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Use of a vaccinia virus gene product to neutralize interferon-alpha and improve the histopathology of HIV encephalitis in a mouse model
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Background and aims: Interferon-alpha plays a key role in neurocognitive defects associated with human immunodeficiency virus (HIV) and HIV encephalitis. The aim of this study was to assess the effects of a novel inhibitor of interferon-alpha (B18R) in an HIV encephalitis severe combined immunodeficiency mouse model.

Methods: Human macrophages were cultured and infected with HIV-1. Mice (5 week old B6.CB17-Prkdcscid/SzJ) were inoculated with HIV-infected (n=16) or uninfected (n=8) macrophages. The B18R was produced by a modified recombinant procedure. Each B18R treated mouse received 50 mcg per day for 10 days. Brain sections were stained by an immunoperoxidase method. The genes ISG15, IFNA4, and Ifrg15 were analyzed using real-time polymerase chain reaction.

Results: Gene expression of interferon-alpha signaling was downregulated in the brain by B18R as shown by polymerase chain reaction (PCR). Mononuclear phagocytes were significantly decreased in mice treated with B18R when compared to untreated mice. However, neuronal arborizations were significantly retained in mice treated with B18R when compared to untreated mice. Significant increase in mononuclear phagocytes and loss of neuronal arborization are prominent signs of HIV encephalitis. Findings of this study indicated that the B18R crossed the blood-brain barrier, blocked interferon-alpha signaling in the brain, and improved defects associated with HIV encephalitis.

Conclusion: Findings of this study might suggest that B18R is a potential alternative to monoclonal antibodies used in the management of HIV encephalitis. Further studies are still needed to fully elucidate the effects of B18R in HIV encephalitis.

Disclosure: Nothing to disclose