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Study reveals how a Rab protein controls HIV-1 replication

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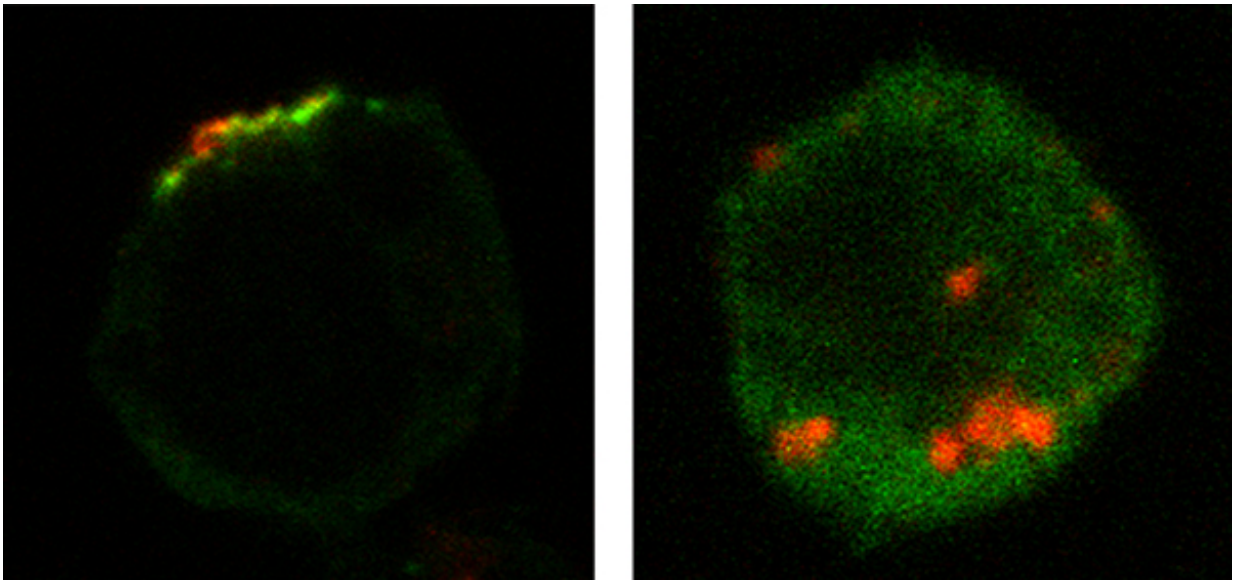

Compared with a control T cell (left), loss of Rab27a (right) blocks the delivery of late endosomes (red) to the plasma membrane, inhibiting the recruitment of Gag (green) to HIV-1 assembly sites. Credit: Pereyra Gerber et al., 2015

HIV-1 replication requires the coordinated movement of the virus's components toward the plasma membrane of an immune cell, where the virions are assembled and ultimately released. A study in *The Journal of Cell Biology* reveals how a Rab protein that controls intracellular trafficking supports HIV-1 assembly by promoting high levels of an important membrane lipid.

New HIV-1 particles assemble at specialized sites in the plasma membrane that are enriched in PIP_2, a phospholipid component of the membrane that recruits a viral protein called $Pr55^{Gag}$ (Gag) that directs HIV-1 assembly. Because certain cell secretion pathways have been suggested to be required for this process, University of Buenos Aires researcher Matías Ostrowski and colleagues investigated whether a role might be played by Rab27a, a protein that guides delivery of membrane-bound compartments called endosomes to the plasma membrane.

Ostrowski and colleagues found that viral replication was impaired in immune cells lacking Rab27a. These cells showed reduced levels of PIP_2 at the plasma membrane and thus failed to recruit Gag to form viral assembly sites. The researchers determined that Rab27a boosted PIP_2 production at the plasma membrane by controlling the endosomal delivery of an enzyme that is necessary for production of the phospholipid to the cell periphery.

Ostrowski believes that these results open a path to investigate whether manipulating endosomal traffic could be a new target for anti-HIV-1 therapies.

More information: Pereyra Gerber, P., et al. 2015. *J. Cell Biol.* DOI: 10.1083/jcb.201409082

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