

Events during the absorption phase of a neutralization assay are predictive of protection in the SHIV – rhesus macaque model.

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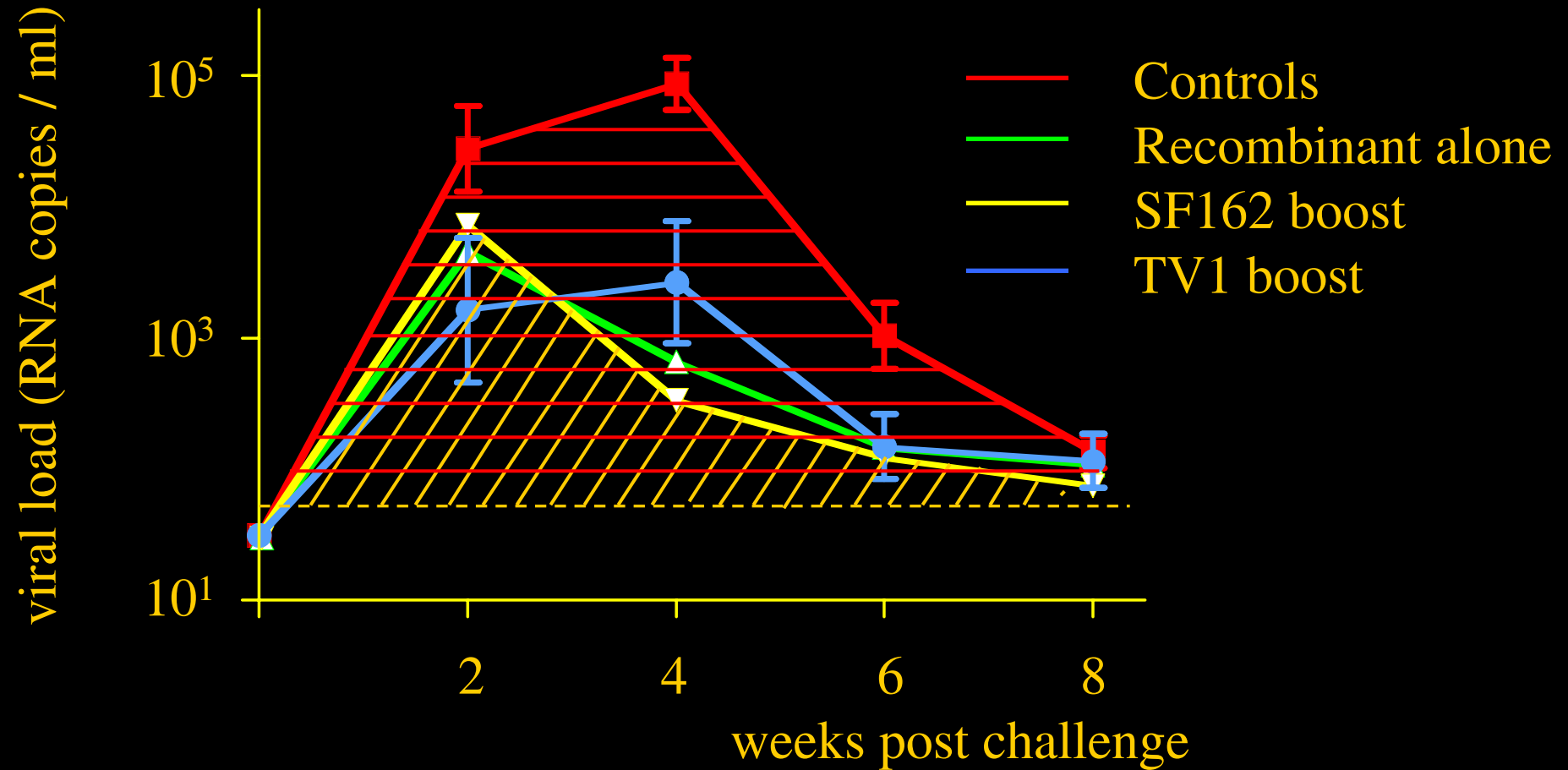
Objective

An assay correlating neutralizing antibodies with protection would facilitate the development of an HIV vaccine.

