

A new multiplication-defective, vaccinia-derived, CHO-manufactured, vaccine vector system (SCV) is effective in preclinical studies

Peter Wulff¹, Preethi Eldi², Tamara H. Cooper², Liang Liu², Natalie A. Prow^{2,3,4}, Eri Nakayama^{3,5}, Kexin Yan³, Jessamine Hazelwood³, Bing Tang³, Thuy Le³, Yin Xiang Setoh⁶, Alexander A Khromykh^{4,6}, Jody Hobson-Peters⁶, Thanh-Thao Le⁷, William B Smith⁷, Kerrilyn R. Diener^{2,8}, Paul M. Howley¹, Andreas Suhrbier^{3,4}, John D. Hayball^{2,8}

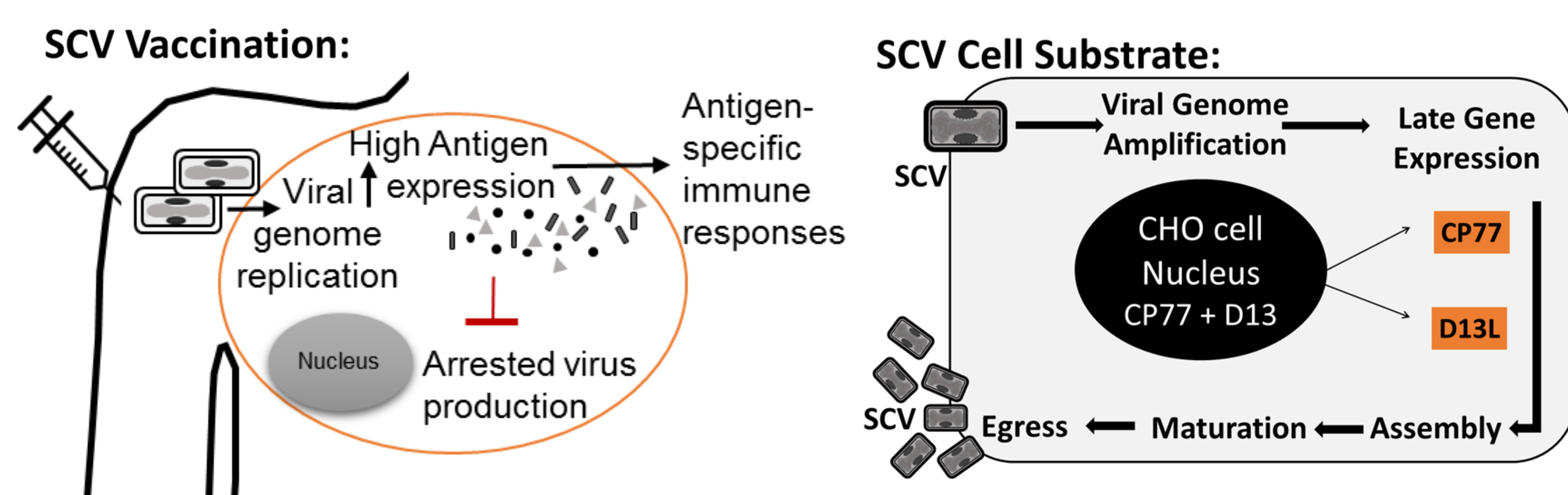


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¹Sementis Ltd., Melbourne, Vic 3000, Australia. ²Experimental Therapeutics Laboratory, Hanson Institute, Sansom Institute, and School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA 5000, Australia. ³QIMR Berghofer Medical Research Institute, Brisbane, Qld 4029, Australia. ⁴Australian Infectious Disease Research Centre, Brisbane, Qld., Australia. ⁵Department of Virology I, National Institute of Infectious Diseases, Tokyo, Japan. ⁶School of Chemistry and Molecular Biosciences, The University of Queensland, St Lucia, Queensland, 4072, QLD, Australia. ⁷Royal Adelaide Hospital, Adelaide, SA, Australia. ⁸Robinson Research Institute and Adelaide Medical School, University of Adelaide, Adelaide, SA 5000, Australia.

