

A dual Chikungunya and smallpox vaccine derived from a novel, replication-incompetent poxvirus vaccine system

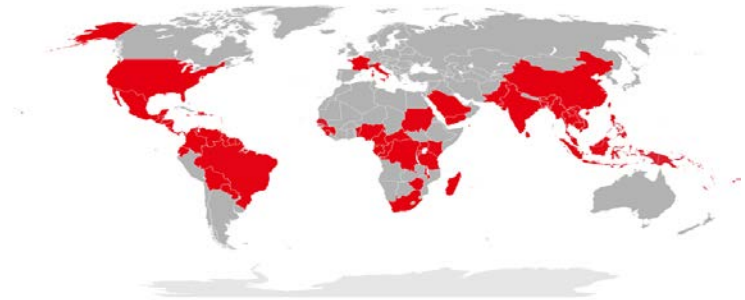
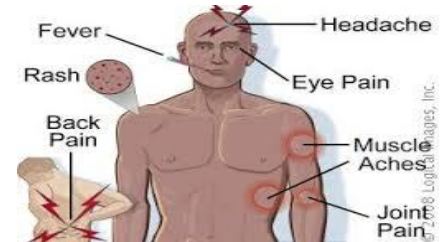
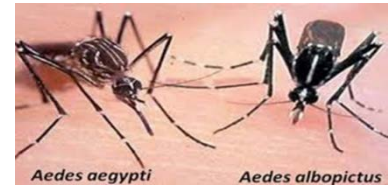
John Hayball

Experimental Therapeutics Laboratory
Sansom Institute, University of South Australia
Hanson Institute, SA Pathology

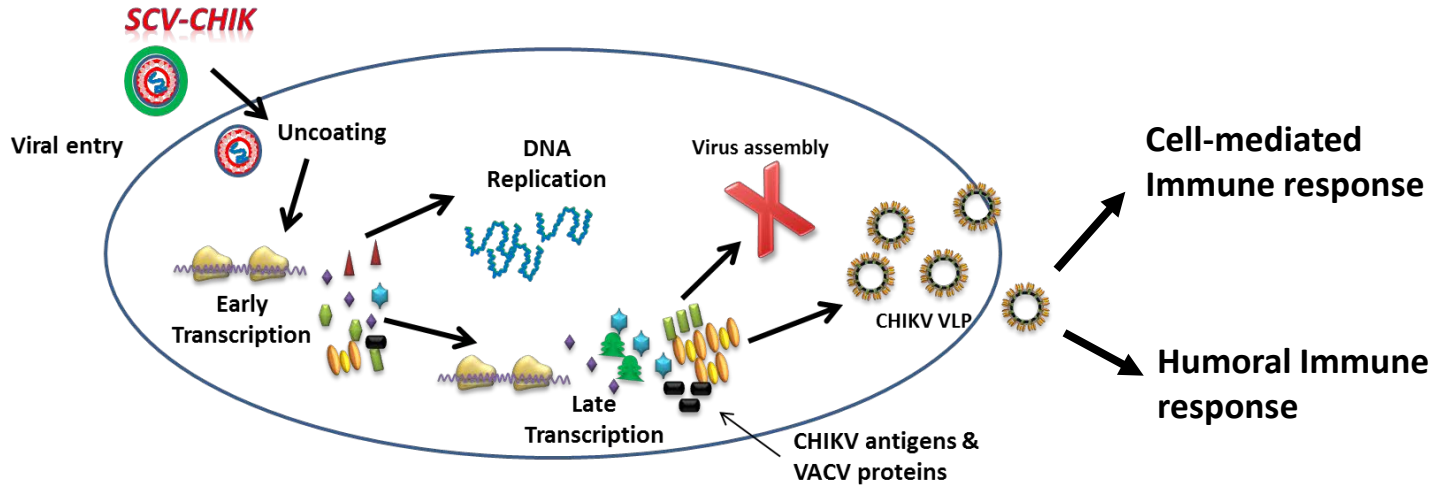


A Collaboration with Sementis to make better vaccines

- SCV (Sementis Copenhagen Vector) Vaccine Vehicle Technology
 - Derived from the Smallpox vaccine (vaccinia)
 - Attenuated to make it safer
 - Multiple disease applications
 - Accelerated preclinical testing
 - Standardised GMP manufacturing
- A prototype vaccine for Chikungunya virus