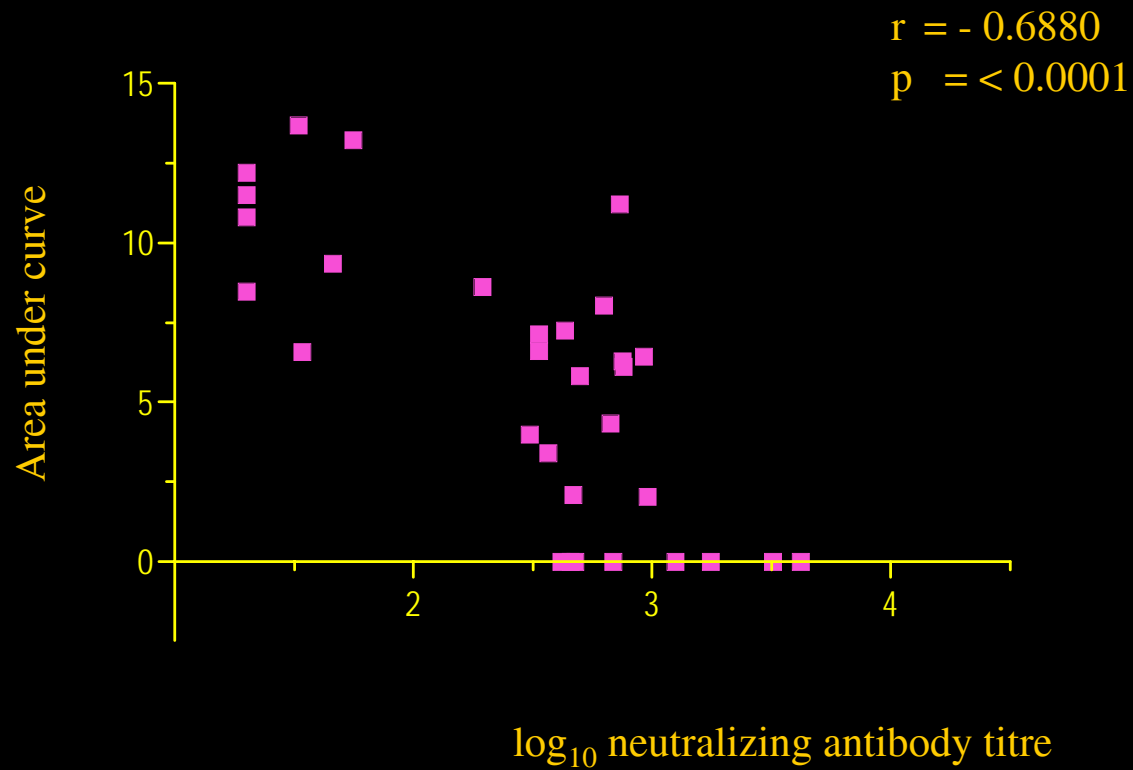
SHIV challenge studies

	Rhesus macaques	Challenge
Trial 1:	Protein prime, peptide boost Imported: 16 + 4 controls	Week 55 i. ven SHIVSF162P4
Trial 2:	Protein prime, mimotope boost Indian: 15 + 5 controls	Week 24 i. rect SHIV SF162P4
Trial 3:	Mimotope prime, protein boost Indian: 15 + 5 controls	Week 24 i. rect SHIV SF162P4
Trial 4:	Adeno/mucosal prime, protein boost Imported: 8 + 4 controls	Week 44 i. rect SHIV SF162P4
Trial 5:	Alpha virus prime, protein boost Mixture: 32 + 8 controls	Week 44 i. rect SHIV SF162P4

