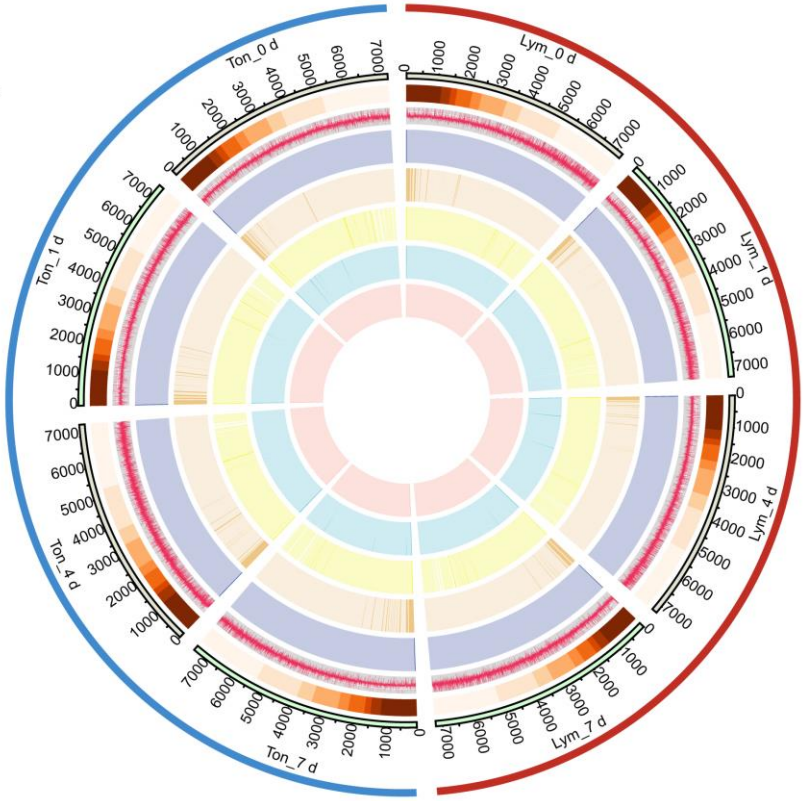
Landscape of the PTMs and succinylation is prominently upregulated

