

## Counteracting mutations in mæði-visna virus and HIV-1

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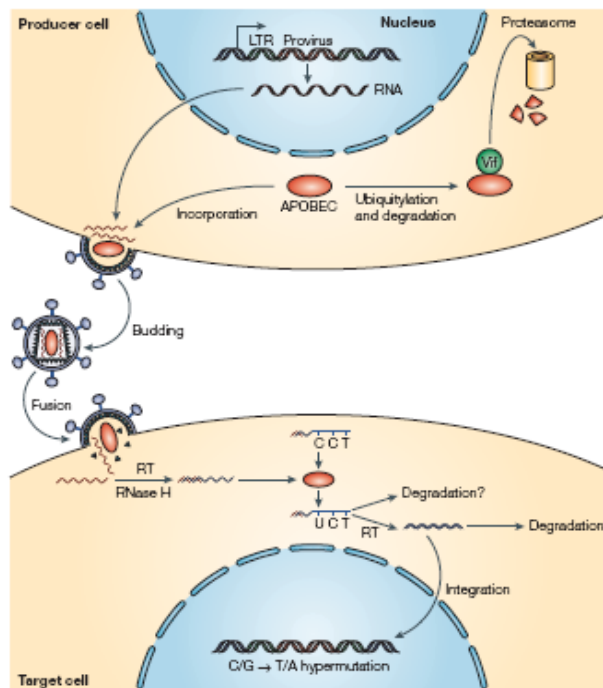
Mæði-visna virus (MVV) in sheep and HIV-1 the causative agent of AIDS are both lentiviruses and have many features in common. Lessons gained by studying MVV can also pertain to HIV-1.

APOBEC proteins catalyze the deamination of deoxycytidine (dC) to deoxyuridine (dU) on the minus DNA strand in the reverse transcription of retroviral genomic RNA. This leads to G->A mutations in the plus strand and in the viral RNA. Both single and multiple mutations can occur, the latter usually leading to degradation of the DNA via host uracil-N-glycosylase enzymes. The viral Vif protein protects the virus against APOBEC mediated inactivation by preventing packaging of APOBEC into virions.

The objective of this study is to increase understanding of the role of the Vif and APOBEC proteins in MVV infections, specifically by using defined mutations to study the interaction of the proteins. These protein interactions have parallels in infections caused by other lentiviruses such as HIV-1.

pCMV plasmids expressing Vif and APOBEC will be co-transfected into COS or 293T cells, Vif being tagged with a myc epitope and APOBEC with an HA epitope. These tags are then used in immunoprecipitation, one at a time, to study the binding interactions. The effects of the mutations introduced into Vif on the stability of both Vif and APOBEC will also be studied.

In addition we have used the expression plasmids pIVEX2,3d and pIVEX2,4d to produce Vif in a special strain of *E. coli* bacteria. The Vif protein produced was purified and used to produce specific antibodies. These antibodies can be used to for various studies of Vif and MVV infections, e.g. by specific histological staining.



The interaction of Vif (green) and APOBEC (red). APOBEC is expressed in the host cell and incorporated into the virion. Vif can ablate packaging of APOBECs by targeting it for proteasome degradation. If APOBEC is not countered by Vif it is packaged in the virion and in a new host cell it can deaminate the viral DNA during reverse transcription. (Harris RS, Liddament MT.2004. Retroviral restriction by APOBEC proteins. Nat Rev Immunol. 4: 868-877.)