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

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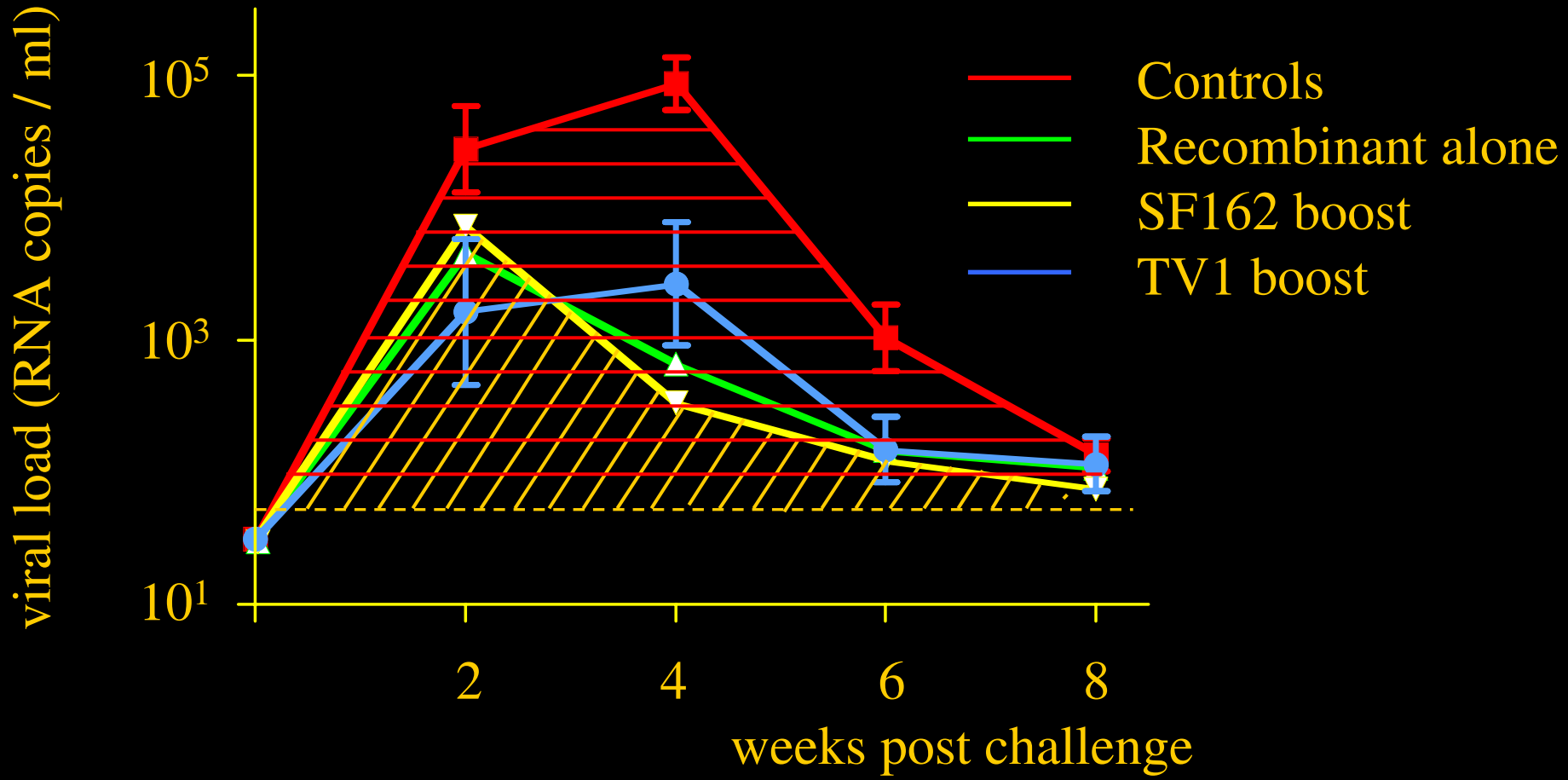
Objective

