Retrovirology

Oral presentation

TRIM5alpha contributes to the anti-viral state

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TRIM5alpha is a host restriction factor that mediates a CA-specific block to retroviral infection. TRIM5alpha binding to the viral protein is only detectable when CA is in the multimeric protein lattice of the retroviral core. This suggested that TRIM5alpha might function as a pattern recognition receptor (PRR) analogous to a TLR. Additionally, *TRIM5* is located within a cluster of interferon-stimulated genes. We therefore sought evidence for functional links between TRIM5alpha and innate immune factors.

TRIM5alpha was induced by type I interferons and PRR agonists in THP-1 cells and monocyte-derived dendritic cells and macrophages. Induction kinetics, knockdown of IRF3, STAT1, STAT2, or IFNaR, and IFNaR-blocking antibodies, demonstrated that TRIM5alpha induction is ISGF3-dependent. In parallel, we found that establishment of an antiviral state with interferon or PRR agonists prevented HIV-1 transduction of THP1 cells or monocyte-derived dendritic cells and macrophages. TRIM5alpha knockdown in THP1 cells largely rescued HIV-1 from the antiviral state, independent of envelope pseudotype. This effect of TRIM5 knockdown was independent of CA and even observed with non-retroviruses. We have now established that TRIM5 contributes to the antiviral state via effects on specific factors that act upstream of NFκB and AP-1.