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Identification of Cellular Proteins Interacting with Human Immunodeficiency Virus-1 Gag

Promotionsfach: Infektiologie
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Human immunodeficiency virus type 1 (HIV-1) Gag is the key structural protein mediating assembly of virions in infected cells. Though Gag is capable of self-assembly *in vitro*, it has become generally accepted that in the environment provided by a living cell, host factors play a decisive role for efficient viral replication.
In this study, a series of affinity purification screens was performed to identify cellular proteins which interact with HIV-1 Gag. Methods applied included Tandem Affinity Purification, GFP nanotrap and affinity purification with paramagnetic anti-GFP microbeads. Protein complexes were analyzed by mass spectrometry. One screen included stable isotope labeling in cell culture (SILAC) yielding quantitative mass spectrometry data. This data provides a rich source of novel HIV-1 Gag interaction candidates for future validation.
In all interaction screens, the cellular protein Lyric was identified as a previously unknown Gag interaction partner. This interaction was verified by co-immunoprecipitations and mapping of the domains mediating the interaction. Gag interacts with endogenous Lyric via its matrix (MA) and nucleocapsid (NC) domains. The interaction requires Gag multimerization. The Lyric domain encompassing amino acids 101-289 is sufficient for the interaction, while deletion of amino acids 107-204 disrupts the interaction with Gag. As a result of its interaction with Gag, Lyric is incorporated into viral particles, where it is cleaved by the HIV protease. The interaction between Gag and Lyric is conserved among retroviruses. Expression of the Gag binding domain of Lyric increases HIV protein expression and infectivity significantly.