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Activation of Toll-like receptor 3 by poly (I:C) inhibits HIV infection of human iPSC-derived microglia

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As a key immune cell in the brain, microglia are essential for protecting the central nerve system (CNS) from viral infections including HIV. Microglia possess functional Toll-like receptor 3 (TLR3), a key viral sensor for activating interferon (IFN) signaling pathway-mediated antiviral immunity. We therefore studied effect of poly I:C, a synthetic ligand of TLR3, on HIV infection of human iPSC-derived microglia (iMg) and found that TLR3 activation of iMg by poly I:C could effectively inhibit HIV infection/replication. Investigations of the mechanisms revealed that TLR3 activation of iMg induced the expression of both type 1 and type 3 IFNs. In addition, the poly I:C-activated iMg expressed significantly higher levels of IFN-stimulated genes (ISGs), including those with anti-HIV activities (ISG15, Mx2, Viperin, Mx1 and OAS-1), than untreated iMg. In addition, TLR-3 activation elicited the expression of the HIV entry coreceptor CCR5 ligands (CC chemokines) in iMg at both mRNA and protein levels. These observations indicate that TLR3 is an important player in the intracellular immunity against HIV in microglia, suggesting the necessity of further investing the clinical potential of TLR3 activation-mediated innate antiviral immunity for control and elimination of HIV infection in microglia.