Elucidating the Interactions between the Envelope Glycoprotein gp41 of HIV-1, gC1qR and C1q: Relevance to HIV-1 Pathogenesis

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Human Immunodeficiency Virus affects more than 33 million individuals globally and is associated with a progressive decline in CD4+ T cell count. The 3S motif of gp41 on the virus induces an activating natural killer (NK) cell signal, NKp44L on uninfected bystander T cells through binding to gC1qR, a ubiquitously expressed multifunctional binding protein that is also the receptor for complement protein C1q. C1q also has been shown to bind to 3S, which facilitates the spread of the infection in the body. This study aimed at clarifying the complex interactions between these three proteins by defining binding sites and developing methods to inhibit the binding of 3S to gC1qR in an effort to prevent cell death. Using enzyme-linked immunosorbent assays (ELISA), residues 14-26 and 155-162 were identified as potential 3S binding sites on the A-chain of C1q and residues 144-162 and 174-180 on gC1qR. Using this information, two methods of inhibition were developed and tested. With peptide-based inhibition, it was seen that only pre-incubations with gC1qR peptides covering residues previously identified as binding sites (144-162 and 174-180) significantly inhibited 3S binding to the receptor on cells. This inhibition was dependent upon concentration of gC1qR peptide. Antibody-based inhibition showed that anti-gC1qR antibodies more effectively inhibited 3S binding than peptide-based inhibition did. All statistical analysis was conducted through IBM SPSS 20 where $p<0.05$ was considered significant. Altogether, investigation in these interactions may provide the foundation for possible future therapies for HIV-1 infection to prevent CD4+ T cell depletion in the body.

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