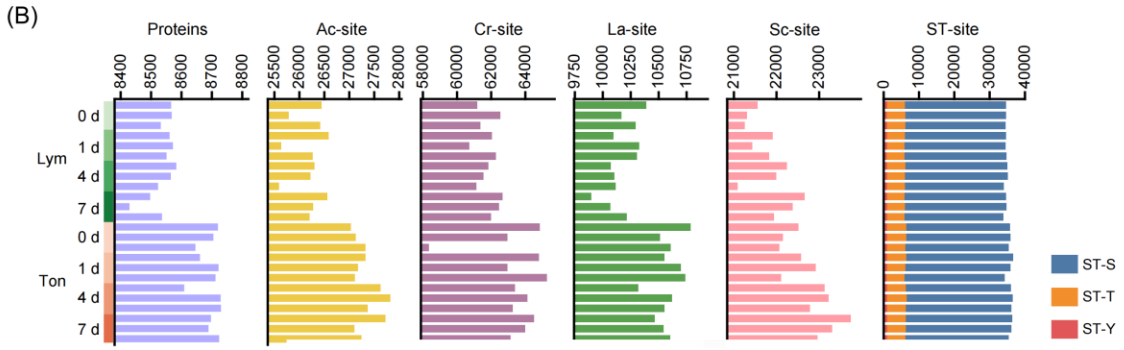






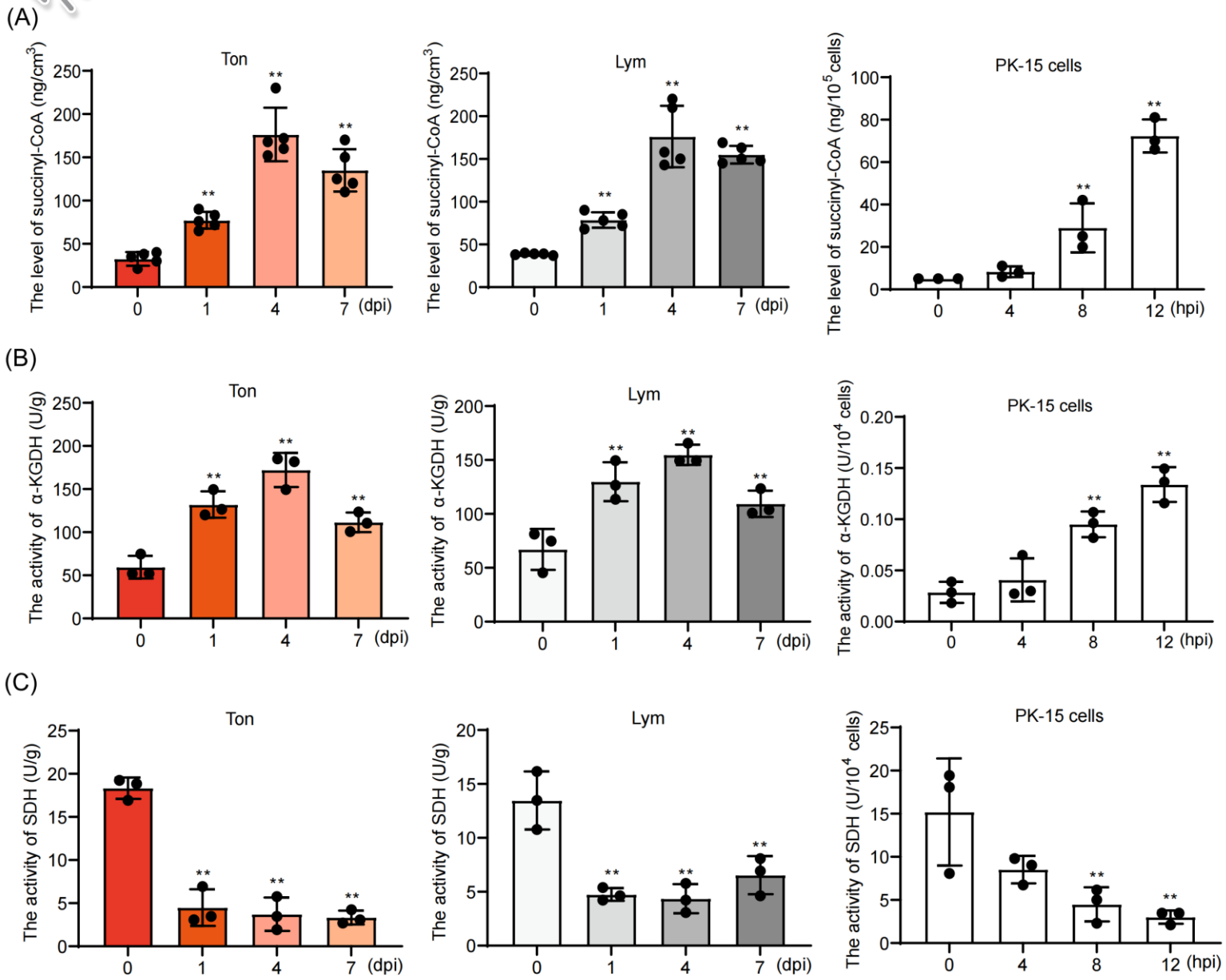


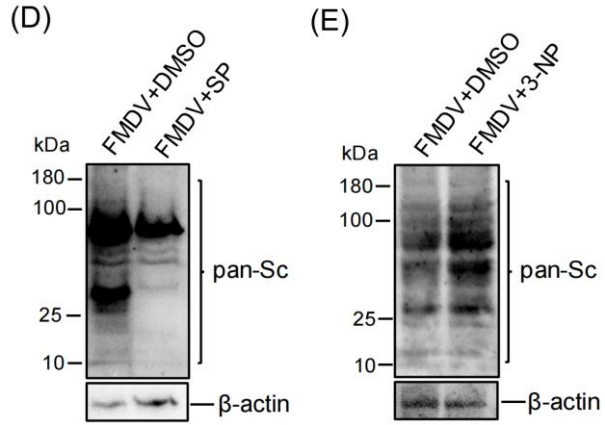


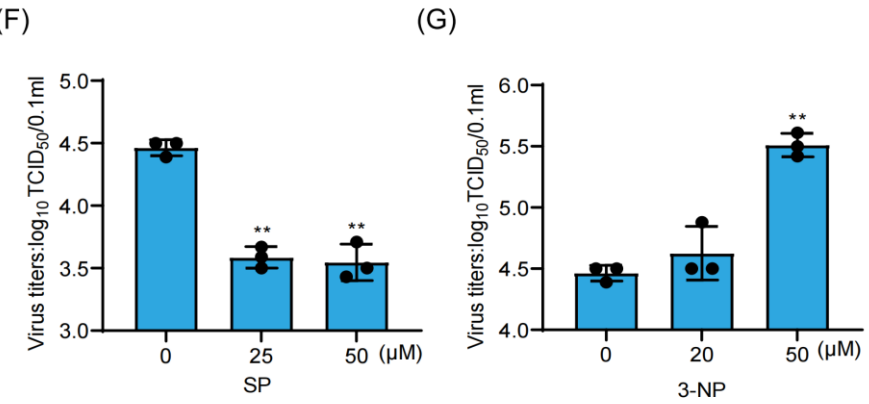


FMDV regulates succinylation, lactylation, acetylation, crotonylation, and phosphorylation, with succinylation showing the most significant upregulation