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

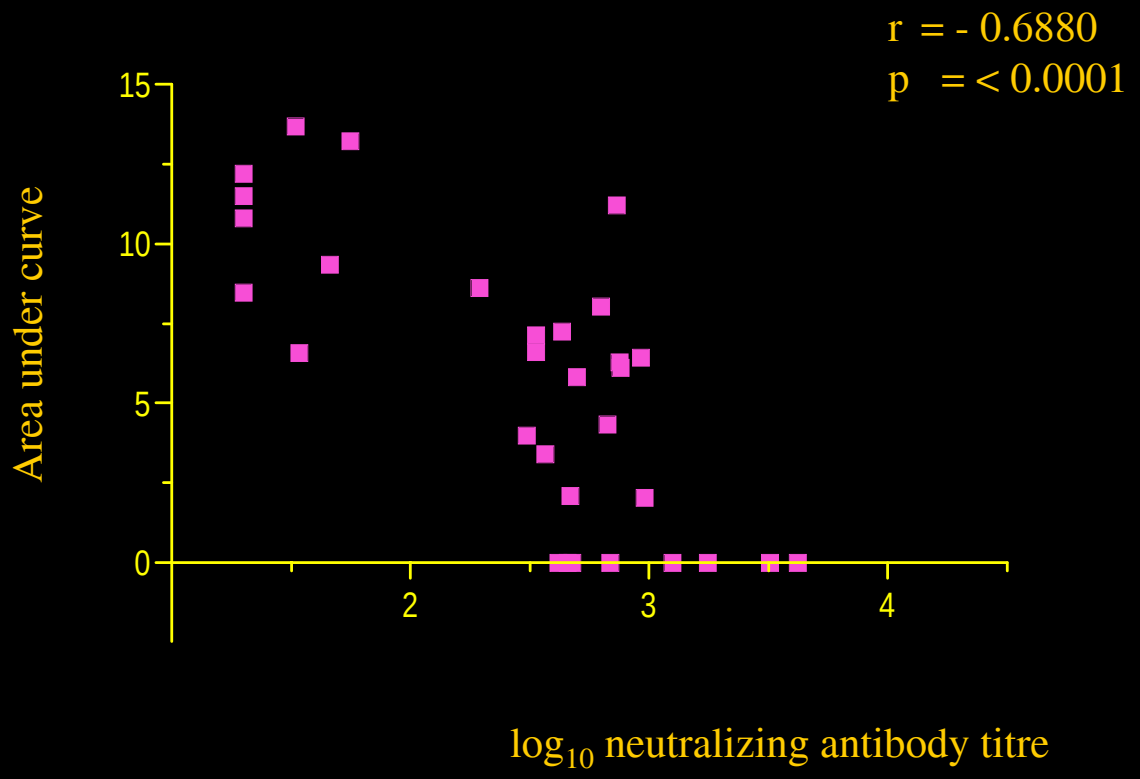
SHIV challenge studies

	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

