BACKGROUND OF THE WORK.....
Human Immunodeficiency Virus (HIV) undergoes tremendous genetic variations by mutations in its genome. The frequency of mutation is very much higher than what is normally observed in other DNA molecules present in the nucleus. Therefore it is imperative that each HIV isolate present in different geographical locations will have a set of envelope glycoproteins which are different from others. Variations in functional domains of gp120 and gp41 will give rise to new virus types which would be selected on the basis of their ability to survive in an immune-competent host.

Numerous studies using HIV isolates obtained from USA, Europe and Africa have been carried out to identify domains in the viral envelope glycoproteins which have some role in viral pathogenesis. But no such studies have been yet reported using any of the Indian isolates of HIV.

Using 19 to 36 amino acid long synthetic peptides, mapping of immunogenic B cell epitopes of gp120 and gp41 of HIV-1 isolates from Europe and USA has been done [128]. It was found that some regions of the gp120 and gp41 have immunosuppressive effect and they may have some role in inducing auto immune responses. When antibodies from both infected humans and immunized rabbits were used it was found that most of the regions of gp120 and gp41 can induce antibody response, but response to HIV-1 peptides was found in infected individuals only. In the case of Indian population where diseases like tuberculosis, malaria etc. persists along with HIV infection, it will be interesting to see what type of antibody response individuals mount against HIV envelope glycoproteins when they are also suffering from tuberculosis or Malaria in the presence or absence of HIV infection. With a view to identify a mixture of neutralizing human monoclonal antibodies against weakly immunogenic epitopes of HIV-1, a phage display system was used [130]. It identified new conformational V2 and CD4 binding domains on the gp120 molecule of HIV-1.
In a study to analyse the effect of sequence variation among different HIV-1 isolates from Africa and North America on seroreactivity by using linear antigenic epitopes of gp120, it was observed that there exist very significant cross reactivity amongst various peptides from certain regions of the molecule [132]. This study has very important implications as far as Indian patients are concerned mainly because the Indian subcontinent have diverse human population with different genetic background.

Monoclonal antibodies are extremely useful tools for mapping B cell epitopes. By making a battery of murine monoclonal antibodies against recombinant gp120 of HIV-1 which can block interaction of the Virus with it's receptors on the host cell surface, three antibodies were found to inhibit this interaction [127]. Two of these epitopes were mapped to the carboxy terminal regions of the gp120 molecule.

It is known that HIV induces virus specific CD8 T Cytotoxic T lymphocyte response in certain infected individuals. Since cell mediated immune response plays an important role in pathogenesis of HIV infection numerous studies have been done using different viral peptides and lymphocytes from infected individuals. But due to the problem of handling infected lymphocytes no such study has yet been reported from India. When peptides obtained from the V3 regions of gp120 molecule of seven different HIV-1 strains were used it was observed that certain strains induced cross reactive CD8+ CTL response in vitro against a broad range of virus strains. This study indicated that peptides representing the V3 region of gp120 of HIV-1 can be used in potential vaccines. But no such information is available for any of the Indian isolates of HIV-1.

The transmembrane glycoprotein gp41 of HIV has received much less attention as far as structural studies are concerned in comparison to gp120. This may be because much less sequence variation has been observed in gp41 molecule.
A highly conserved six amino acid long (ELDKWA) sequence was identified in C-terminal region of the gp41 molecule of HIV-1 by using infected individuals from widely separated geographical locations like Argentina and Sweden [136]. In an interesting study to identify the domains of the transmembrane glycoprotein gp41 which interact with gp120 for virus assembly and propagation using 47 different monoclonal antibodies raised in mice by immunizing them with oligomeric envelope protein, six distinct determinants were identified and mapped [137]. No such study has been done using Indian isolates of HIV-1. In comparison to envelope glycoproteins of HIV-1, much less work has been done on the same molecules of HIV-2. Our present preliminary study reported in this thesis has been carried out with this background. Due to lack of P3 facility we have neither used lymphocytes from HIV infected individuals nor even inactivated viruses. Our study has been done by using peptides, derived from the known sequences of envelope glycoproteins of Indian isolates of HIV-1 and HIV-2 [158, 159, 160] and sera from confirmed HIV-1, HIV-2 and HIV 1 and 2 infected (Mixed infection) individuals made non-infective after proper heat treatment and lymphocytes from healthy individuals from diverse genetic background.