FMDV enhances succinylation by promoting the level of succinyl-CoA



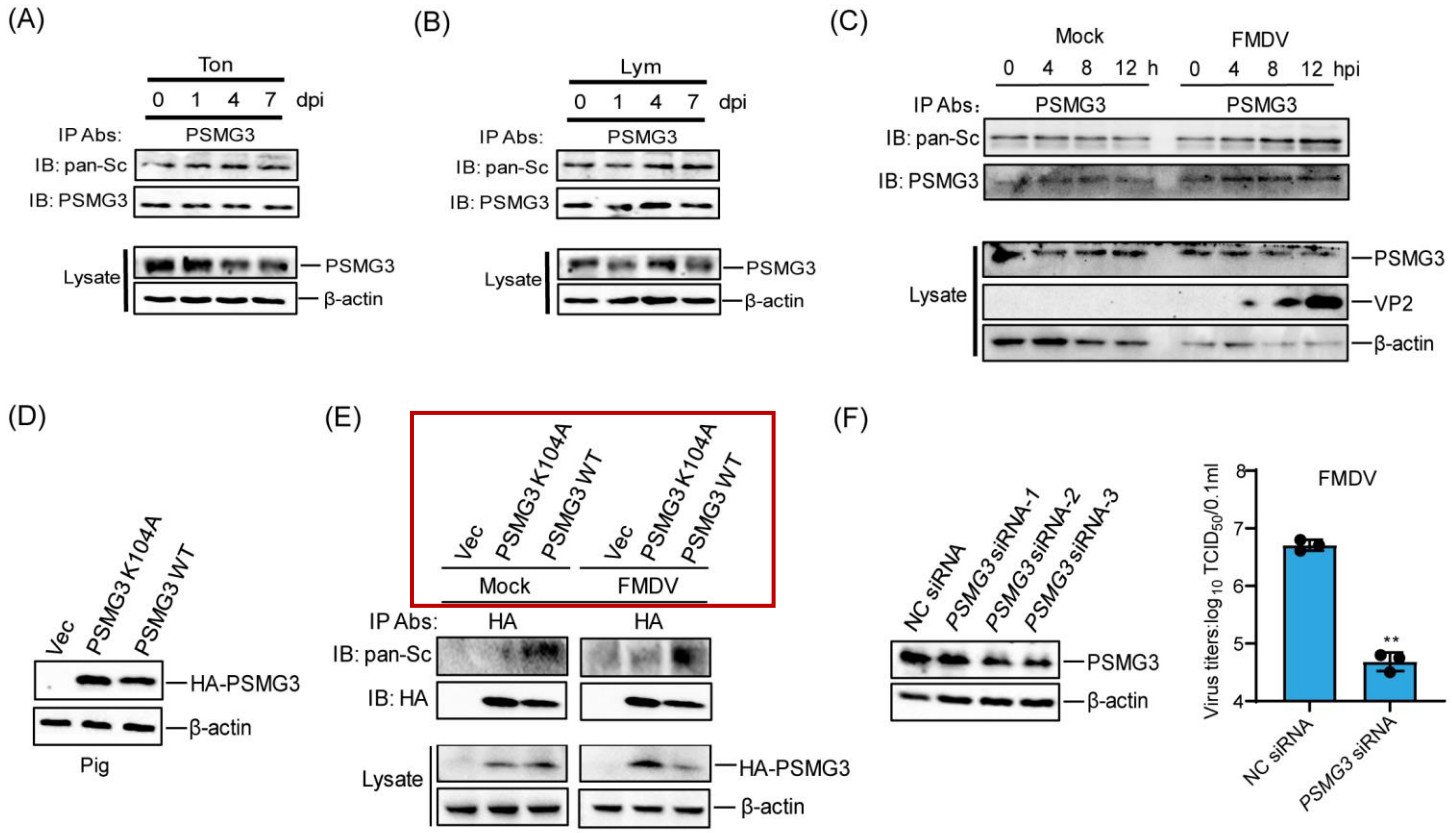


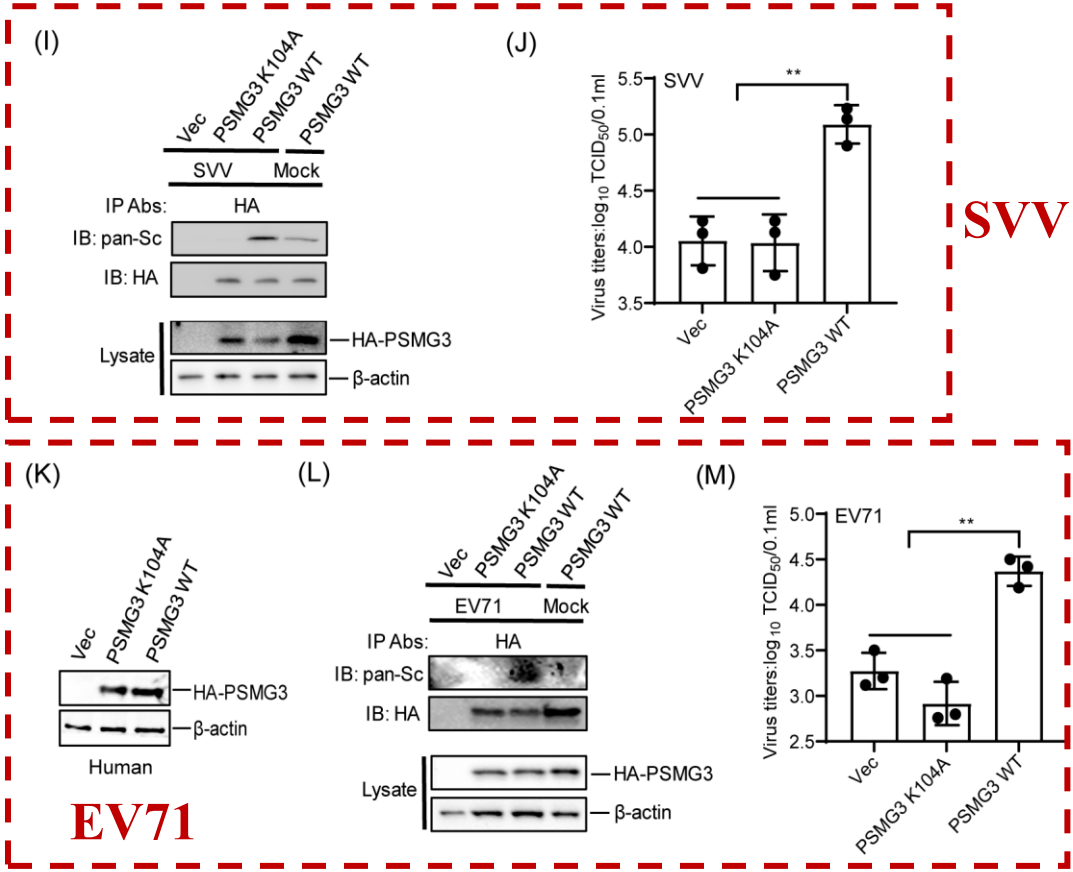


SP: α-KGDH inhibitor
3-NP: SDH inhibitor

FMDV upregulates α-KGDH activity and downregulates SDH activity

The succinylation of PSMG3 K104 residue promotes picornavirus replication