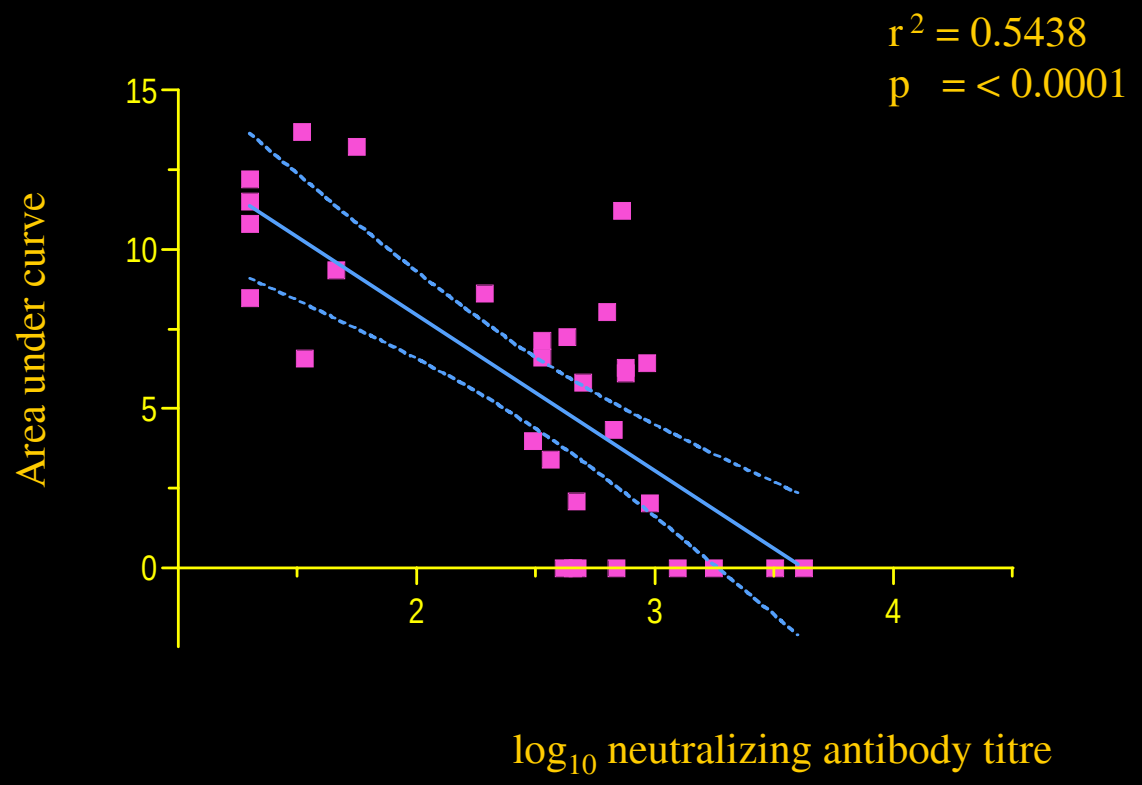
Areas under curve



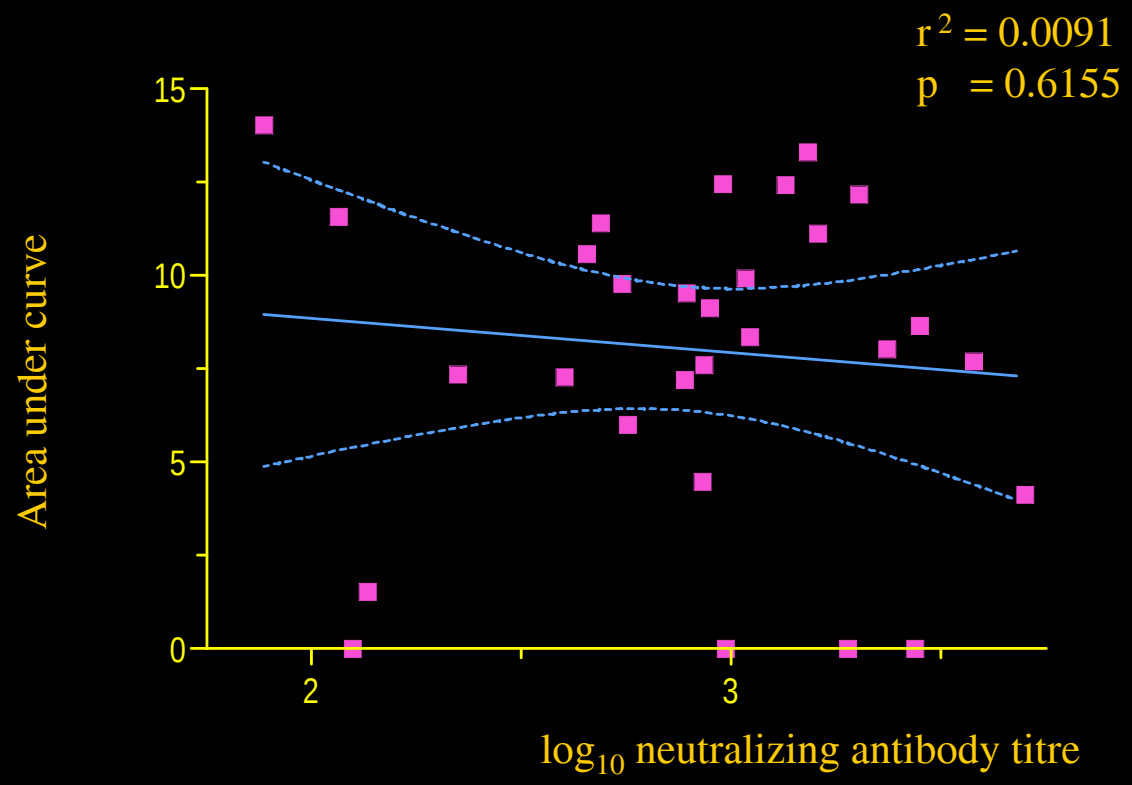
Positive example



Coefficient of determination



Negative example



Summary: Coefs. of Determination

