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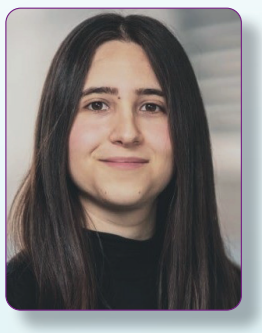

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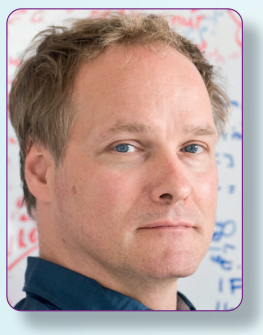

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iScience

An HIV-1 CRISPR-Cas9 membrane trafficking screen reveals a role for PICALM intersecting endolysosomes and immunity

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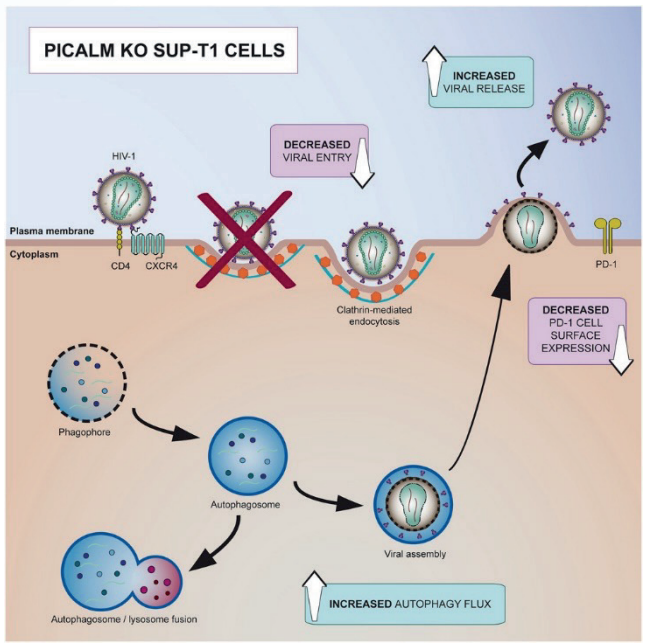
Human immunodeficiency virus type 1 (HIV-1) infects 1.5 million people per year and represents a prominent global threat despite progress made with prevention and combined antiretroviral drug therapies.

HIV-1 hijacks host proteins involved in membrane trafficking, endocytosis, and autophagy that are critical for virus replication. Yet, the complete network of host proteins and their mechanisms of action during HIV-1 replication are unknown.

Despite their potential as clinical targets, only a few membrane trafficking proteins have been functionally characterized in HIV-1 replication. To further elucidate roles in HIV-1 replication, we performed a CRISPR-Cas9 screen on 140 membrane trafficking proteins.

In this study, we demonstrate that PICALM, a component of both clathrin-mediated endocytosis and autophagy pathways, plays an important role in HIV-1 entry into CD4+ T cells, and that it is also an important protein in the host response to HIV-1 infection. The absence of PICALM leads to the accumulation and release of HIV-1 viral Gag protein by infected cells and most astoundingly, it decreases the expression of the immune checkpoint PD-1, eliciting a highly active state and possibly disturbing CD4+ T cell differentiation.



Considering that the SupT1 is a CD4+/CXCR4+/CCR5- cell line is derived from a T cell lymphoblastic lymphoma which likely differs from primary T cells found in vivo, it will be interesting to knock-out PICALM in primary CD4+ T cells to confirm the observations made in this study.

In conclusion, PICALM modulates a variety of pathways that ultimately affect HIV-1 replication, underscoring the potential of this host protein as an interesting, future target to control HIV-1 and benefit cancer patients.

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