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Poster presentation

P05-11. Yeast mannan genetics controls the molecular specificity of anti-carbohydrate antibodies cross-reactive to the HIV envelope

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Background

Immunologically self carbohydrates protect the human immunodeficiency virus type -1 (HIV-1) surface glycoprotein, gp120 from antibody recognition. However, one broadly neutralising antibody, 2G12, can protect against primary viral challenge by direct recognition of these "self" glycans on gp120. Immunogens capable of eliciting antibodies of similar specificity are candidates for HIV/AIDS vaccine design. The polysaccharides of common yeasts exhibit significant structural and antigenic mimicry with the immunologically "self" glycans of gp120; 2G12 also recognises yeast mannans.

Methods

Wild-type and genetically modified *Saccharomyces cerevisiae* was used to intravenously inoculate rabbits. Sera from these animals was subjected to gp120-binding ELISAs, carbohydrate microarray analysis, and *ex vivo* neutralisation assay.

Results

Here we report that manipulation of yeast mannan biosynthesis controls the molecular specificity of cross-reactive antibodies to gp120. Carbohydrate microarray analysis of gp120-reactive sera produced following immunization by *Saccharomyces cerevisiae* (SCWT) revealed serum with high reactivity to "self" Man8GlcNAc2 glycans. In contrast, immunisation with *S. cerevisiae* deficient for the Mnn1 a1,3 mannosyl transferase gene (SCMnn1), elicited gp120-reactive antibodies directed to Man9GlcNAc2 glycans. Terminal Mana1-3 linkages that cap the common repeating (Mana1-2Man) core motif are absent in the SCMnn1 strain.

Conclusion

These data reveal that anti-carbohydrate antibodies that bind gp120 can be reliably elicited by microbial mimicry. The specificities of these antibodies can be controlled by genetic manipulation of mannan biosynthesis, suggesting a route towards HIV vaccine design.