Purification and Antigenicity of the Putative gp41 Fusion Peptide of the Human Immuno-deficiency Virus

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The problem of drug resistance in HIV-AIDS therapy requires continued research for novel drug targets. Gp41 (an envelope glycoprotein) may be an important target for the development of novel HIV fusion inhibitors. The HIV-1 gp41 envelope glycoprotein mediates fusion of the viral and cellular membranes. The core of the gp41 ectodomain undergoes a receptor-triggered conformational transition forming a trimeric, alpha-helical coiled-coil structure. This trimer-of-hairpins species facilitates insertion of the viral envelope protein into the host cell membrane promoting viral entry. The prefusogenic conformation of gp41 is capable of stimulating a neutralizing antibody response and is therefore an attractive therapeutic target[1]. Previous work showed that the sera from HIV positive patients contain antibodies to fragments of the gp41 membrane fusion protein.

Here the extent to which an immune response is elicited in HIV positive patients is reported. Gp41 peptides of 80 amino acids were designed using molecular modeling and PCR. The antigenicity of these peptides was determined by making use of the ELISA assay. HIV antibodies in the sera of all 58 HIV positive patients reacted with the MBP-HIV gp41 constructs (80 amino acid peptides) in contrast to the 21 HIV negative sera. When antigenicity of a hydrophilic construct of gp41 was compared to the CD4 counts of test patients, a correlation between the antigenicity and the CD4 counts was apparent. In contrast the antigenicity of a hydrophobic construct showed no correlation with CD4 count of the patient. This may be explained by taking into consideration that some hydrophobic molecules are known to be presented by APC on CD1 to CD4 T-cells to produce antibodies even at very low CD4 counts. This research may contribute to the development of gp41 based vaccines to either prevent infection (hydrophilic peptide) or further progression (hydrophobic peptide) after HIV infection.

[1]McGaughey GB, Barbato G, Bianchi E, Freidinger RM, Garsky VM, Hurni WM, Joyce JG, Liang X, Miller MD, Pssi A, Shiver JW, Bogusky MJ. (2004) Progress towards the development of a HIV-1 gp41-directed vaccine. Curr HIV Res. 2(2):193-204