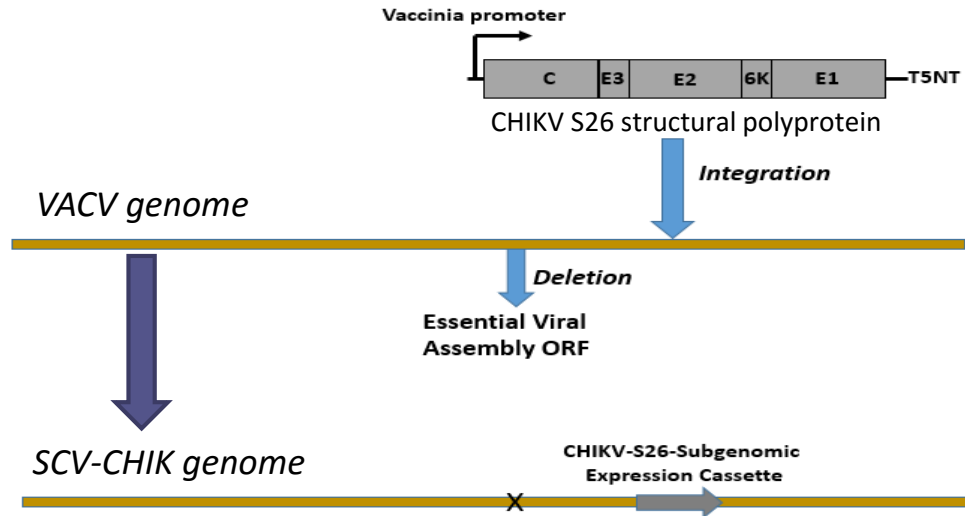
SCV-Chikungunya (SCV-CHIK)



SCV infectious life cycle is arrested at the viral assembly stage. No infectious progeny virus is produced

SCV-CHIK Vaccine Construction

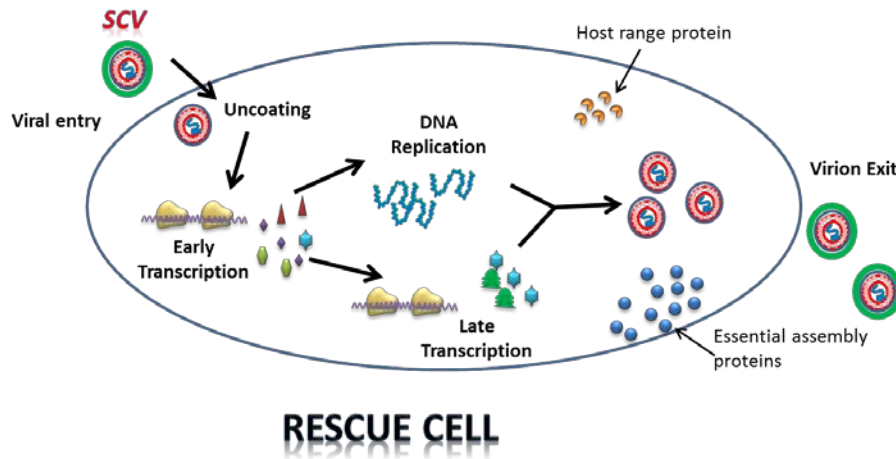
- Entire CHIKV structural polyprotein inserted
- Essential assembly protein deleted to attenuate



Human cell line		VACV	SCV-CHIK
HEK-293	Kidney		
HeLa	Cervical		
143B	Bone		
MRC-5	Lung		