	Serum taken:		
Trial	- 6 weeks	- 2 weeks	Day of challenge
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

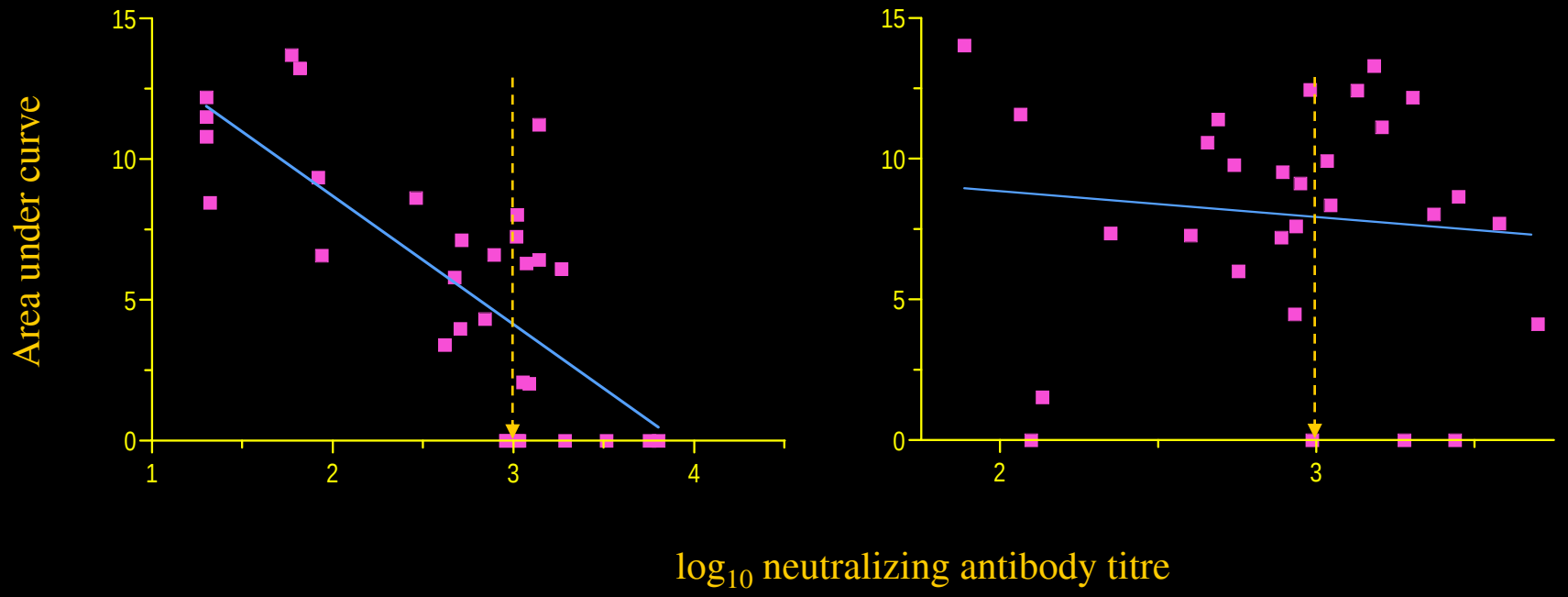
Neutralizing antibodies are not protective;

