A longitudinal study on the dynamics of plasma neutralising antibodies and its determinants in HIV-2 infected individuals

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**BACKGROUND**

- HIV-2 is known to be less virulent and less pathogenic than HIV-1, and the majority of HIV-2 infected individuals remain asymptomatic much longer than HIV-1 infected individuals. Plasma viral load is approximately 1 log unit lower in HIV-2 than HIV-1 when matched for CD4+ T cell count, whereas the proviral load does not appear to differ between the two infections. Therefore, HIV-2 infection represents a model for the studies of immune responses that may control HIV infection and possibly functional cure.
- In HIV-1 infection, broad plasma neutralizing antibody (NAb) response develops in only 15% of individuals after two to four years of infection. Moreover, potency of NAb seems to be low at around 1:30 and fluctuating.
- To study dynamics of NAb response in HIV-2 infected individuals is difficult because of usually unknown seroconversion time and relatively silent disease course.
- Guinea-Bissau is a small country in West Africa with the highest HIV-2 prevalence in the world (2%). In 1990, we initiated an occupational cohort of police officers in Guinea-Bissau. Regular follow-up visits enabled us to investigate evolution of NAb response longitudinally in fifteen HIV-2 infected individuals with known seroconversion time.

**QUESTIONS**

- Where does broad and potent p-NAb response develop in HIV-2 infected individuals?
- What are the modulators of broad and potent p-NAb response?

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**RESULTS**

**Neutralization assay by plaque reduction**

- Target cell: GHOST(3)-CCR5 cells
- Complement-inactivated plasma: Starting plasma dilution was 1:20.

**Neutralization**

- Neutralization (%): The ratio of the number of virus plaques + p = 100
  - + p = 100

**Potent NAb response developed during the first two years of infection and was persistent**

- During the first two years after seroconversion, seven out of seven participants succeeded to develop potent NAb response at a score of 10000.
- Potent NAb response was persistent during the whole follow-up period in all participants.
- In the immunocompromised group, potency score stabilized around 30000 in the end of 5 years after seroconversion.
- In the immunocompetent group, potency score showed persistent increase throughout the whole follow-up period and reached approximately 20000 in the end.
- Potency score: was significantly higher at the end of follow-up period in immunocompetent group compared to the immunodeficient group (20000 vs 25000).

**NAb response at 1:10000 dilution differentiates immunocompetent from immunocompromised group**

- NAbs were able to neutralize only one isolate during the first 2 years after seroconversion.
- In the immunocompromised group, breadth score stabilized at around 3 in the end of 5 years after seroconversion.
- In the immunocompetent group, breadth score showed persistent increase throughout the whole follow-up period and reached approximately 4.5 in the end.
- Breadth score was significantly higher at the end of follow-up period in favor of immunocompetent group (4.5 vs 2.5).

**Modulators of Breadth and Potency of p-NAb Response**

- Age at seroconversion correlated negatively with CD4+ and CD8+ T cell count (r= -0.64 and -0.41, respectively, p<0.05).
- There was a positive correlation between breadth and potency (r=0.75, p<0.05).
- In the immunocompromised group, CD4+ and CD8+ T cell count tended to decrease with years after seroconversion (r = -0.62 and -0.88, respectively, p<0.05).
- Decreasing number of cellular immunity cells correlated negatively with potency of humoral immunity (r = -0.57 and -0.78, p<0.05).
- In the immunocompetent group, both breadth and potency of NAb response tended to increase with years after seroconversion (r = 0.53 and 0.51, respectively, p<0.05). Furthermore, potency of NAb response correlated positively with CD4+ T cell count (r = 0.72, p<0.05).

**CONCLUSION**

This study represents the most diverse longitudinal seroconversion infection cohort studied to date for HIV-2 neutralization.
- Broad and potent NAb response developed in all participants within the first two years of HIV-2 infection and persisted throughout the whole follow-up period. This strong humoral immunity response may contribute to the control of HIV-2 infection and functional cure.
- Immunosenescence may play a role in the development of humoral immunity against HIV-2. Individuals infected at a younger age seem to keep both humoral and cellular immunity active against HIV-2. However, older individuals with relatively impaired cellular immunity display blunted humoral immunity against HIV-2.
- Our results indicate that CD4+ T cells stimulate potent antibody production in immunocompetent individuals. Interestingly, in immunosuppressed individuals, despite decrease in CD4+ T cell count, potent antibody production continues. We speculate that increasing viremia in the immunodeficient group is responsible for potent antibody production.

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