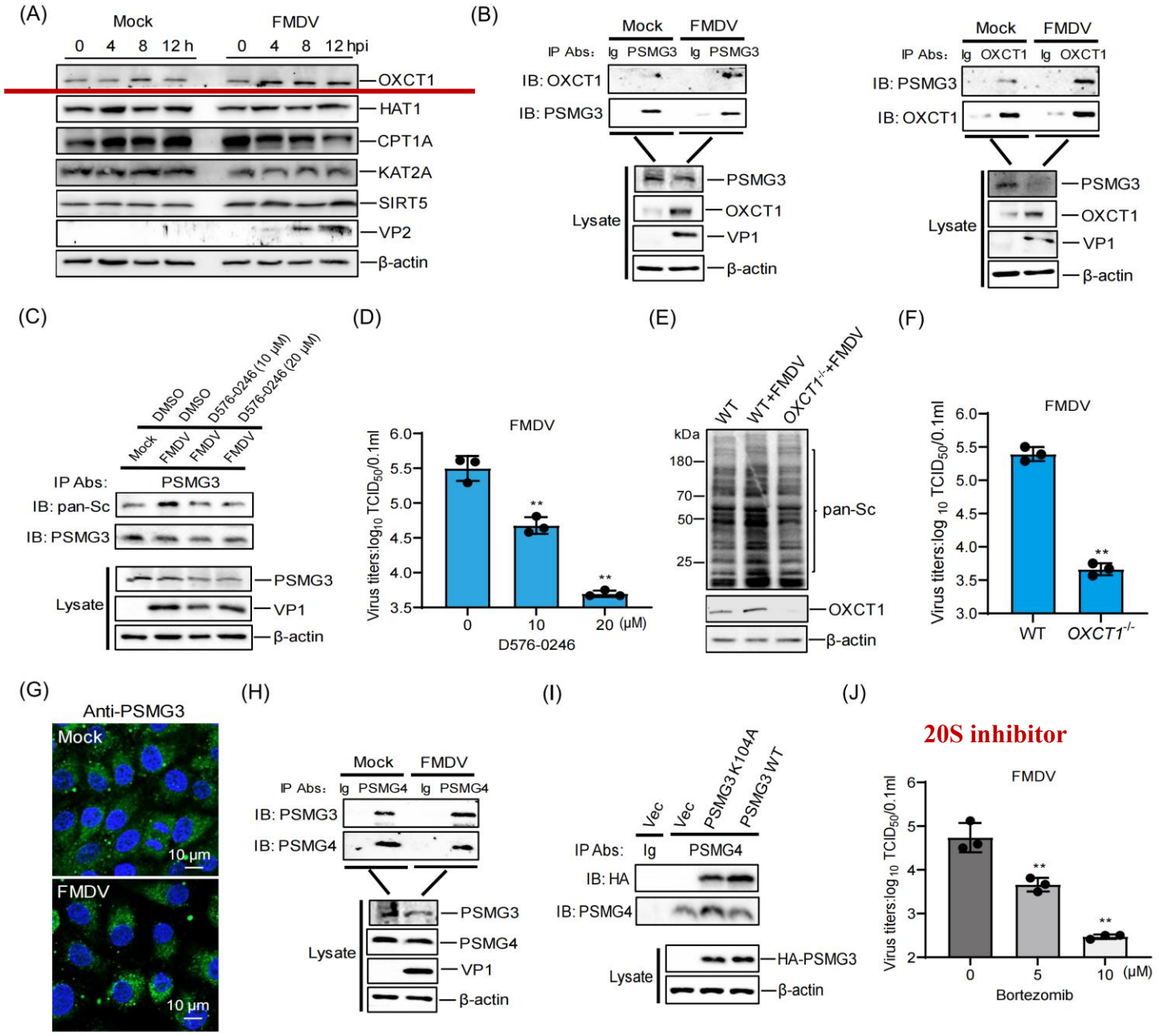




PSMG3: proteasome assembly chaperone 3

Both human and porcine PSMG3 can undergo succinylation at the K104 residue

FMDV utilizes OXCT1 to succinylate PSMG3, enhancing viral replication

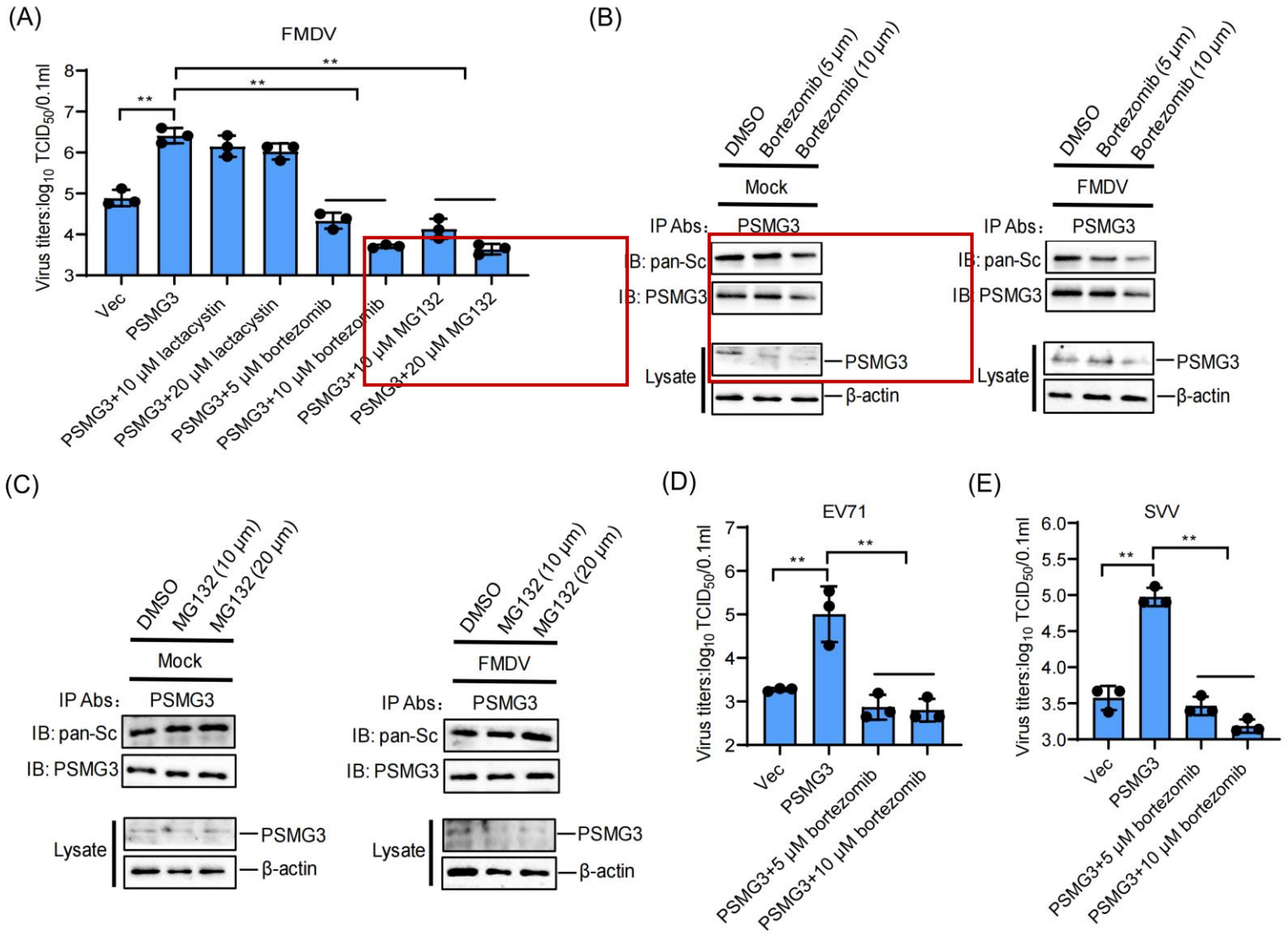


OXCT1: 3-oxoacid CoA-transferase 1

