



POSTER PRESENTATION

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# HIV-1 envelope characteristics that coincide with the development of cross-reactive neutralizing activity in HIV-1 infected patients

Tom van den Kerkhof<sup>1\*</sup>, Marit van Gils<sup>1</sup>, Zelda Euler<sup>1</sup>, Naomi Verwer<sup>1</sup>, Rogier Sanders<sup>2</sup>, Hanneke Schuitemaker<sup>1</sup>

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## Background

The HIV-1 envelope glycoprotein (Env) on the viral surface is the target for anti-HIV-1 neutralizing antibodies. In some HIV-1 infected patients broadly neutralizing antibodies (BrNAb) develop that neutralise HIV-1 from different subtypes and therefore are considered to be directed against conserved regions [2]. The most vulnerable epitopes can be shielded from antibody recognition by steric hindrance and N-linked glycans [3]. Moreover, length and glycosylation of the envelope V1V2 region seem to play a role in resistance against neutralizing antibodies [4]. Understanding of factors involved in BrNAb development will help the rational design of an effective antibody-based vaccine immunogen.

## Methods

From a previous screening of 299 patients for broadly neutralizing activity (BrNAb), we selected 13 patients with high BrNAb in serum, 9 patients without BrNAb (non-BrNAb) and 10 patients with intermediate BrNAb, at 2-4 years after SC. From these patients clonal viruses were obtained within the first year after SC from which gp160 was sequenced and analyzed for length of different regions and number of potential N-linked glycosylation sites (PNGS). Additionally we tested the neutralization sensitivity of the viral variants from the patients with and without BrNAb against different already identified broadly neutralizing antibodies (BrNAbs).

## Results

We observed a correlation between length of the variable regions 1 and 2 (V1V2) of *env*, especially for variable region 1 (V1), and the presence of BrNAb. Patients with non-BrNAb in their serum had HIV-1 variants with longer V1 regions. Remarkably, differences in length of the V1 region did not coincide with differences in the number of PNGS on V1. Only the number of PNGS in gp41 correlated with BrNAb, where a higher number of PNGS correlated with the absence of BrNAb. No significant differences were observed between HIV-1 variants from individuals with and without BrNAb in their sensitivity to the known BrNAbs b12, 2G12, 2F5, 4E10, PG9, PG16 and VRCO1.

## Conclusion

The observed correlation between a shorter V1 of *env* in patients with BrNAb could indicate that the development of BrNAb in HIV-1 infected patients is associated with a more accessible and more open structure of the viral envelope glycoprotein, which is achieved by having fewer glycans and shorter variable loops. However these *env* characteristics on early viruses isolated from patients who developed BrNAb did not coincide with a higher sensitivity to BrNAbs as compared to early viruses from patients who did not develop BrNAb. Identification of *env* characteristics that coincide with BrNAb in patients could help the rational design of an effective antibody-based vaccine immunogen.

## Author details

<sup>1</sup>Dept of Exp Immunology and Landsteiner Laboratory of the Academic Medical Center at the University of Amsterdam, Amsterdam 1105 AZ, The Netherlands. <sup>2</sup>Dept of Med Microbiology and Experimental Virology of the Academic Medical Center at the University of Amsterdam, Amsterdam 1105 AZ, The Netherlands.

<sup>1</sup>Dept of Exp Immunology and Landsteiner Laboratory of the Academic Medical Center at the University of Amsterdam, Amsterdam 1105 AZ, The Netherlands

Full list of author information is available at the end of the article

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