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In a new study, a group of WiScan® Hermes users from the University College London (UCL) found that although macrophages have a protein that shields human immunodeficiency virus (HIV), the virus is able to make it past the defense.

A G1-like state allows HIV-1 to bypass SAMHD1 restriction in Macrophages

Petra Mlcochova et al. ***The EMBO Journal,*** 2017; Jan 25; Volume 36, Issue 2 , pp 129 – 244

Macrophages produce an antiviral protein called SAMHD1, which prevents HIV from replicating in these cells - except for when the protein is switched off.
The researchers found that HIV infection is limited to macrophages at G1-like stage, which is induced in about 20% of the macrophages.

The reason why SAMHD1 gets switched off is yet to be determined, however the authors suggest it occurs in order to repair damaged DNA, as part of the normal functioning of the macrophage.

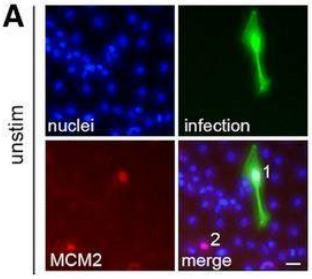
The researchers also explored the use of Histone Deacetylase (HDAC) inhibitors, which induce SAMHD1 activity and therefore prevent HIV infection of the microphages.

These findings explain the ability of microphages to sustain high levels of HIV but also offer a therapeutic target to enhance macrophages resistance to HIV infection.

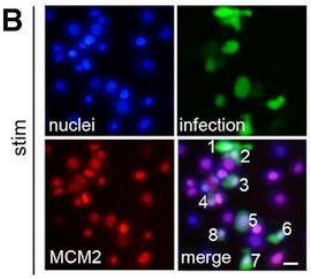
Imaging Data obtained with WiScan® Hermes automated imaging system

G1-like phase macrophages are preferential targets for HIV at the single-cell level

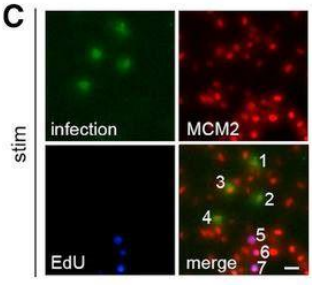
The authors employed a high-throughput single-cell co-localization analysis, aiming to measure the association between SAMHD1, markers of cell cycle progression and HIV-1 infection at the single-cell level.



A,B: MCM2 expression correlates with HIV infection under both stimulatory and non-stimulatory conditions.

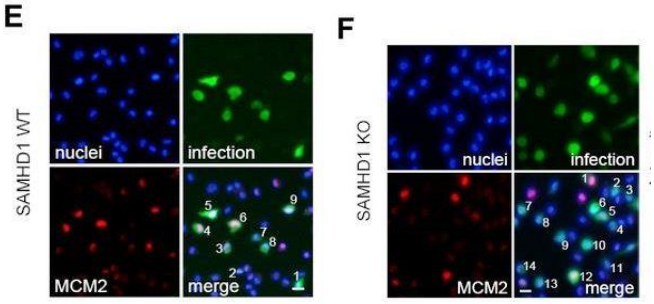


C: HIV infection did not co-localize with EdU incorporation in single-cell analyses, which indicates that entry into S phase and DNA synthesis is not required for enhanced HIV-1 infection.



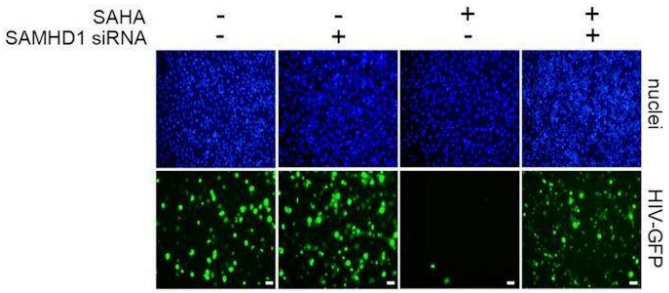
This analysis illustrates that macrophages in a G1-like state, measured by MCM2 expression, are preferential targets for HIV at the single-cell level.

Tissue-resident macrophages commonly reside in a G1-like phase and are preferential HIV-1 targets



Preferential infection of MCM2-positive cells is observed in WT(E) but not in SAMHD1 knock-out cells(F).

HDAC inhibitors induce a SAMHD1-dependent block to HIV-1 in human MDM



SAMHD1 depletion using siRNA completely rescued HIV-1 infection from the inhibitory effect of HDACi.

These data indicate that HDACi possess antiretroviral activity that is SAMHD1-dependent in macrophages.