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Evaluation of a candidate WHO International Standard for Zika antibody as a vaccine reference reagent

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Challenges for Vaccine Development against Emerging Diseases

- ❑ Many emerging diseases agents require high containment facilities
  - ❑ Limited facilities for handling whole agent
  - ❑ Extremely limited facilities for pre-clinical challenge studies
- ➢ Prevent academics and SME's entering field

- ❑ Dispersed and fragmented research field
  - ❑ How to compare data from different groups
  - ❑ How to compare data throughout pre and clinical development

- ➢ The availability of a common reference standard addresses these difficulties

Aims

- To create a serological **vaccine** reference reagent which would
  - Set a benchmark for immunogenicity studies
  - Facilitate all stages of vaccine development by harmonising data
  - Overcome biocontainment / bio-security restrictions can limit vaccine development

- NIBSC works with the WHO to produce over 90% of the International Standards for biological medicines.

Anti-Zika Standard

- Candidate International Standard (IS) material (16/320-14)
- Freeze dried 0.25mL
- Included in WHO International collaborative study
- Convalescent plasma pooled (2 individuals)

Old World vs. New World Models

		Serology (d42pi)				Viremia
		Euroimmun ZIKV IgG (RU/mL)	Mikrogen RecomLine Tropical		NT_{50}	copies/mL
			ZIKV NS1	ZIKV E		
Old World	Cynomolgus Macaque	4.96	+	-	71	1.91E+04
		4.82	+	-	95	6.64E+04
		8.76	++	-	292	1.12E+04
		4.42	-	-	40	4.06E+04
	Rhesus Macaque	10.67	+	-	184	3.49E+01
		180.77	+++	++	3620	8.53E+05
		81.52	+++	-	956	9.83E+04
		70.75	+++	-	1170	8.27E+04
New World	Marmoset	73.15	+++	+	2230	5.06E+03
		18.45	+++	+	1210	1.63E+04
		30.16	+++	-	2870	2.85E+03
		70.55	+++	-	3620	1.62E+03
	Tamarins	4.54	+	-	90	1.05E+07
		7.85	+	-	718	6.69E+06
		7.96	++	-	570	4.33E+05
		3.64	++	+	394	8.96E+05