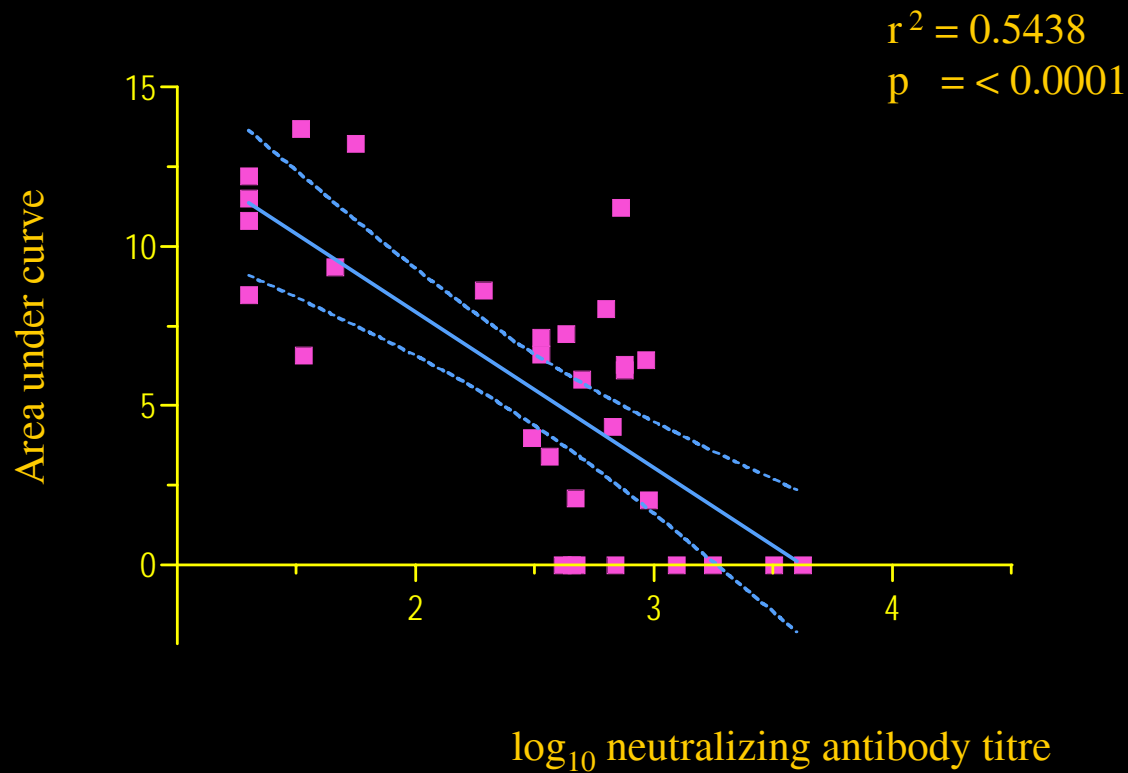
Areas under curve



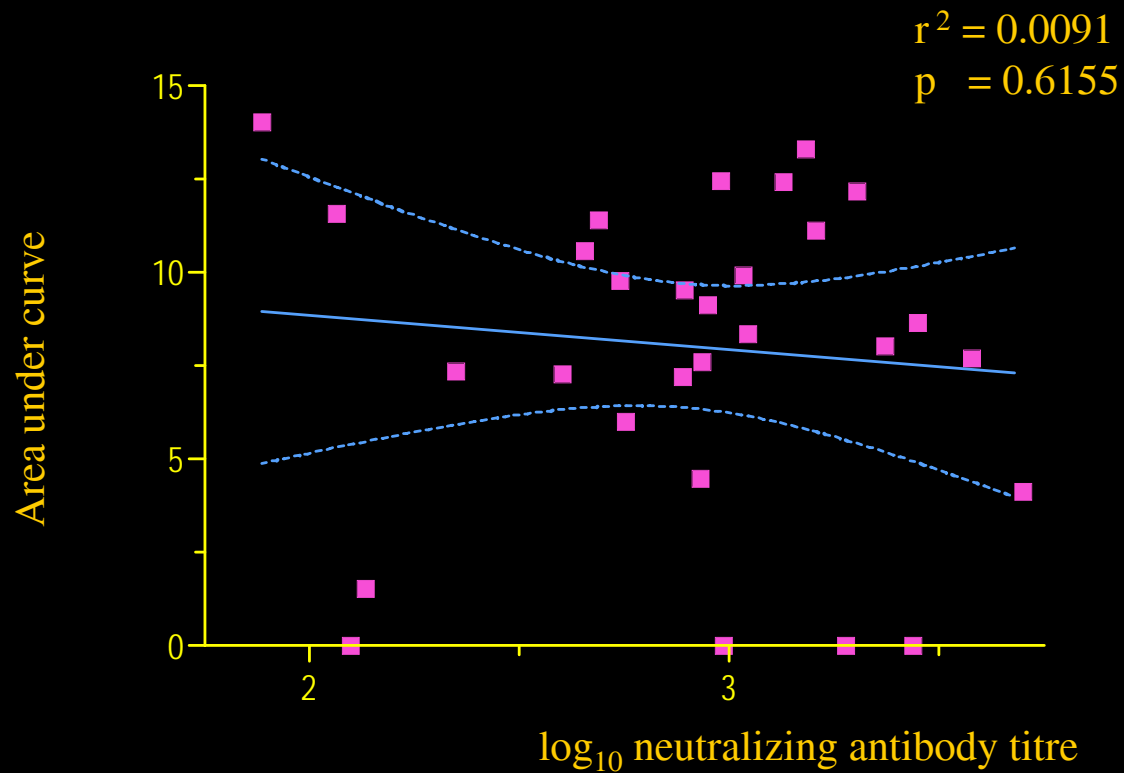
Positive example



Coefficient of determination



Negative example



Summary: Coefs. of Determination

Trial	Serum taken:		Day of challenge
	- 6 weeks	- 2 weeks	
1	0.3729	0.4221	Not available