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

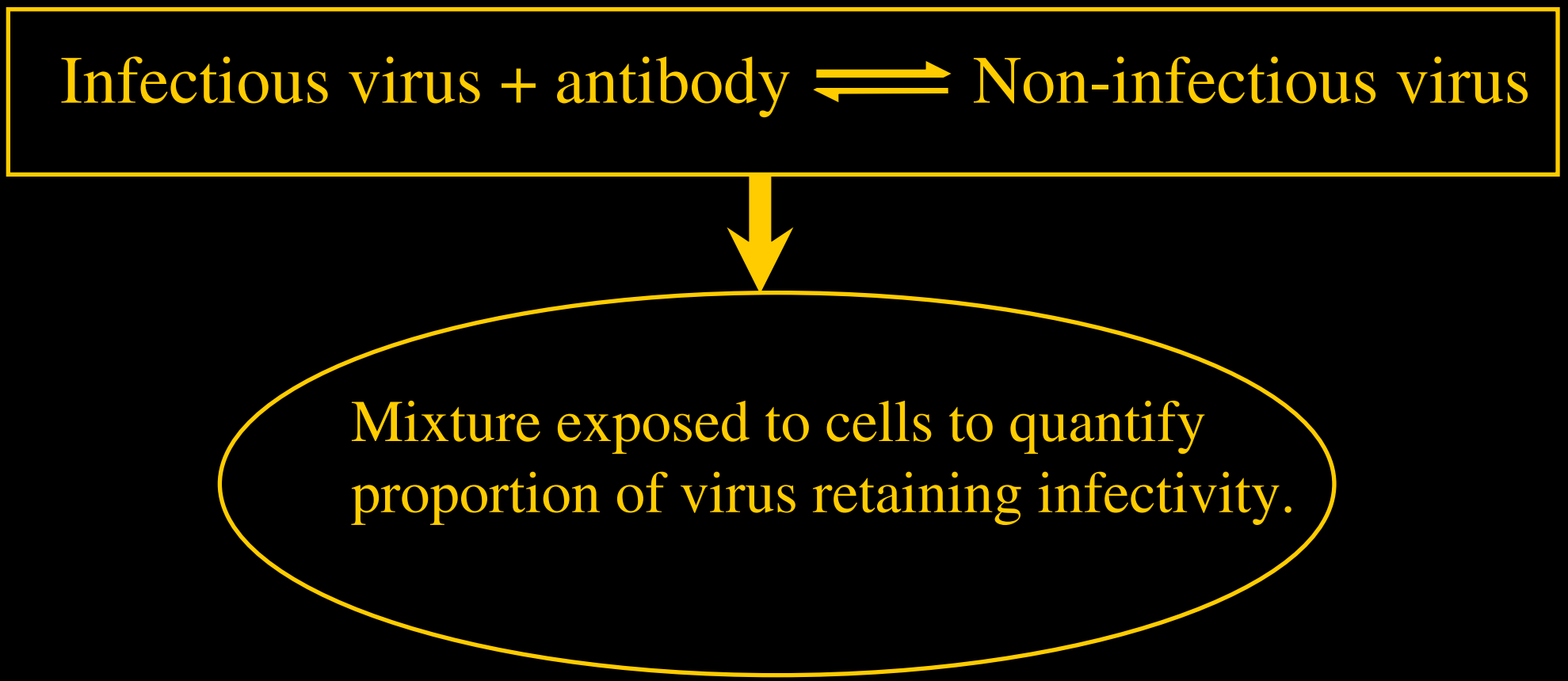
Protection not related to concentration of neutralizing antibody;

Qualitative differences between protective and other antibodies.