Cynomolgus macaque

Indian rhesus macaque

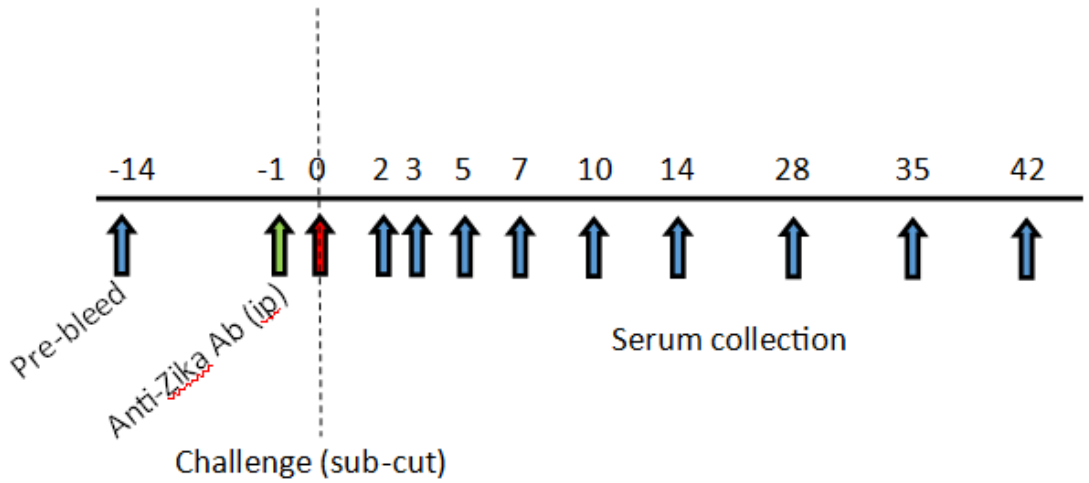
Common Marmoset

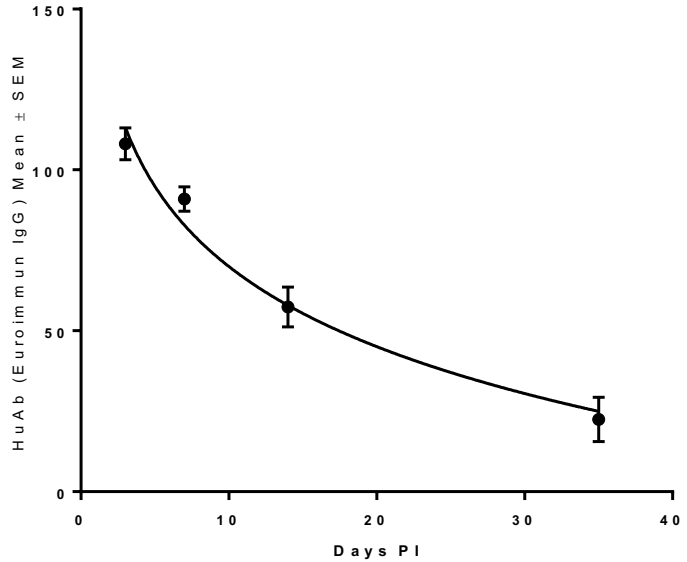
Red-bellied Tamarin

PRVABC59 challenge. Virus provided by NCPV.

Passive transfer model

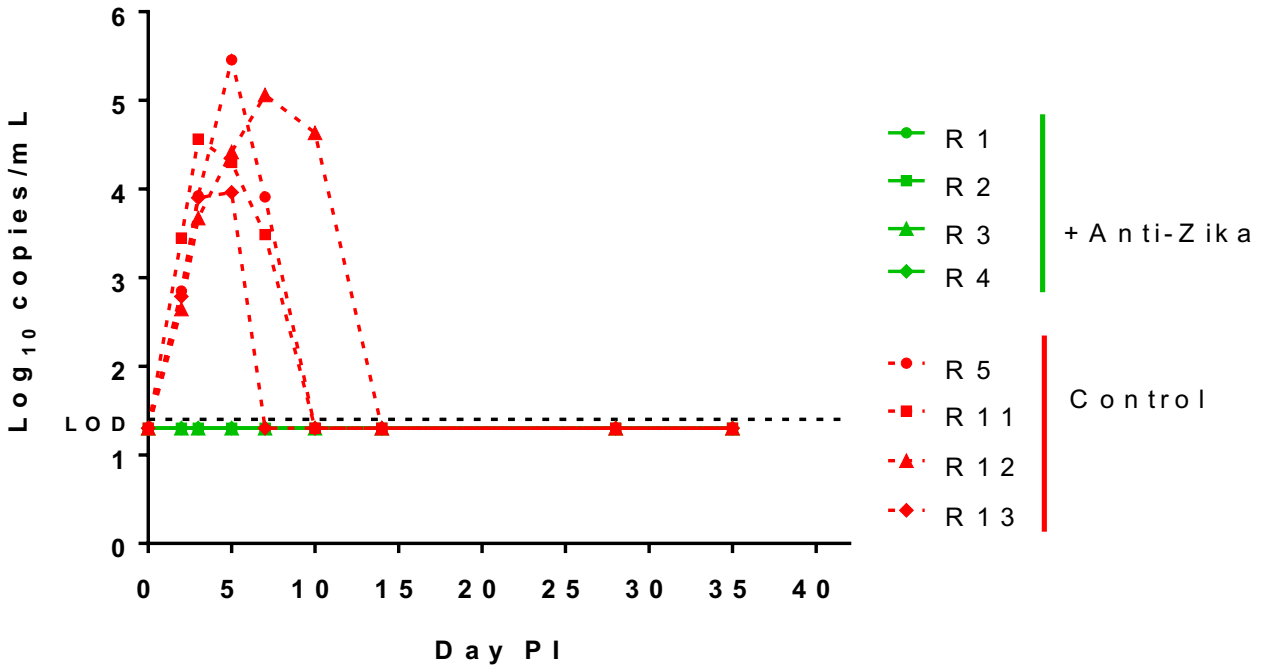
- ❑ 25mLs administered intraperitoneal to Cynomolgus macaques.
- ❑ Challenge at 24 hours with PRVABC59 (sub-cut).
- ❑ Blood collected at set intervals.