2	Not available	0.01239	0.0001344
3	Not available	0.1362	0.1182
4	0.8602	Not available	0.6377
5	0.4947	0.5510	0.5438

Potential explanations

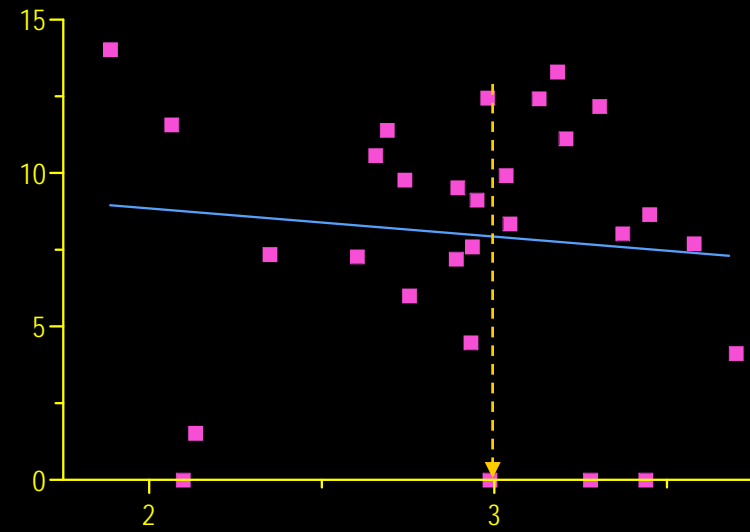
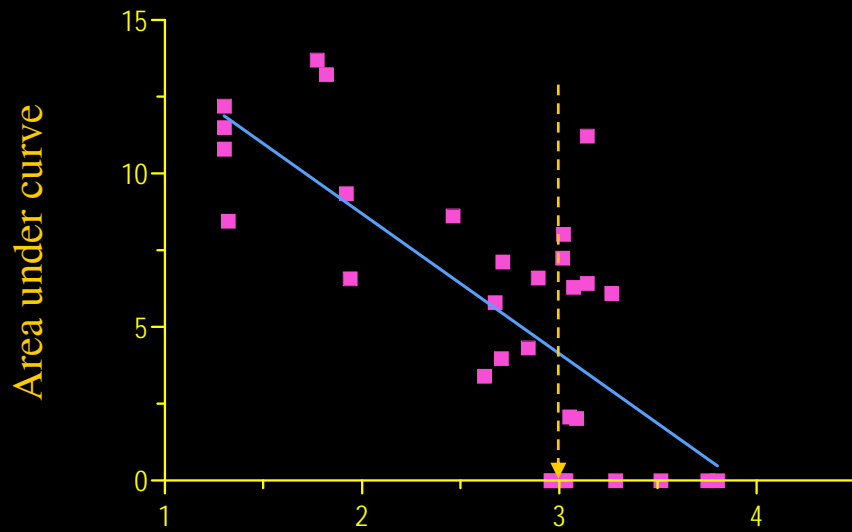
Neutralizing antibodies are not protective;