FMDV promotes OXCT1 expression, thereby upregulating PSMG3 succinylation

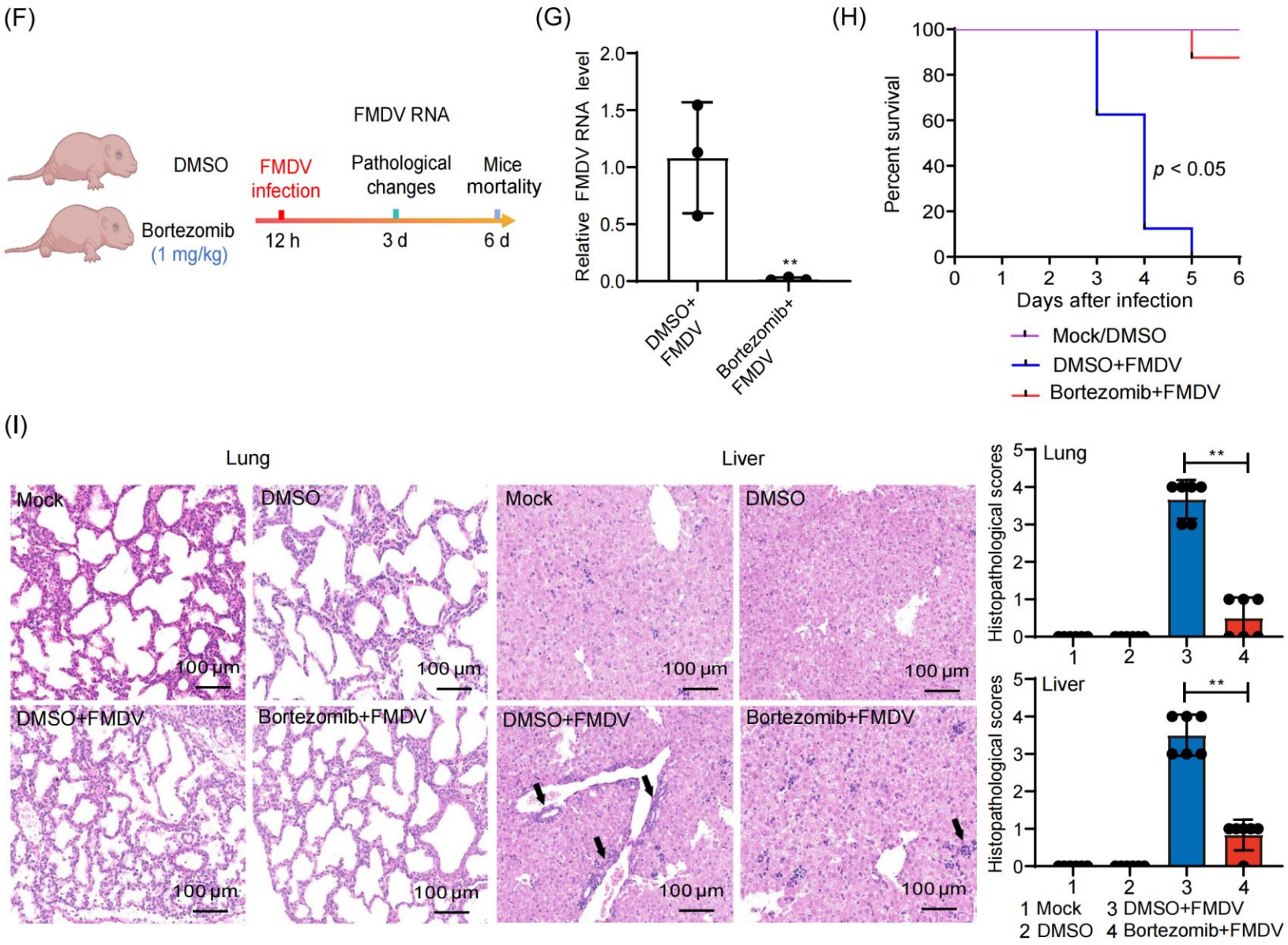
PSMG3 succinylation further promotes the PSMG3–PSMG4 interaction, thereby stabilizing the proteasome and facilitating viral replication

Bortezomib inhibits viral replication by targeting PSMG3 succinylation (in vitro)



In vitro experiments show that the Bortezomib inhibitor inhibits picornavirus replication by targeting PSMG3 succinylation

Bortezomib inhibits viral replication by targeting PSMG3 succinylation (in vivo)



In vivo experiments show that bortezomib inhibits FMDV replication and reduces mouse mortality

