Abstract

Members of the interferon regulatory factor (IRF) family control the expression of numerous proteins, many of which are central to regulating host immune responses. IRF1 is one of the central mediators of the innate and adaptive immune responses required for antigen processing and presentation, Th1/Th2 differentiation, and natural killer (NK) cell and macrophage function. Many viruses have evolved mechanisms to target the IRF1 pathway in order to promote viral pathogenesis. During early HIV infection, IRF1 acts as a double-edged sword, critical for driving viral replication as well as eliciting antiviral responses. In this review, we describe the strategies that HIV-1 has evolved to modulate IRF1 in order to enhance viral replication and to disarm the host immune system. IRF1 has been shown to be an important factor in natural protection against HIV in highly exposed seronegative (HESN) individuals and is crucial in regulating the initial stages of HIV replication and HIV disease progression, as well as the establishment of latency. An understanding of how the protective effects of IRF1 responses are controlled in HESN individuals, naturally resistant to HIV infection, may provide important clues on how to regain control of HIV and tip the balance of immunity in favor of the host, or provide new opportunities to eliminate HIV in its host altogether.