Reduction in area under viral load curve does not quantify protection;

Protection not related to concentration of neutralizing antibody;

Qualitative differences between protective and other antibodies.

Selection of sera



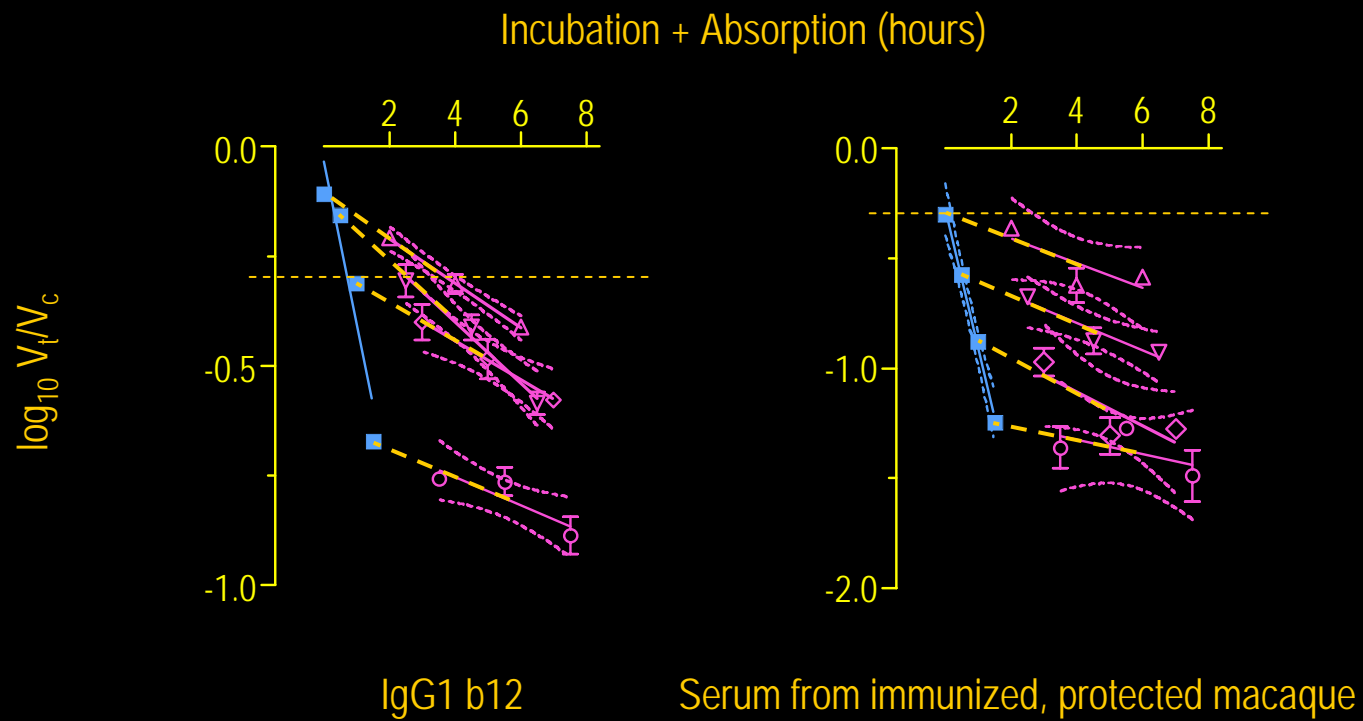
