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Neutralizing and non-neutralizing antibody responses in HIV-1 subtype C chronically infected patients with divergent rates of disease progression

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Background

Development of an efficacious HIV-1 vaccine able to elicit the production of broadly neutralizing antibodies (nAbs), capable of retaining potent activity against a diverse panel of viral isolates remains a significant challenge. The evolutionary forces that shape envelope and ensuing nAb and non-neutralizing antibodies in HIV-1 subtype C are incompletely understood and these two parameters have been rarely studied concurrently.

Methods

We characterized patterns of virus-specific nAbs and non-neutralizing antibodies in four slow progressors and four progressors with chronic HIV-1 subtype C infection, over a median of 21 months. Single cycle neutralization assays was performed. In addition, the binding affinities of HIV-specific immunoglobulins (IgGs) and the affinities of the IgGs to various Fcγ receptors (FcγRs) were assessed.

Results

NAbs evolved significantly in progressors (p=0.003) from study entry to study exit. NAb IC50 titers significantly correlated with amino acid lengths for V1-V2 (p=0.04), C3-V5 (p=0.03) and V1-V5 (p=0.04). Both groups displayed preferential heterologous activity against the subtype C panel. Both groups displayed preferential heterologous activity against the subtype C panel. There were no significant differences in breadth of responses between the groups for either subtype A or C. Neutralization breadth and titers to subtype B reference strains was significantly higher in progressors compared to slow progressors (both p<0.03) with increasing nAb breadth from study entry to study exit in progressors. Progressors had cross-reactive neutralizing antibodies that targeted V2 and V3. Binding affinities of non-neutralizing antibodies to HIV-specific gp120, gp41 and p24 and to activating and inhibitory Fcγ receptors (FcγRs) were similar in both groups. However, in slow progressors, CD4 T-cell counts correlated inversely with antibody binding affinity for the activating FcγRIIa (p=0.005).

Conclusion

Overall, the data suggest that neither nAbs nor non-neutralizing antibodies could be directly associated with disease attenuation. However, continuous evolution of nAbs was a potential marker of disease progression.

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