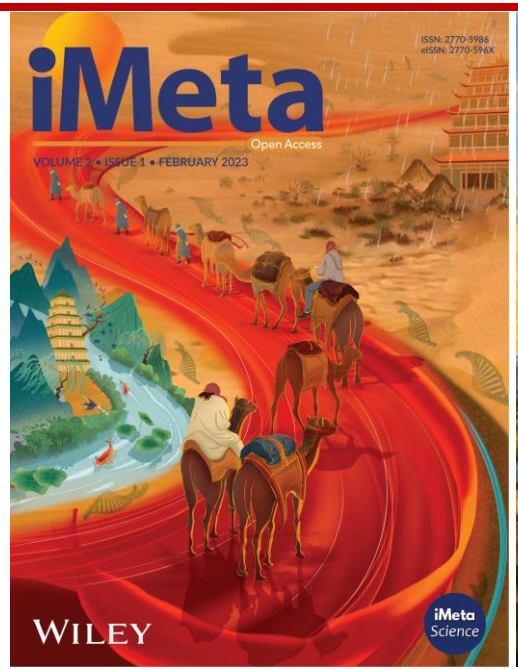
Summary

- OXCT1-mediated PSMG3 succinylation supports rapid FMDV replication in pigs.
- Bortezomib inhibits picornavirus replication by targeting PSMG3 succinylation (in vitro and in vivo).
- This study deepens our understanding of the pathogenic mechanism of FMDV and provides data support for improving the immune efficacy of foot-and-mouth disease vaccines.

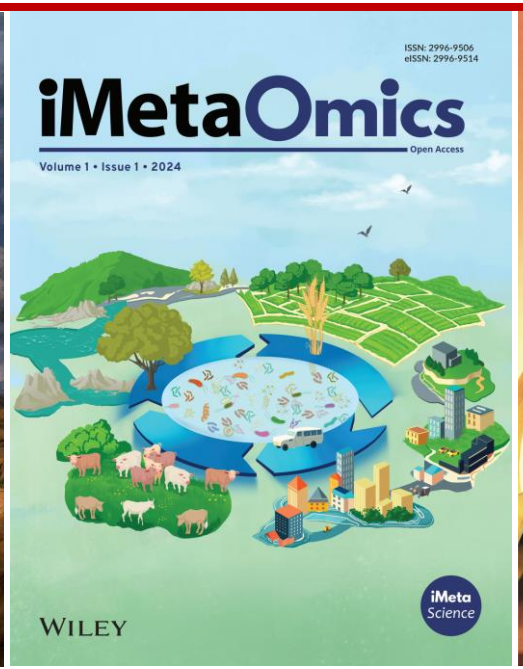
Huisheng Liu, Qiao Xue, Pengfei Liu, Zhihua Dong, Weijun Cao, Fan Yang, Yingming Zhu, et al. 2026. OXCT1 driven succinylation of PSMG3 stabilizes the proteasome to facilitate picornavirus replication. ***iMetaOmics*** 3: e70151. https://doi.org/10.1002/imo2.70151

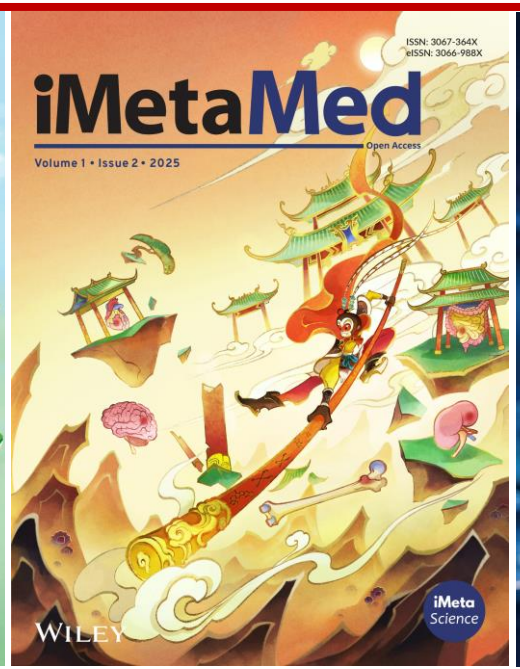
iMeta: Biology and Medicine in Info and Meta Era

WILEY











"***iMeta***" launched in 2022, 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**, 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.

"***iMetaBio***" launched in 2026, with a target IF>15, similar to *Cell Reports, Cell Reports Medicine, eBioMedicine, eClinicalMedicine*

Society: http://www.imeta.science

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

Submission: iMeta: https://wiley.atyponrex.com/journal/IMT2
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
2026/10/19