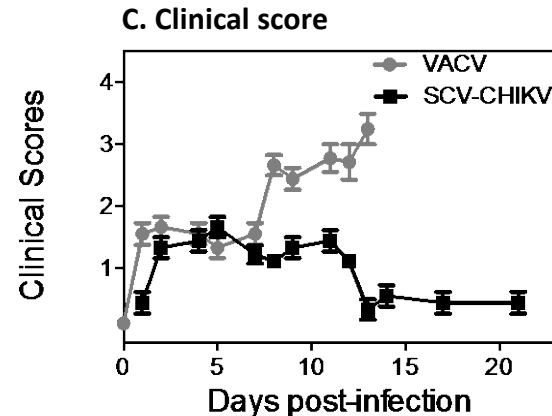
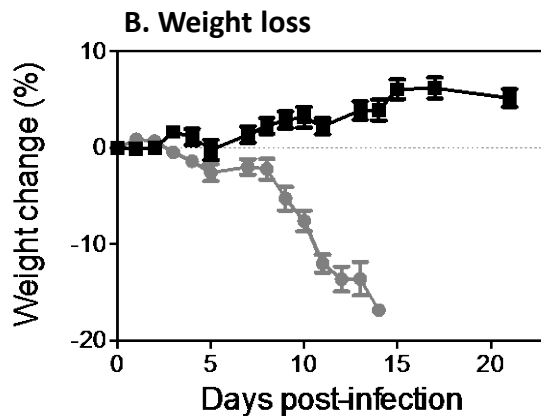
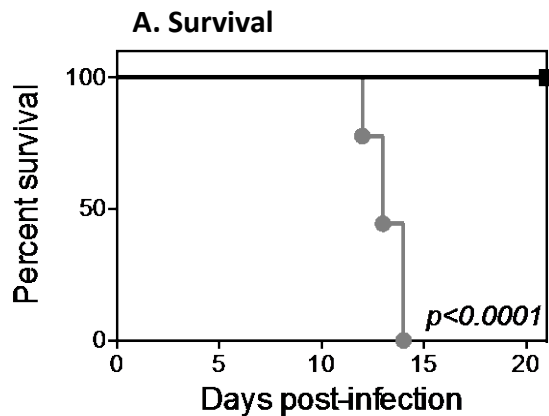
SCV Vaccine Production

- In trans* provision of host range and essential viral assembly proteins rescues SCV production in biotech friendly CHO cells



	CHO-AP	CHO-HR	RCL
VACV			
SCV-CHIK			
Assembly protein (AP)	+	-	+
HR protein (HR)	-	+	+

SCV vaccine platform is safe in immunocompromised mice



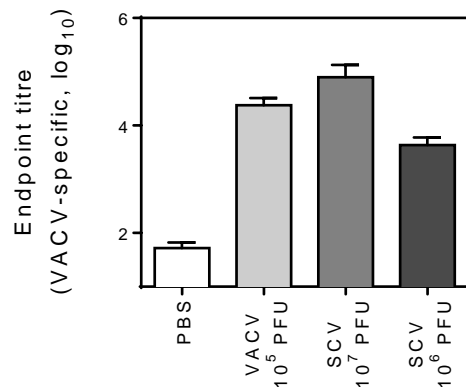
D. Vaccinia viral load in key organs

	Ovary		Spleen		Liver		Lung	
	VACV	SCV-CHIK	VACV	SCV-CHIK	VACV	SCV-CHIK	VACV	SCV-CHIK
Day 3	++++	-	++	-	++	-	++	-
Day 5	++++	-	+++	-	++	-	++	-
Day 10	++++	-	+++	-	++	-	+++	-
Day 15	++++	-	+	-	+	-	+++	-

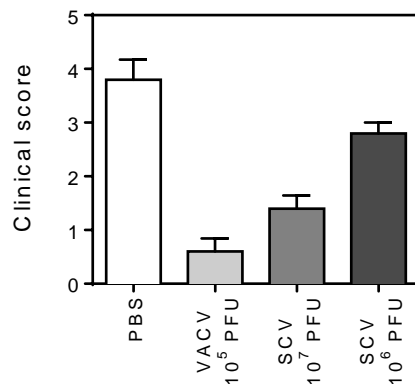
- : No infectious virus
 + : $1 - 10^2$ PFU/organ
 ++ : $10^2 - 10^4$ PFU/organ
 +++ : $10^4 - 10^6$ PFU/organ
 ++++ : $> 10^6$ PFU/organ