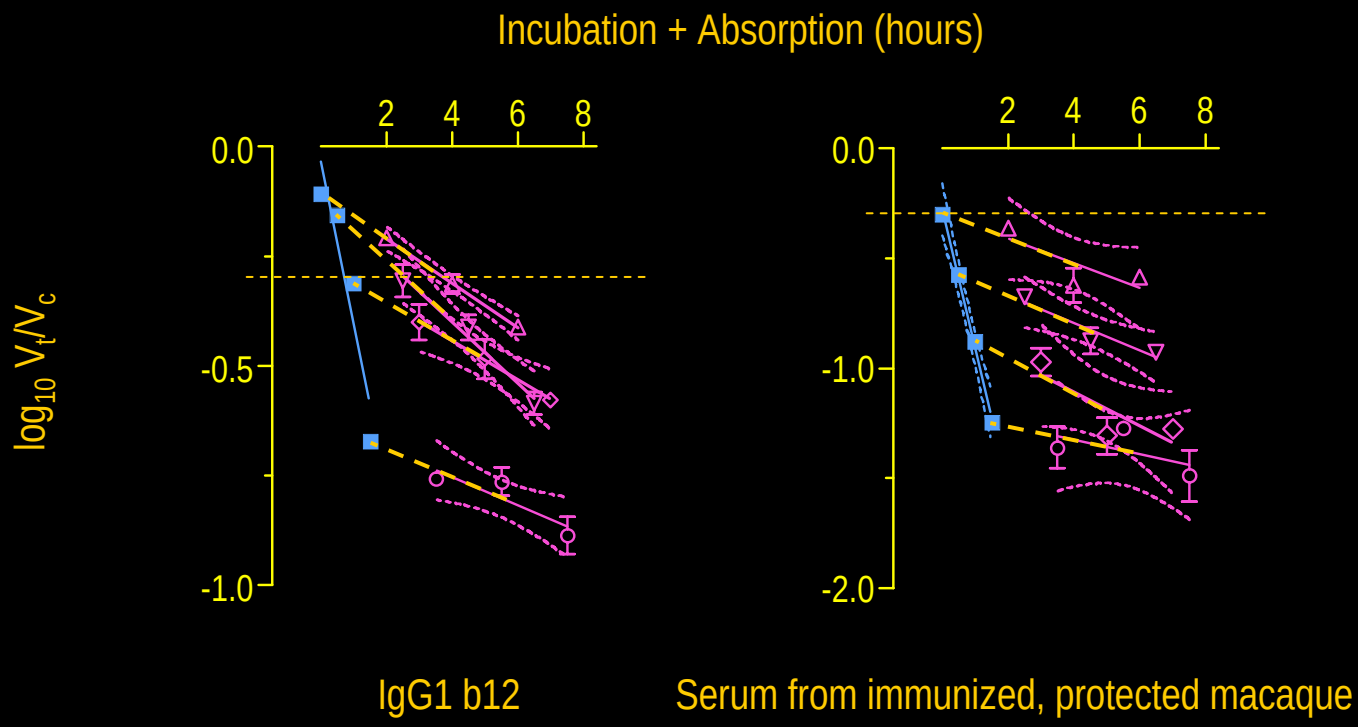
Selection of sera



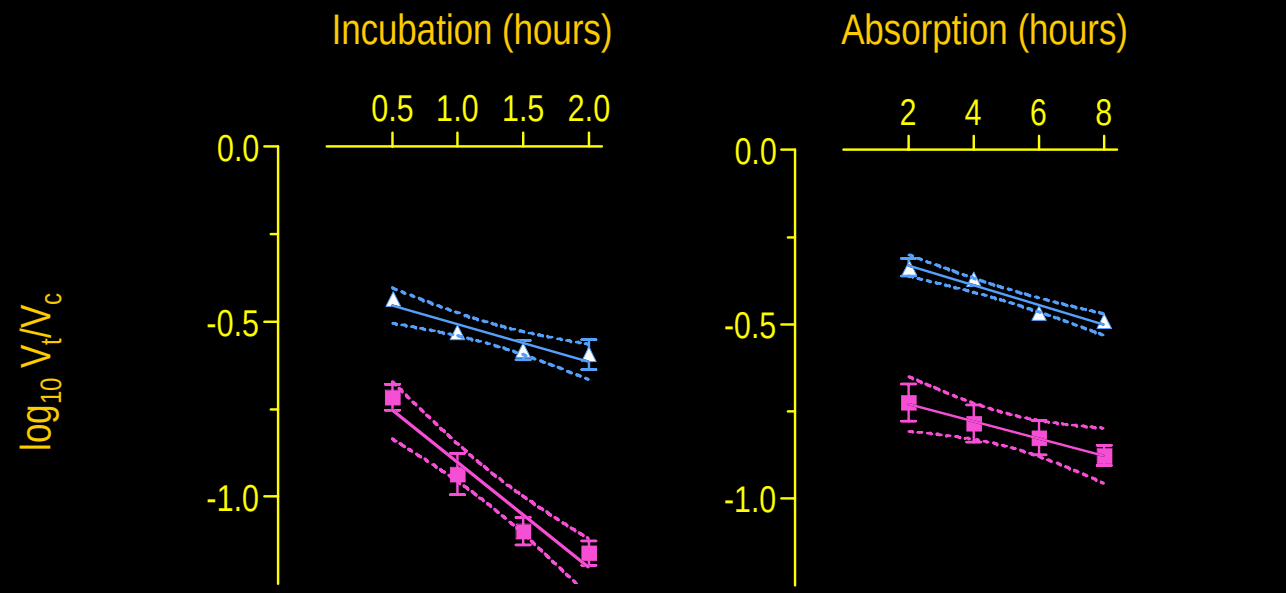
Neutralization reaction



Extrapolation back to zero absorption.