log₁₀ neutralizing antibody titre

Neutralization reaction

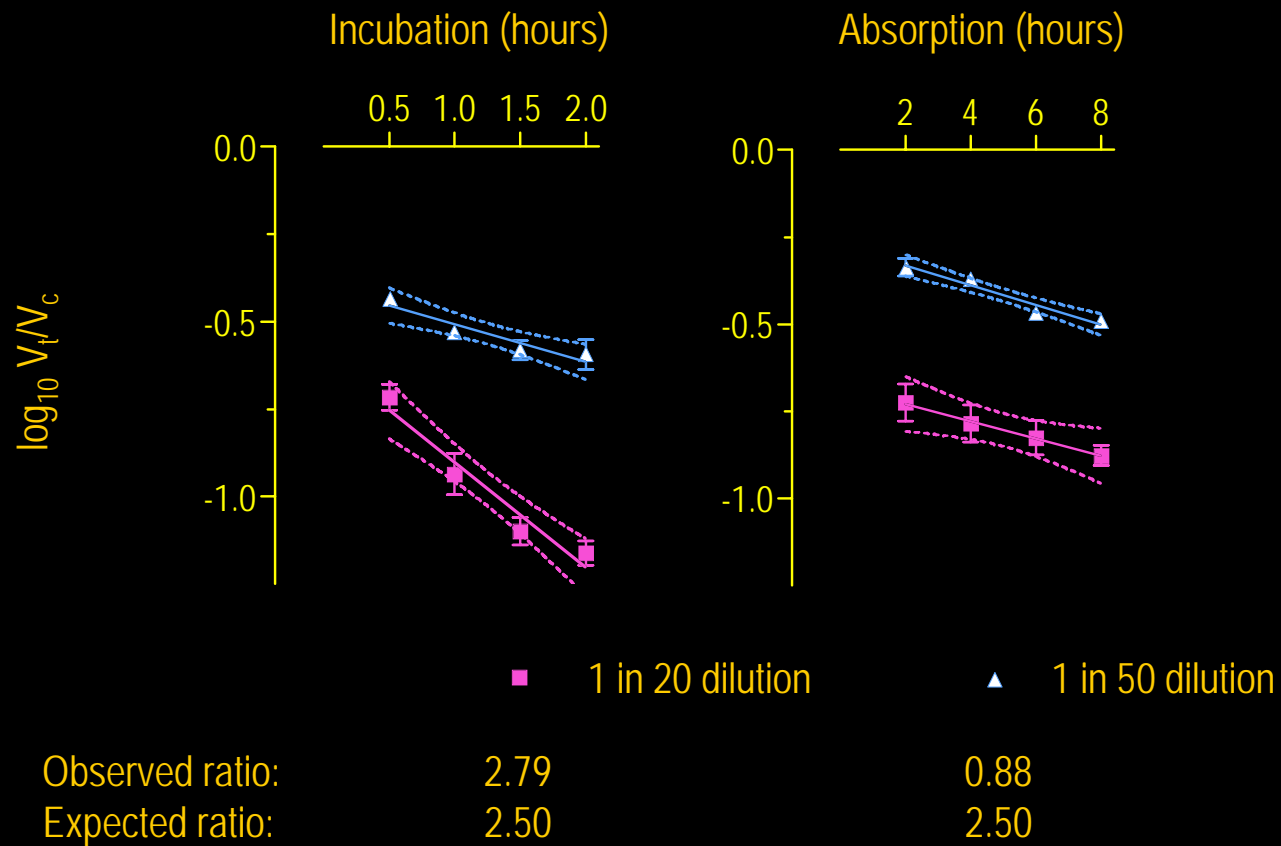
Infectious virus + antibody \rightleftharpoons Non-infectious virus

Mixture exposed to cells to quantify proportion of virus retaining infectivity.

