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P04-13. Complex pattern of neutralization of cell-to-cell HIV transmission to activated CD4+T cells

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Background

Virological synapses formed between HIV-infected and CD4+T cells contribute to HIV spread *in vivo* and may be less sensitive to neutralization than cell-free virus infection. However, anti-gp120 and anti-gp41 antibodies block cell-to-cell HIV transmission to unstimulated CD4+T cells. Since HIV infection is characterized by an immune hyperactivation, we evaluated the effect of neutralizing antibodies on cell-mediated transmission using activated primary CD4+T cells.

Methods

We cocultured HIV infected cells with PHA/IL-2 stimulated CD4+T cells and analyzed the effect of anti-gp120 (IgGb12, 2G12) and anti-gp41 (4E10, 2F5) antibodies and soluble-CD4 on HIV transfer, cell-to-cell fusion, cell death and infection of target cells. Antibodies blocking LFA-1, ICAM-1 and ICAM-3 were also tested.

Results

4E10 and 2F5 failed to block early events (HIV transfer) although efficiently inhibited late events (cell-to-cell fusion, target cell death and infection). 2G12 also failed to block early events but partially inhibited late events, including infection. IgGb12 (and soluble-CD4) blocked early and late events with IC50 values of 0.3–1 μg/ml, except cell-to-cell fusion that was observed even at the highest concentration tested (100 μg/ml). Anti-LFA-1 and anti-ICAM-1 antibodies slightly increased whereas anti-ICAM-3 antibodies decreased IgGb12 neutralization, suggesting a secondary role for adhesion molecules in stimulated cells. The paradoxical effect of IgGb12 and soluble-CD4 suggests a direct competition between these inhibitors and CD4 expressed by target cells for gp120 in the virological synapse, allowing cell-to-cell fusion events. Conversely, infection mediated by viruses released to the synaptic space was completely blocked.

Conclusion

Infectious cell-to-cell transmission to stimulated CD4+T cells is sensitive to anti-gp41 antibodies but partially resistant to 2G12, although none of these antibodies blocked early transfer events. The observed activity of IgGb12 in early events may be compromised by high synaptic CD4 concentrations. Therefore, activated CD4+T cells show a complex neutralization pattern that may challenge *in vivo* activity of anti-gp41 and anti-gp120 antibodies.