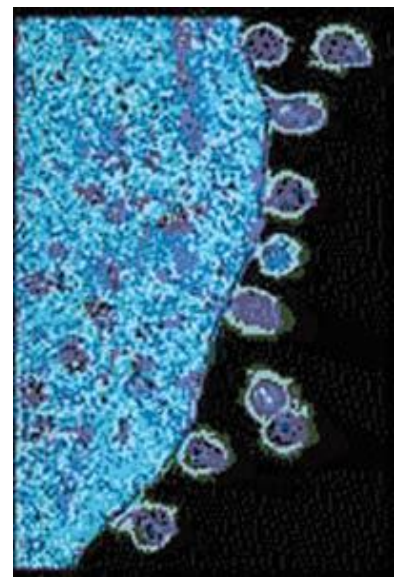
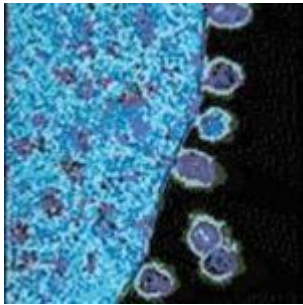


# $\alpha 4\beta 7$ -MAdCAM interaction promotes HIV replication.



HIV shedding from T cell

Several studies with non-human primates (NHPs) have shown that *in vivo* administration of an antibody against the integrin can induce persistent Simian immunodeficiency virus (SIV) control, delay disease progression, and reduce viral titres (Ansari, 2011; Byraredddy, 2014, Byraredddy 2016). The precise mechanism of protection, however, had remained uncertain.  $\alpha 4\beta 7$  integrin serves as a gut-homing receptor on T cells by interacting on with MAdCAM, present on the surface of gut high endothelial venules. Recently, Guzzo *et al.*, (2017) found that  $\alpha 4\beta 7$  can be incorporated in HIV virions, thereby facilitating infection of MAdCAM expressing cells and

intestinal homing of the virus.

Nawaz *et al.*, now show in this study, that the interaction of MAdCAM with its ligand  $\alpha 4\beta 7$ , present on the surface of CD4 T cells, costimulates these T cells and thereby promotes HIV replication. Further, stimulation of CD4<sup>+</sup> T cells with MAdCAM induced proliferation of  $\alpha 4\beta 7$  expressing cells, activated both, naïve and memory CD4<sup>+</sup> T cells, and upregulated expression of CCR5. All effects could be blocked by the addition of an anti- $\alpha 4\beta 7$  antibody.

Retinoic acid, which can upregulate  $\alpha 4\beta 7$  on naïve T cells, was found to act as an essential cofactor in MAdCAM-induced proliferation and viral replication in naïve CD4 T cells. As the combined presence of MAdCAM and retinoic acid is limited to gut associated lymphoid tissues (GALT), the findings of Nawaz *et al.*, could explain the prominent role of GALT in acute HIV infection. This study thus provides novel insight on how the antibody blocking  $\alpha 4\beta 7$  might protect against disease progression SIV infected NHPs by protecting GALT of increased viral replication.

Journal Article: Nawaz *et al.*, 2018. [MAdCAM costimulation through Integrin- \$\alpha 4\beta 7\$  promotes HIV replication.](#) Mucosal Immunology

Article by Kathrin Held