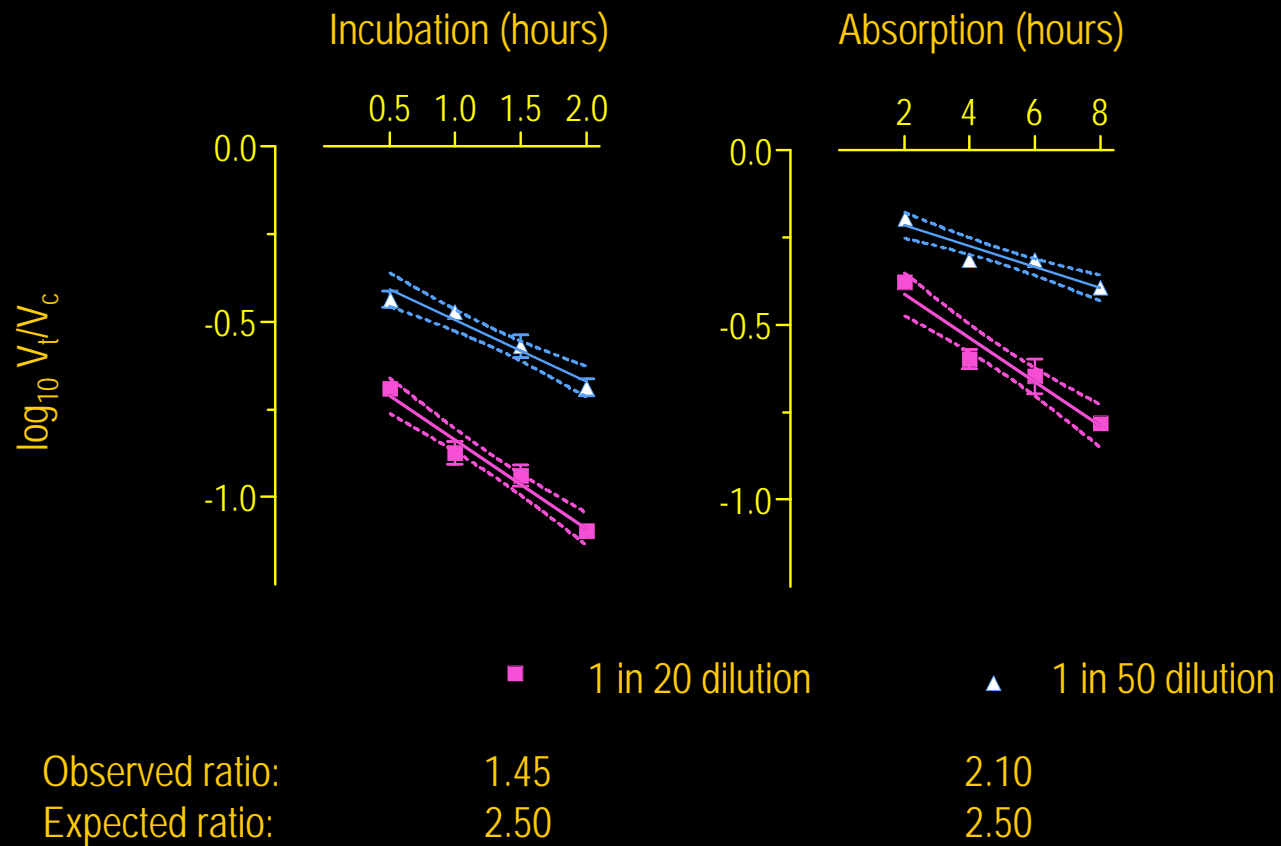
Extrapolation back to zero absorption.



