Retrovirology

Poster presentation

Characterisation of FEZ1-mediated inhibition of retroviral replication

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The brain specific cytoskeletal regulatory protein FEZ1 (fasciculation and elongation protein zeta 1) has been shown to block retroviral infection including human immunodeficiency virus type 1 (HIV-1). Previous work has shown that FEZ1 blocks HIV-1 early in the viral life cycle, after reverse transcription but before nuclear entry. To begin to dissect the mechanism by which FEZ1 functions in host cell resistance yeast-two-hybrid assays were performed to identify FEZ1 interacting proteins. Two of the interactors, talin1 and vinculin, were identified as strong candidates for potential involvement in FEZ1-mediated inhibition of retroviral infection due to their cytoskeletal regulatory functions. Talin 1 and vinculin directly interact with each other and are involved in the linkage of integrins to the actin cytoskeleton. To assess the potential role of talin1 and vinculin in retroviral infectivitiy we have used an siRNA approach to reduce expression of each gene followed by infection with pseudo-typed HIV-1 virus. Two independent infection assays confirmed that cells with reduced expression of either talin 1 or vinculin become more susceptible to HIV-1 infection. Interestingly, when expression of either the talin 1 or vinculin gene is reduced FEZ1 expression levels also decrease. We can conclude that FEZ1, talin 1 and vinculin play an important role in the HIV-1 lifecycle and we are currently examining whether these proteins function independently or as part of a larger protein complex that regulates cellular susceptibility to retroviral infection.