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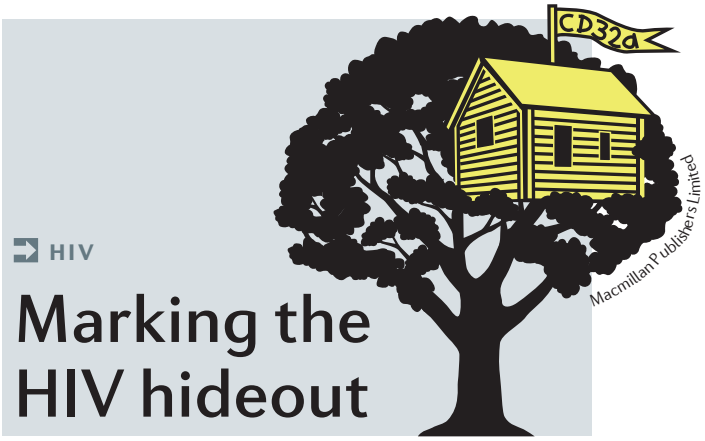

HIV

Marking the HIV hideout

Antiretroviral therapy has greatly reduced mortality from HIV-1 infection, but the virus can persist in a small proportion of infected CD4$^+$ T cells, forming a latent HIV reservoir. The eradication of this reservoir has proved difficult as markers for these cells have been lacking. Now, Descours, Petitjean *et al.* show that CD32a is specifically expressed on the surface of dormant CD4$^+$ T cells that harbour HIV-1.

To investigate the HIV reservoir the authors developed an *in vitro* model of HIV latency in which dormant CD4$^+$ T cells were generated by inducing degradation of SAMHDI — a protein previously shown to be responsible for HIV-1 restriction in resting CD4$^+$ T cells. Peripheral blood mononuclear cells (PBMCs) from HIV-negative controls were subjected to SAMHDI degradation and then infected with an HIV-1-derived vector expressing green fluorescent protein. RNA sequencing revealed 103 differentially expressed genes — 16 of which encode cell surface transmembrane proteins — in infected quiescent CD4$^+$ T cells compared with uninfected cells. The most highly expressed gene was *FCGR2A*, which encodes CD32a — a low-affinity receptor for the IgG Fc fragment.

> “CD32a is a specific marker of HIV-1-infected resting CD4$^+$ T cells”

The expression of CD32a was examined in the HIV latency *in vitro* system using PBMCs from HIV-negative individuals. CD32a expression was selectively induced on HIV-1-infected resting CD4$^+$ T cells. Of note, infection of T cells stimulated with phytohaemagglutinin and interleukin-2 was not associated with induction of CD32a expression compared with infection of resting CD4$^+$ T cells. Thus, CD32a is a specific marker of HIV-1-infected resting CD4$^+$ T cells *in vitro*.

Finally, the authors tested whether CD32a could be used as a marker to separate HIV-infected dormant CD4$^+$ T cells from other PBMCs isolated from individuals treated with antiretroviral therapy. CD32a immunostaining showed a continuum of expression that correlated with HIV infection frequency, and CD32a$^+$ CD4$^+$ T cells constituted approximately 50% of the total CD4$^+$ T cell reservoir. Further experiments showed that CD32a$^+$ CD4$^+$ T cells contain inducible replication-competent provirus and depletion of these T cells led to delay in virus production and spreading, indicating that CD32a$^+$ CD4$^+$ T cells contribute to the inducible viral reservoir in CD4$^+$ T cells.

To conclude, the identification of CD32a as a cell surface marker of the CD4$^+$ T cell HIV reservoir will facilitate the study and, hopefully, therapeutic targeting of HIV latency.

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ORIGINAL ARTICLE Descours, B. *et al.* CD32a is a marker of a CD4 T-cell HIV reservoir harbouring replication-competent proviruses. *Nature* http://dx.doi.org/10.1038/nature21710 (2017)