Estimating the probability of polyreactive antibodies disabling a gp41 trimer after T cell-HIV adhesion

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***Short Abstract* — A subset of broadly neutralizing monoclonal antibodies (mAbs) recognize epitopes in the membrane proximal external region (MPER) of gp41 that are transiently exposed during viral entry. We present a model that allows us to calculate, for a given antibody concentration, the probability that during the transient period when the epitopes in the MPER are exposed, a trivalent gp41 will be rendered incapable of completing the fusion process. The model elucidates the parameters that determine the ability of polyreactive MPER-binding antibodies to disable epitopes and predicts how the IC50 for neutralization depends on these parameters.**

***Keywords* — HIV neutralization, antibody, gp41, probability.**

I. Purpose

Although numerous studies have determined rate constants for the binding of 4E10 and 2F5 to peptide epitopes in solution and peptides conjugated to liposomes [1-4] and the lifetime of the exposure of the MPER on HIV-1 has been estimated [5-8] a quantitative description of how these parameters determine the mAb concentrations that are effective in inhibiting fusion has been lacking.

Here we present a model that allows us to calculate, as a function of the serum antibody concentration, the probability of a trivalent MPER being disabled by polyreactive mAbs.

II. Methods

A computational model was developed to the study the probability of polyreactive antibodies disabling a gp41 trimer after T cell-HIV adhesion. Rate constants determined for the binding of 4E10 and 2F5 to peptide conjugated liposomes [1] were used to compare these two antibodies.

III. Conclusion

We show that for the rate constants determined for the binding of 4E10 and 2F5 to peptide conjugated liposomes [1] and for lifetimes of the pre-hairpin intermediate longer than a few minutes [5–8], probabilities greater than a half are predicted for 4E10 and 2F5 when their concentrations are in the nM range. The model shows how the probability depends on the rate constants and the lifetime of the pre-hairpin intermediate and what the limitations are on achieving a high probability of disabling an epitope at low antibody concentration.

Acknowledgements: This work was supported by National Institutes of Health Grant R37-GM035556 and DOE contract DE-AC52-06NA25396.

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