

P021 Differential roles for Alix and ESCRT-III in cytokinesis and HIV-1 release

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Retroviral late domains (L-domains) recruit the ESCRT machinery to sites of viral assembly to effect a membrane fission event that allows viral particle release. For example, the PTAP L-domain within HIV-1 Gag binds to Tsg101; however, when this L-domain is disrupted, HIV-1 employs an auxiliary LYP(X)nL L-domain that recruits the ESCRT machinery through binding Alix. Alix-dependent HIV-1 release is dependent upon Alix's extreme C-terminus, suggesting that this region encodes a novel activity mediating this release. Additionally, we have shown that the ESCRT machinery is recruited to the midbody of dividing cells through interactions of Alix and Tsg101 with the midbody protein, Cep55. Here, the ESCRT-machinery regulates a membrane fission event topologically equivalent to retroviral release and allows the separation of daughter cells through cytokinesis. Here we show that disruption of Cep55/Alix/ESCRT-III interactions causes formation of aberrant midbodies and cytokinetic failure. Further, we analyse the role of the extreme C-terminus of Alix in both HIV-1 release and cytokinesis and show that this region is required for Alix-multimerisation. We explore requirements for Alix-multimerisation in viral budding and cytokinesis and highlight functional differences between cytokinesis and HIV-1 release by analysing differential roles for the ESCRT-III subunits Chmp4a -4b and -4c in these processes.