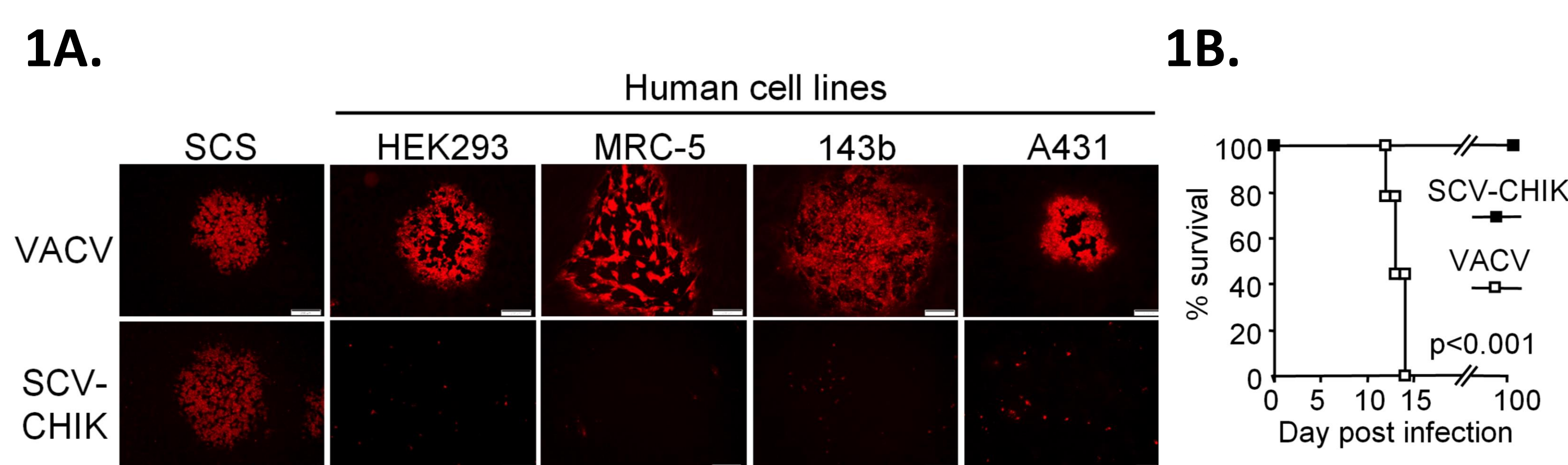
What is the SCV vaccine platform technology?

- The Sementis Copenhagen Vector (SCV) system is a novel vaccine platform designed to confer the advantages of live vaccinia virus (VACV) vector.
 - Highly immunogenic.
 - Easy to genetically manipulate with capacity for a large transgene antigen payload.
 - Manufacturing yields high titres.
- SCV was rendered multiplication-defective by the targeted deletion of D13, essential for virus assembly.
 - Enhanced safety profile
- SCV vaccines can be manufactured in Chinese Hamster Ovary (CHO) cells engineered to express D13 and the VACV host-range factor CP77 (SCS cell line).
 - Fast growth to high cell densities in suspension.
 - Animal component-free, chemically defined medium.
 - CHO cells are characterised and in use for production of biologicals.



Schematic representation of SCV vaccination depicting preserved gene amplification for high levels of antigen production to stimulate immune responses in the absence of virus replication (left) and production of SCV in the SCS cell line derived from CHO cells engineered to produce D13 and CP77 (right).

SCV is multiplication-defective *in vitro* and *in vivo*



Production of infectious progeny virus is restricted to the SCS cell line (Figure 1A).

- SCV replicates and spreads in the SCS cell line shown by fluorescent immunostaining using a polyclonal vaccinia antibody.
- SCV was unable to spread in a range of human cell lines permissive to VACV infection.

In the absence of a complete anti viral immune response *in vivo*, SCV is not pathogenic (Figure 1B).