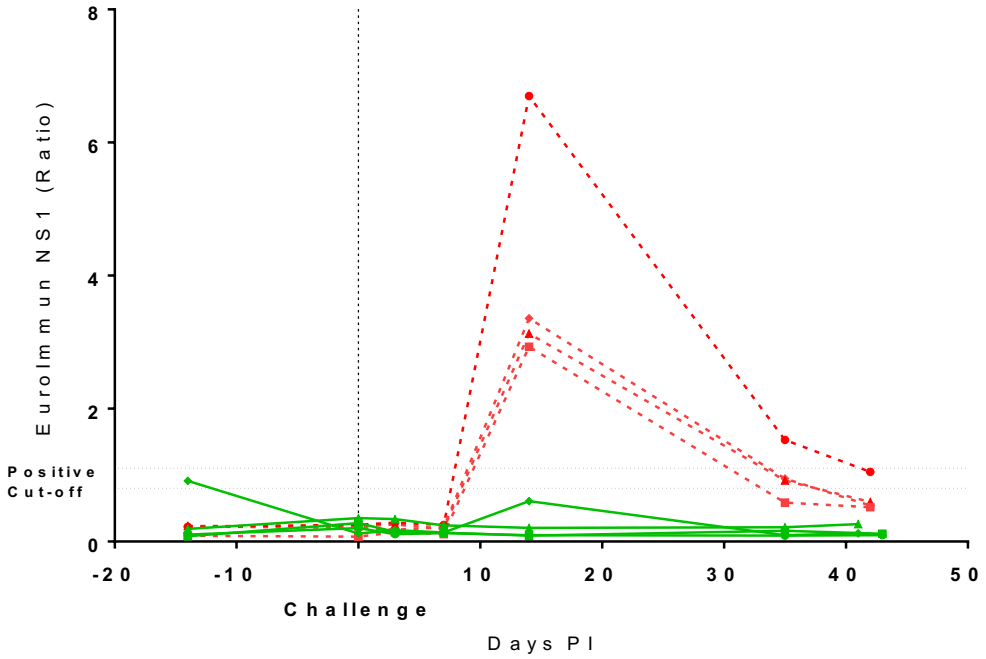
Half-life approx. 18 days.