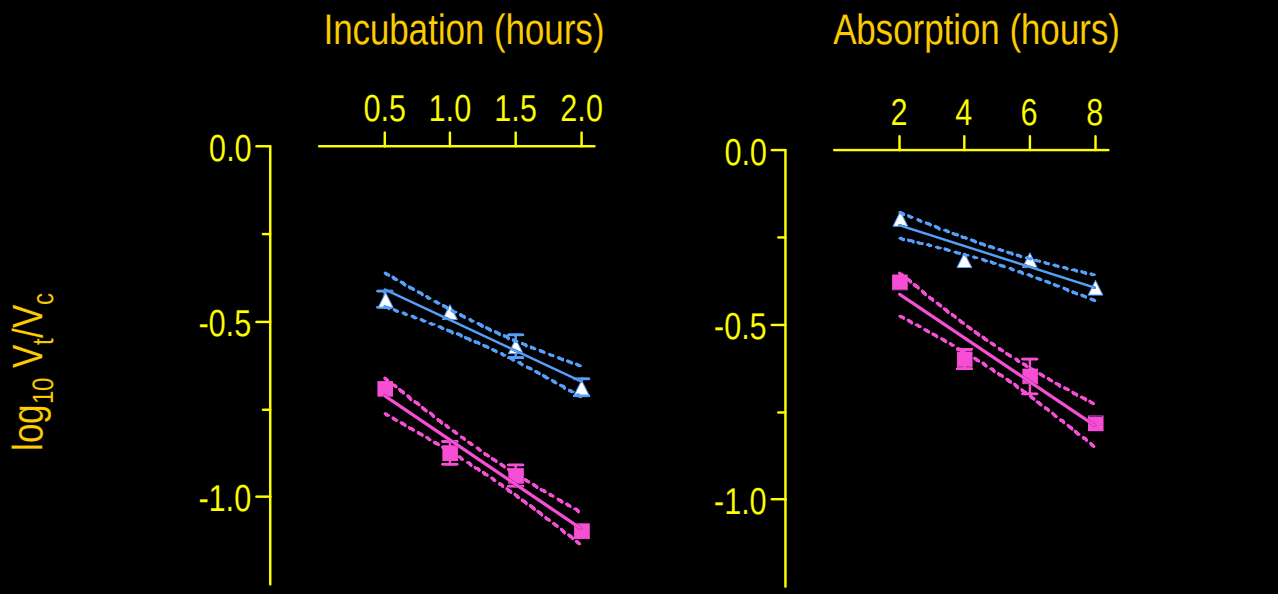


Kinetics with serum from protected macaque.



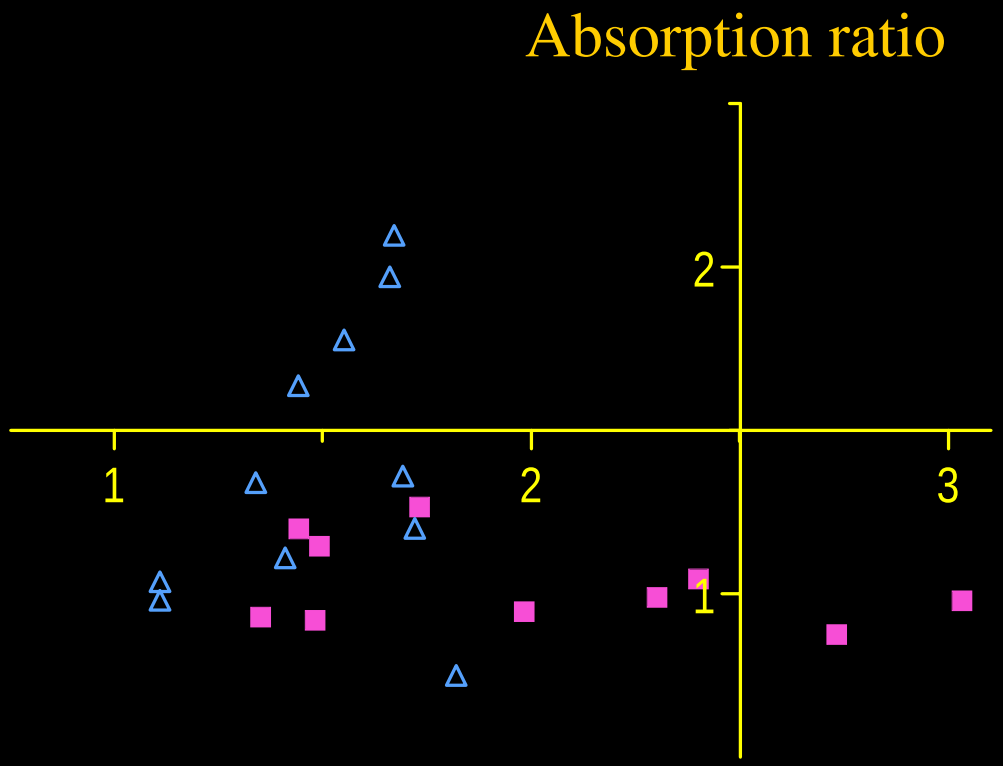
Observed ratio:	2.79	0.88
Expected ratio:	2.50	2.50

Kinetics with serum from infected macaque.



Observed ratio:	1.45	2.10
Expected ratio:	2.50	2.50

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.

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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