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Title: HIV infection of CD4+ T cells: innate sensing and host dependency factors

Abstract: Despite decades of research and public health efforts, HIV/AIDS remains a major global health issue with more than 36 million people infected with the virus in 2016. Effective HIV treatment has enabled HIV infected patients to live longer than ever before. However, over the last decade it has become increasingly evident that successfully treated HIV patients develop age-related illness at a younger age than the general population. The pre-mature aging seen in these patients is partially due to chronic inflammation associated with treatment side effects and residual viral replication. Moreover, due to the emergence of multidrug-resistant virus, some patients have little or no treatment options. We have found that during cell-to-cell transmission of HIV to CD4+ T cells, endosomal virus that fails to fuse with the membrane can be degraded and subsequently detected by the innate immune receptor TLR8. Activation of TLR8 by viral nucleic acid induced an inflammatory response by CD4+ T cells. In addition, stimulation of TLR8 by synthetic ligands augmented HIV replication and reactivated latent virus. We have also performed a CRISPR/Cas9 based screen in a CD4+ T cell line and identified novel host genes that promote HIV replication.

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