Amino Acid Residue-Specific Interaction between gC1qR and Cytotoxic Peptides of Various Pathogenic Microorganisms with Homology to HIV-1 gp41 3S

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Recently, complement component C1q and its corresponding receptors (gC1qR and cC1qR) have generated interest due to their involvement in autoimmunity, inflammation, and infectious disease. During HIV-1 infection, viral envelope proteins composed of glycoprotein 41 (gp41) and gp120 bind to CCR5 and CD4 receptors respectively, allowing them to manipulate the host's immune system to fuse with and proliferate inside healthy CD4+ cells. gC1qR binds to gp41, recognizing its 3S amino acid motif (PWNASWSNKSLDDIW), preventing viral fusion. Utilizing the gp41 3S motif, eleven distinct, suspected virulence proteins from nine pathogenic microbes were identified via sequence homology screening. Peptides derived from these pathogenic proteins were subjected to ELISA analysis to determine if they were capable of binding to either microplate bound recombinant gC1qR or MOLT-4 cells expressing surface gC1qR. 36.3% (4 out of 11 peptides) exhibited affinity for gC1qR. Notably, three peptides, LVIVD repeat protein from L. weilii str., nucleotidyltransferase of A. actinomycetemcomitans, and PG_0027 of P. gingivalis exhibited the highest affinity to gC1qR. Interestingly, a randomized gp41 peptide sequence serving as a negative control demonstrated higher than expected selective binding in both assays. As both the negative control (WNDWDSKILSDPAWNS) and LVIVD repeat (PWNASWSYVLDSAWS) peptides retained a serine residue in register with wild-type gp41, it is proposed that this serine serves as a crucial anchor residue in the gp41-gC1qR interaction. Furthermore, these studies suggest that pathogenic microorganisms expressing surface antigens with sequence homology to the gp41 3S motif may induce NKP44L expression on CD4+ cells thereby rendering them susceptible to NK-mediated desctruction.