SARS-CoV Papain-like Protease Suppresses Rac1/TRAF6/TAK1 Signaling in TLR7-mediated Immune Responses

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Background/Objective

Severe acute respiratory syndrome coronavirus (SARS-CoV) papain-like protease (PLpro) has proteolytic and deubiquitinating enzymatic activities, showing interferon (IFN) antagonistic potential.

Method

In this study, dual luciferase reporter, real-time PCR, Western blotting, and immunoprecipitation assays were used to investigate the role of SARS-CoV PLpro in Toll-like receptor 7 signaling pathway.

Result

This study deomstrated SARS-CoV PLpro suppressing TLR7 agonist (R837) induced innate immune responses, such as IRF3, NF- κ B and STAT1 mediated signaling pathways, as well as mRNA expression of cytokines, including TNF- α , IFN α , IFN β and IL-8. Immunoprecipitation assays indicated that SARS-CoV PLpro removed the poly-ubiquitin chains of Rac1, TRAF3, TRAF6, and TAK1. SARS-CoV PLpro influenced the degradation and signal transduction of Rac1, TRAF6, and TAK1 in R837- induced innate immune responses.

Conclusion

These results reveal SARS-CoV PLpro suppressing TLR7-mediated immune responses via Rac1/TRAF6/TAK1 signaling pathway.