Retrovirology

Poster presentation

P07-03. HIV gp120 interaction with CD4+ T cells induces local intracellular signaling and creates an F-actin depleted zone in the virological synapse

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Background

HIV can be transferred from cell to cell via a virological synapse (VS). Through the VS, the infected cells direct the release of viral particles toward the non-infected cells. While this involves polarization of the infected cells, the response of the non-infected, target cells has not been well investigated.

Methods

We have utilized the supported planar bilayers presenting laterally mobile, fluorescently labeled gp120 and ICAM-1 as a model to mimic virus-infected cells. After applying primary target CD4+ T cells onto the bilayers, we monitored changes in cell morphology and motility, intracellular signaling, and cytoskeletal rearrangement by microscopy.

Results

The data show that gp120 and ICAM-1 on the bilayers can induce the formation of a synaptic structure by non-infected CD4+ T cells with some characteristics of an immunological synapse (IS). There is a transient stop signal and the interface contains a central supramolecular activation cluster (cSMAC) of gp120-CD4 interactions surrounded by a peripheral supramolecular activation cluster (pSMAC) of ICAM-1-LFA-1 interactions. As with the IS, the cSMAC is also formed from microclusters that are enriched in active Src family kinases. However, while Src kinase signaling is suppressed in the cSMAC of the IS, the Src family kinases and other TCR signaling components remain active for a prolonged period in the cSMAC of the VS. Notably, the gp120-enriched cSMAC region of the VS is depleted of f-actin.

Conclusion

These results indicate that, in addition to its role in initiating virus infection, HIV envelope gp120 interaction with target CD4+ T cells triggers activation signals that lead to formation of an f-actin-depleted zone in the VS, which is important for viral entry.