SCV vaccine platform confers Ectromelia protection

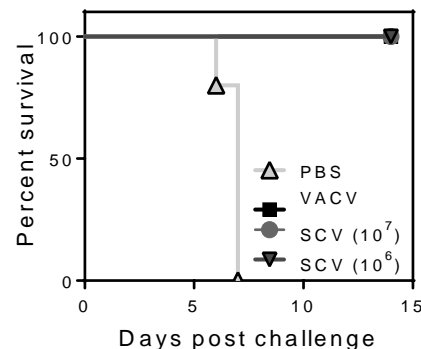
**A. Pre-challenge
VACV-specific IgG**



B. Clinical score (D7)



C. Survival

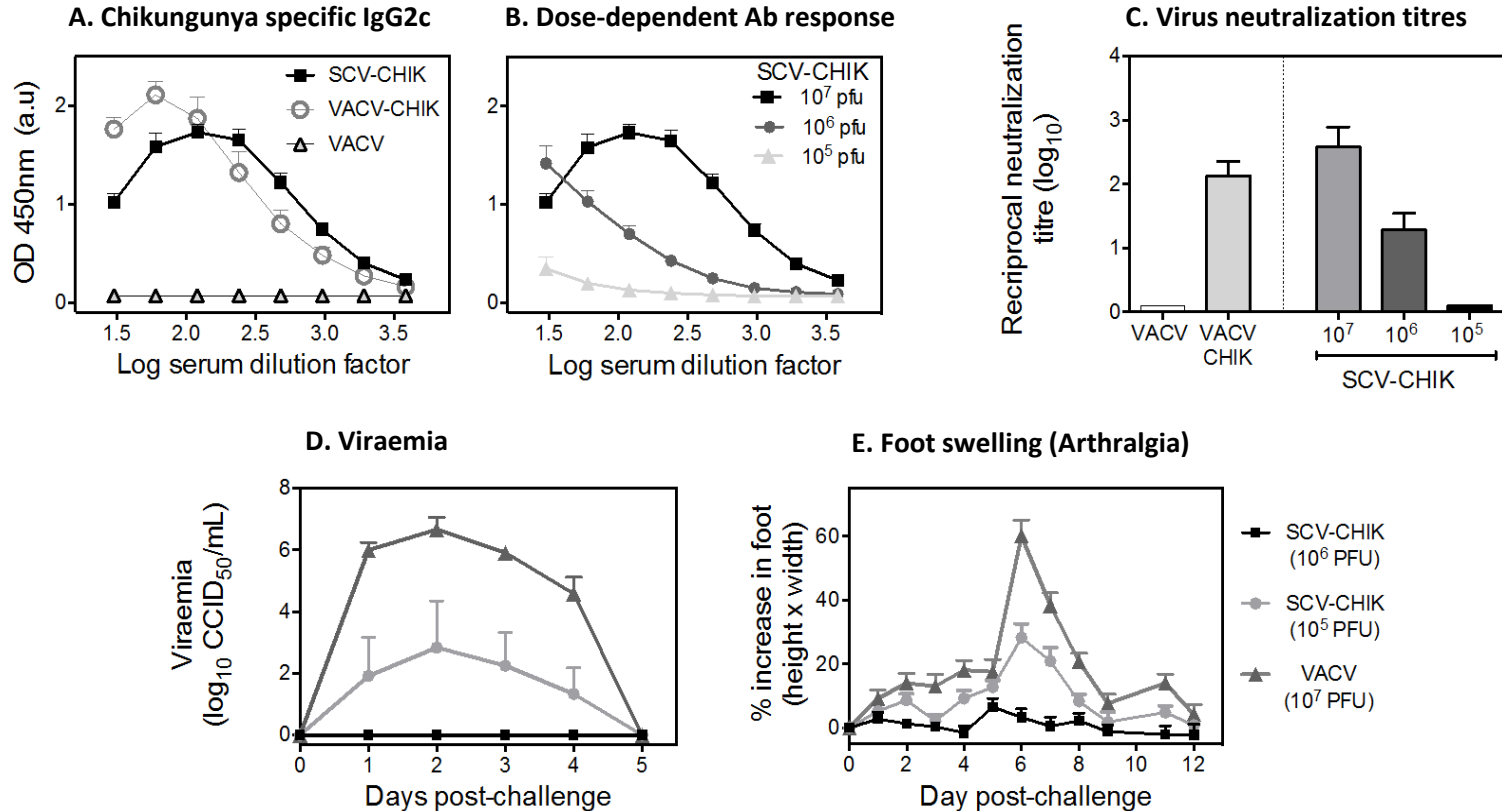


D. Ectromelia viral load in organs

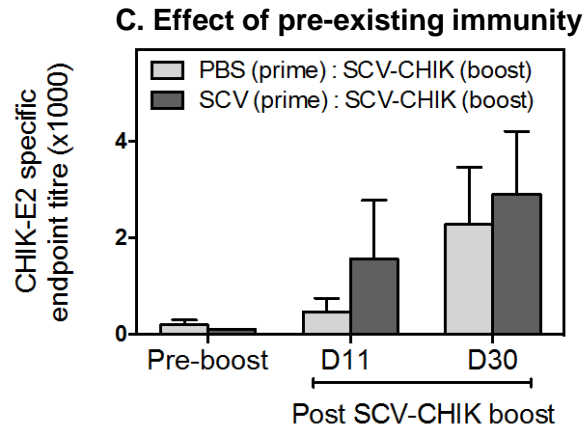
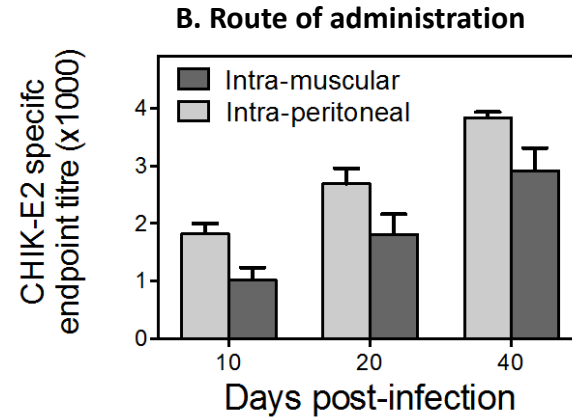
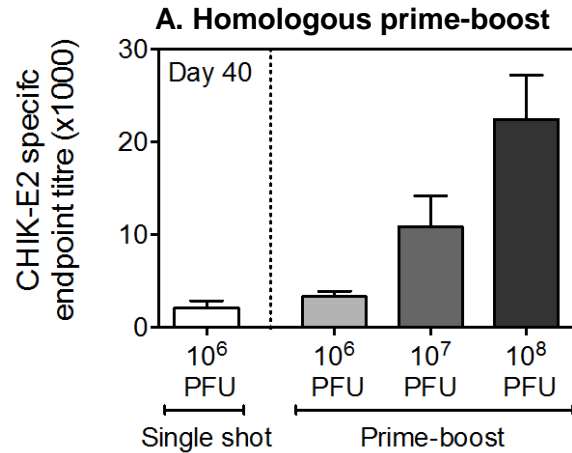
	Ovary	Spleen	Liver	LN	Lung
PBS	++	+++	+++	++	++
VACV	-	-	-	-	-
SCV 10 ⁷ pfu	-	-	-	-	-
SCV 10 ⁶ pfu	-	-	-	-	-

- : No infectious virus
++ : 10⁴ -10⁶ PFU/organ
+++ : 10⁶ – 10⁸ PFU/organ

Single dose SCV-CHIK vaccination elicits protective immune responses



Efficient vaccination strategies and translation potential



Summary

- SCV is replication-defective *in vitro* and *in vivo* - safe vaccine platform.
- A stable rescue cell line derived from biotech-proven CHO cells provides for scalable production of SCV vaccines.
- Immunogenicity is maintained - evidenced by protection from heterologous poxvirus challenge in mice.
- Introduction of exogenous CHIKV antigens elicited protective immune responses – neutralizing antibodies as a correlate of protection

Acknowledgements



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