Genome-wide analysis of host factors in HIV replication

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HIV-1 and AIDS

- >40 million individuals are infected with HIV
- Most of these do not have access to therapy
- Therapy is not curative and must therefore be lifelong
- It is unclear whether an individual can be cured of HIV infection; withdrawal from even the most effective available therapy invariably leads to virus rebound
HIV replication cycle

Known host factors affecting HIV replication

- CD4 (1986)
- Cyclophilin A (1993)
- CCR5 and CXCR4 (1996)
- Cyclin T1 (1998)
- Vps proteins involved in virus budding (2001)
- APOBEC3 proteins (2002)
- TRIM5α and TRIMCyp (2004)
- Bst2/tetherin (2008)
Approaches to identify host genes involved in HIV infection

• Mechanistic studies
• Library screening assays
  – Yeast two-hybrid
  – Gene transfer/selection
• Biochemical approaches
  – Fishing with viral baits
• Gene expression analysis
Tsg101 and the Vacuolar Protein Sorting Pathway Are Essential for HIV-1 Budding

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miRNA processing and export

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siRNA

- 21 bp duplex RNAs with identity to mRNAs
- Can be transfected into cells and target specific mRNAs
- Silencing is transient but effective
- Sold by several commercial sources
- Being developed as a therapeutic strategy


Fig. 5. Model of HDF roles in the HIV life cycle. With the stages of the HIV life cycle as a framework, each HDF was placed at the position most likely to elicit HIV dependency. The function and subcellular location of HDFs were determined with the use of multiple databases (rationale, table S4). Some proteins are in multiple locations to represent more than one possible role in the HIV life cycle. Newly identified HDFs (red or blue, the latter if they inhibited HIV in part two only); previously implicated HDFs detected in the screen (green), or not detected but with a relevant interaction (gray); HIV protein (black); matrix (MA), reverse transcriptase (RT), integrase (IN), envelope (gp41, gp120) (ENV). Unfolded protein response, UPR.