Results - Viremia

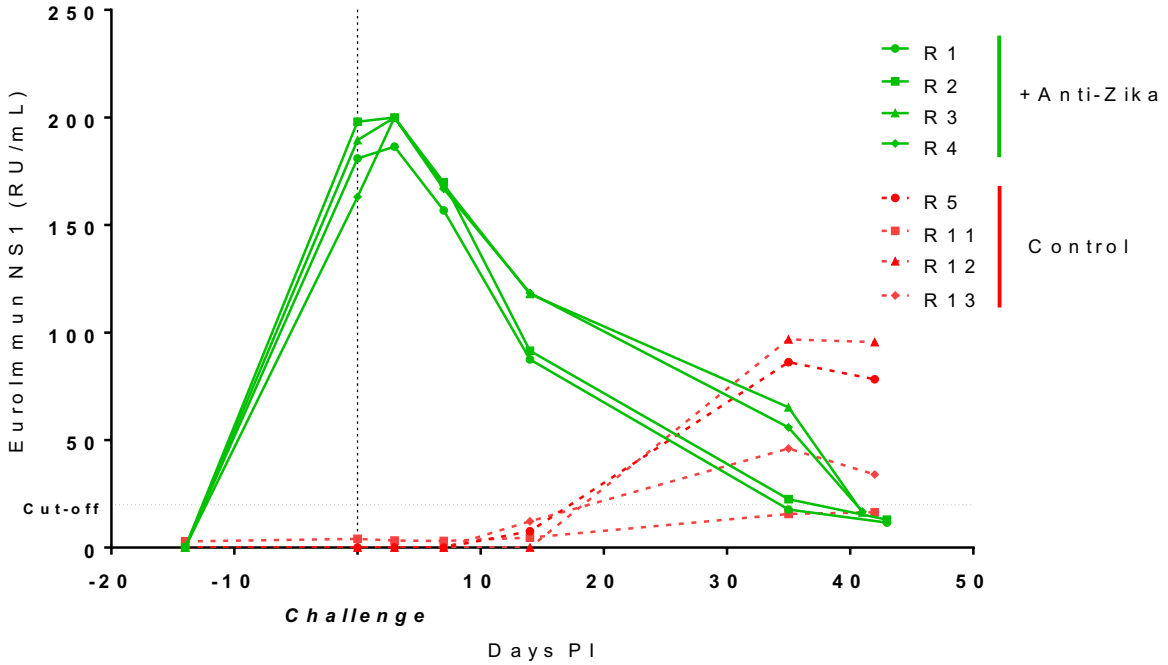


Results - Serology

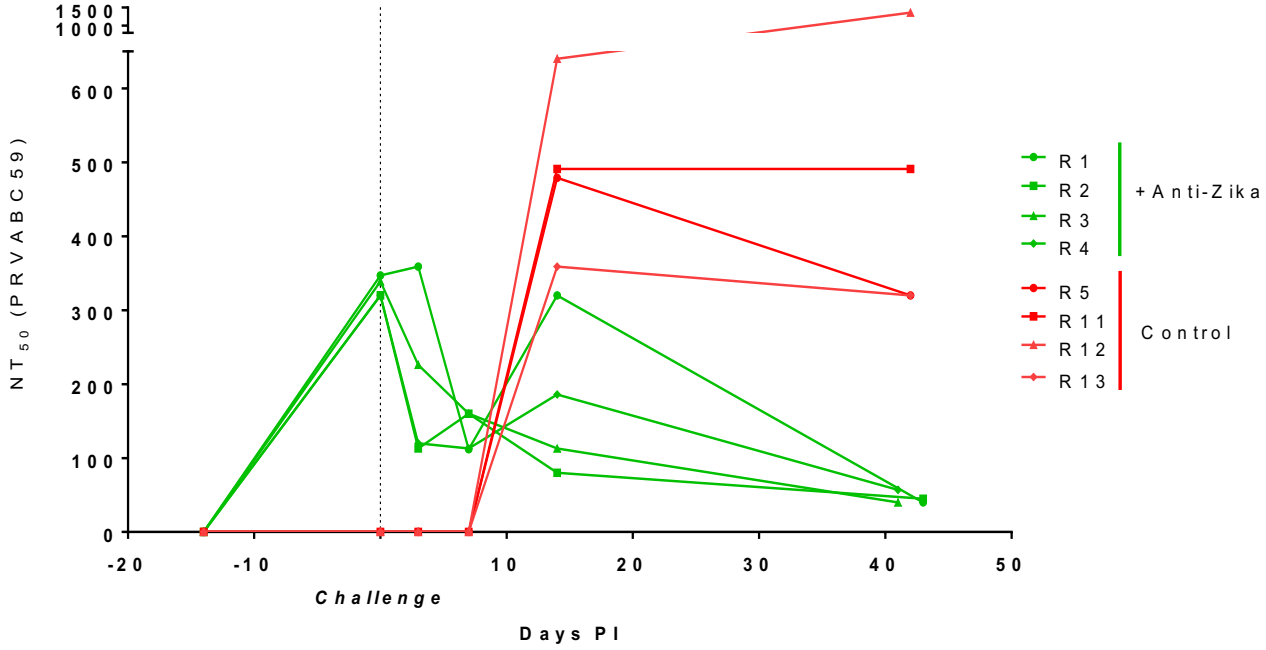
IgM

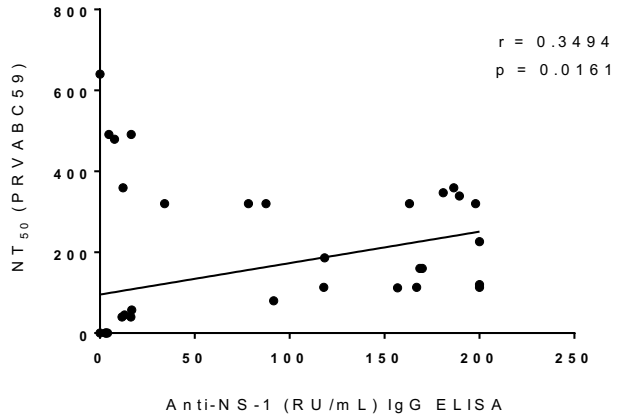


IgG



In vitro neutralisation

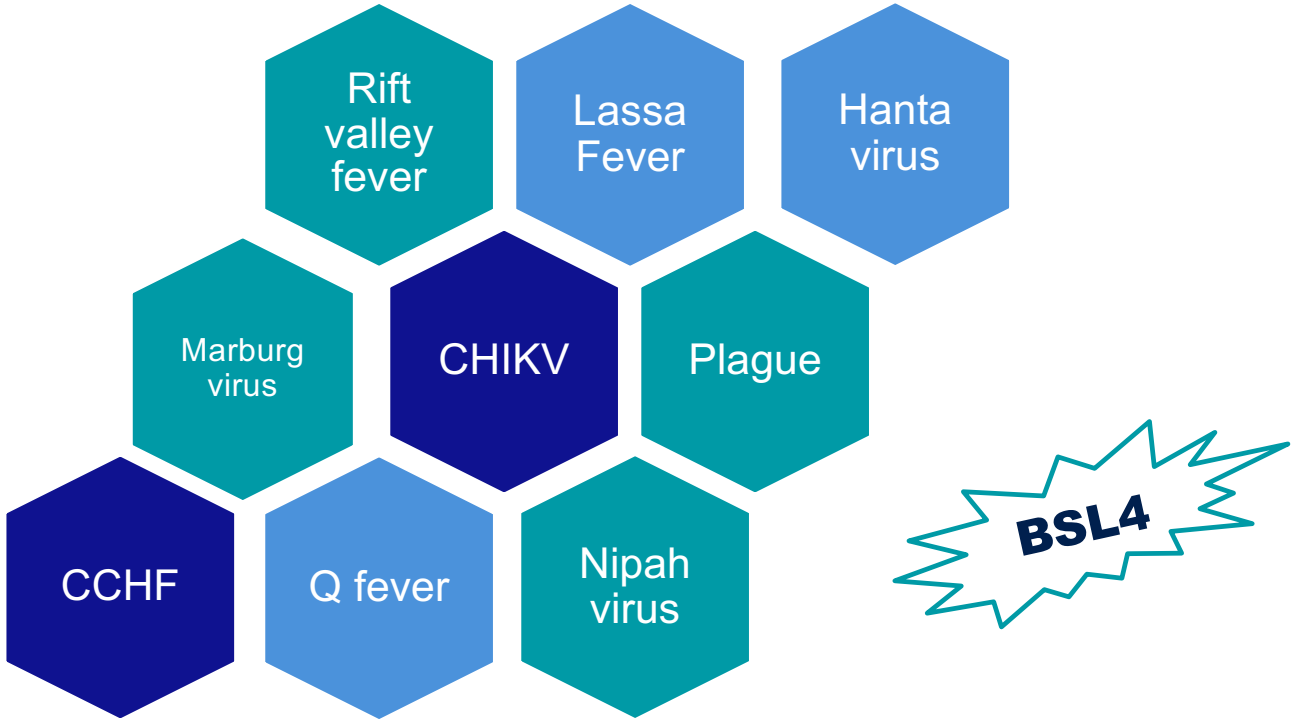




Conclusions

- The anti-Zika reference material alone is sufficient to confer protection *in vivo*.
- Further study ongoing to establish the lowest titre that can provide protection.
- This study sets a paradigm to produce serological vaccine reference reagents for other Priority Emerging Pathogens.

Future projects



- Vaccine reference reagents will enable the efficacy of candidate vaccines to be compared.

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