The landscape of ifn/isg signaling in hiv-1-infected macrophages and its possible role in the hiv-1 latency

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Abstract

A key characteristic of Human immunodeficiency virus type 1 (HIV-1) infection is the generation of latent viral reservoirs, which have been associated with chronic immune activation and sustained inflammation. Macrophages play a protagonist role in this context since they are persistently infected while being a major effector of the innate immune response through the generation of type-I interferons (type I IFN) and IFN-stimulated genes (ISGs). The balance in the IFN signaling and the ISG induction is critical to promote a successful HIV-1 infection. Classically, the IFNs response is fine-tuned by opposing promotive and suppressive signals. In this context, it was described that HIV-1-infected macrophages can also synthesize some antiviral effector ISGs and, positive and negative regulators of the IFN/ISG signaling. Recently, epitranscriptomic regulatory mechanisms were described, being the N6-methylation (m6A) modification on mRNAs one of the most relevant. The epitranscriptomic regulation can affect not only IFN/ISG signaling, but also type I IFN expression, and viral fitness through modifications to HIV-1 RNA. Thus, the establishment of replication-competent latent HIV-1 infected macrophages may be due to non-classical mechanisms of type I IFN that modulate the activation of the IFN/ISG signaling network.

Author keywords

Epitranscriptomic; IFN/ISG response; Latent HIV-1 reservoir; Macrophages; Regulation HIV