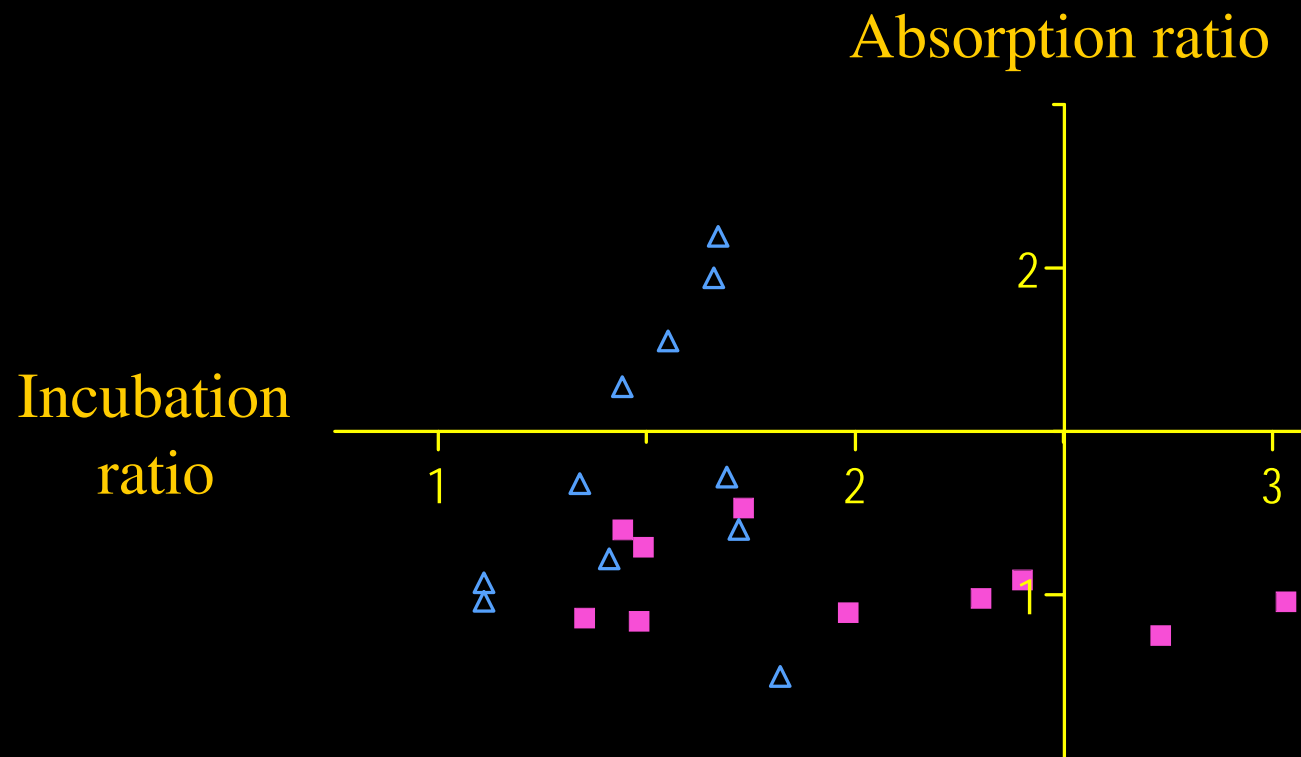
Kinetics with serum from protected macaque.



Kinetics with serum from infected macaque.



Ratios (so far)



Expected ratios = 2.5

■ Protected Infected △

Conclusions

Antibodies which conform to the traditional definition of neutralization are more likely to be associated with protection.

Consortium

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The way to get something done is not to mind who gets the credit for doing it.

Benjamin Jowett, Master of Balliol College, Oxford