Retrovirology

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Oral presentation

Complement supports progression of HIV and turns neutralising antibodies at low concentration into infection enhancing antibodies

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HIV is largely resistant to complement-mediated lysis primarily due to binding of factor H from the fluid phase and secondarily to incorporation of additional complement control proteins (DAF, MCP, CD59) from the host cell into the viral envelope. Since HIV by itself activates the complement system – and even more so, if antibodies are bound to its surface, fragments of C3, i.e. C3b – are deposited on the virus. We could document this situation for exvivo HIV, isolated from human plasma.

Depending on the quantity of activation this may reach such a degree that gp120 is not accessible any more. It could be clearly shown that HIV carrying C3b binds to complement receptor typ 1 (CR1) on human erytrocytes (E). Thereby, with the help of the C3b inactivator, C3b is converted into iC3b and further to C3d. HIV-iC3b/HIV-C3d bind to B lymphocytes (CR2, CR1), to FDCs (CR2, CR3, CR1) and to DCs (CR3).

HIV-C3d/B cell- and HIV-C3d/FDC – complexes very efficiently infect resting (!) CD4+ T lymphocytes. HIV-iC3b, bound to DCs, causes a productive (!) infection of these cells! HIV – IgG or HIV-IgG-iC3b allows only attachment of HIV to DCs. In both cases HIV can be transmitted to T cells and productively infect these cells.

These complement-mediated infection enhancement mechanisms can be overcome by sufficient large quantities of broadly neutralising antibodies.

But if these drop to low concentrations, then the fact that these antibodies activate complement and cause opsonisation of HIV with C3 fragments becomes the salient feature and the before neutralising antibodies begin to enhance infection.

In our judgment, this complement-deposition by antibodies to surface epitopes is one of the aspects, which make development of a vaccine so difficult.