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An Infection-Triggered SUMO Switch Controls Induction of an Antiviral Program by TRIM28

Content

Dynamic post-translational modification of diverse proteins with SUMO (small ubiquitin-like modifier) is critical to orchestrate cellular recovery from genomic damage, proteotoxic stress and pathogen insult. Using a quantitative affinity proteomics approach, we surveyed the pan-viral host SUMOylation response and identified a spectrum of common and unique SUMO remodelling events that are mounted during influenza A and B virus infections, as well as during viral innate immune stimulation. Notable among common infection-triggered events was the complete loss of SUMO-modified TRIM28, a multifunctional host E3 ligase that acts as a SUMO-dependent transcriptional co-repressor and restriction factor for several endogenous and exogenous retroviruses, as well as some DNA viruses. Loss of SUMOylated TRIM28 during influenza virus infection did not correlate with stress-induced phospho-regulated proteasome-mediated degradation of TRIM28 or activation of canonical antiviral RNA sensors, but could be mimicked by the forced action of selected deSUMOylating enzymes, which are known redox stress-sensors. Using a CRISPR/Cas9-based knockout/reconstitution strategy, combined with system-wide transcriptomics, we found that deSUMOylated TRIM28 potentiates induction of the host antiviral interferon response during infection, and thereby acts to limit efficient influenza virus replication. Our data suggest that virus-triggered deSUMOylation of TRIM28 contributes to cellular innate immune defences by derepressing expression of host genes involved in the antiviral response.

Choose primary session

Virus host cell interaction

Choose secondary Session

Innate Immunity

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