Retrovirology

Poster presentation

P11-20. HIV-1 gp41-specific mucosal IgAs from highly exposed but IgG seronegative women block HIV-1 epithelial transcytosis and neutralize CD4+ cell infection

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Background

AIDS is mainly a sexually transmitted disease and accordingly, mucosal tissues are the primary sites of natural HIV-1 transmission. Mucosal IgA antibody specific for HIV-1 envelope gp41-subunit is one correlate of protection in individuals who are highly sexually exposed to HIV-1 but remain persistently IgG seronegative (HEPS). Understanding these peculiar IgAs at the gene and functional level is only possible with monoclonal IgAs.

Methods

We have constructed a mucosal Fab IgA library from HEPS and have characterized a series of HIV-1 IgAs specific for gp41 at the functional level against HIV-1 transcytosis and CD4+ cell infection and analyzed the *IgA fab* genes

Results

These IgA are transcytosis-blocking and infection-neutralizing in the nM range using primary B clade viruses. Characterization of their *IgA* genes shows that Fab specific for gp41-membrane proximal region harbors a long CDRH3 similar to the two broadly neutralizing IgG monoclonal antibodies, 2F5 and 4E10. Furthermore, the selected Fab IgA exhibits extensive somatic mutations that cluster in the CDR regions, indicating that affinity maturation due to an antigen driven process had occurred in HEPS, presumably upon multiple exposures to HIV.

Conclusion

The present analysis of HEPS monoclonal IgA gives a unique opportunity to correlate antibody function (resistance to a pathogen *in vivo*) to antibody gene. Such neutralizing monoclonal IgA could be used in microbicide formulation.