Variability of V3 loop in gp120 protein of HIV

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Considering the pandemic proportions the Acquired Immunodeficiency Syndrome (AIDS) has assumed, it has rather become imperative to find a radical cure for this disabling condition. On such a quest, at our lab at All India institute of Medical Sciences we have been quantifying the response of various antigens, seen as potential vaccine candidates, against a spectrum of broadly neutralising antibodies. The antigen under our focus was V3 loop (a variable region present in the gp120 envelope of Human Immunodeficiency Virus). Though having a variable nature, it has an urgent need to be conserved mostly, since it plays an important part in entry of virus into its target cell, whether its a macrophage or a CD4+ helper T-cell. Till date not much work has been done, especially in India, in paediatric HIV-infected population, which acquires the infection through vertical transmission, i.e. from the mother. Further, the risk of a secondary infection is minimal in children due to the absence of high-risk behaviour. We enrolled 27 children in the study after obtaining informed consent from their parents. For sequence analysis, 18 samples were sent to Macrogen Inc.(S.Korea), either as conjugated to E.coli plasmid (where transduction was successful), or as independent amplified sequences.A vaccine which covers the latest evolved viruses and covers most of the grounds, i.e. which elicits broadly cross-reacting antibodies is urgently needed. The major barrier between the science community and HIV- vaccine seems to be the rate at which this virus mutates and hence evolves. Majority of the vaccines that are available today act by producing neutralizing antibodies which prevent the infecting virus from entering the target cells in the human body. Neutralizing antibodies are those antibodies which bind to the infectious agent and clear it from the system thereby preventing further entry of the organism into its target cell. In the present study, we studied the variability in the V3 loop of HIV-1 in the paediatric patients visiting our hospital by amplifying and sequencing the V3-V5 region of the viral envelope.In my project, I sequenced the V3-V5 region, determined the clade of virus, its variability, co-receptor tropism, garnering the required details since we are aiming it as a vaccine candidate and need to complete the groundwork before we project it such. We found that all of the patients were infected with subtype C virus which is the most common clade found in our country. Sequence analysis of the V3 showed that it is highly conserved in length and sequence showing only minor variations. It is essential to highlight here of the fact that CXCR4 usage was predicted in one of the patient's sequences (out of the 9 sequences that we received) that was analyzed in this study. The use of entry inhibitors (eg. Maraviroc), which is one of the second line drugs to treat HIV-1, is contraindicated in patients with CXCR4 usage. It is, therefore, important to analyze the sequence of the viruses infecting patients, to know the viral diversity. This quantitative and qualitative analysis of epidemiological data is an important cornerstone for establishing a preventive/curative vaccine.