- Immune-compromised SCID mice (n=9) vaccinated with SCV remained in good health for the 100 day experiment whereas VACV caused progressive disease to humane endpoints by day 15.



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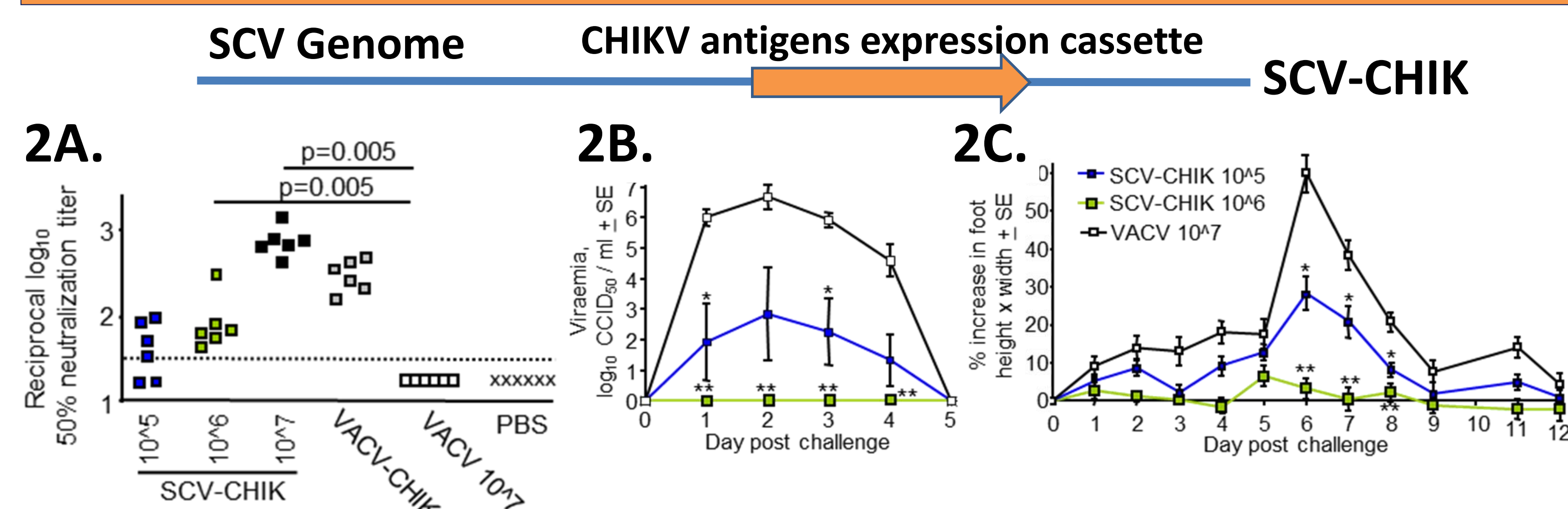
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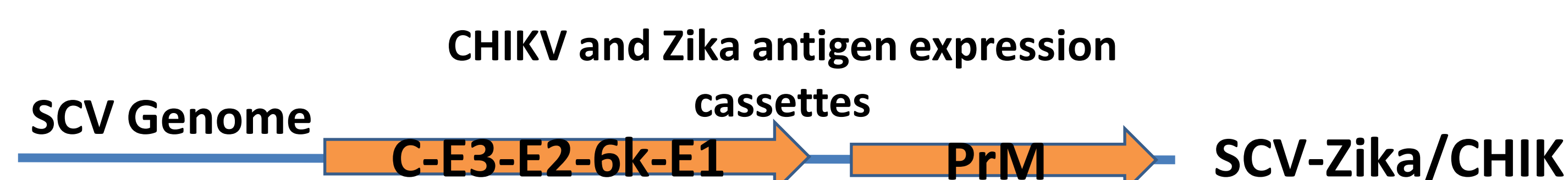
Royal Adelaide Hospital

Pre-clinical development of SCV as an infectious disease vaccine



SCV-CHIK vaccination (Eldi, P. et al, *Molecular Therapy*; Jul 2017):

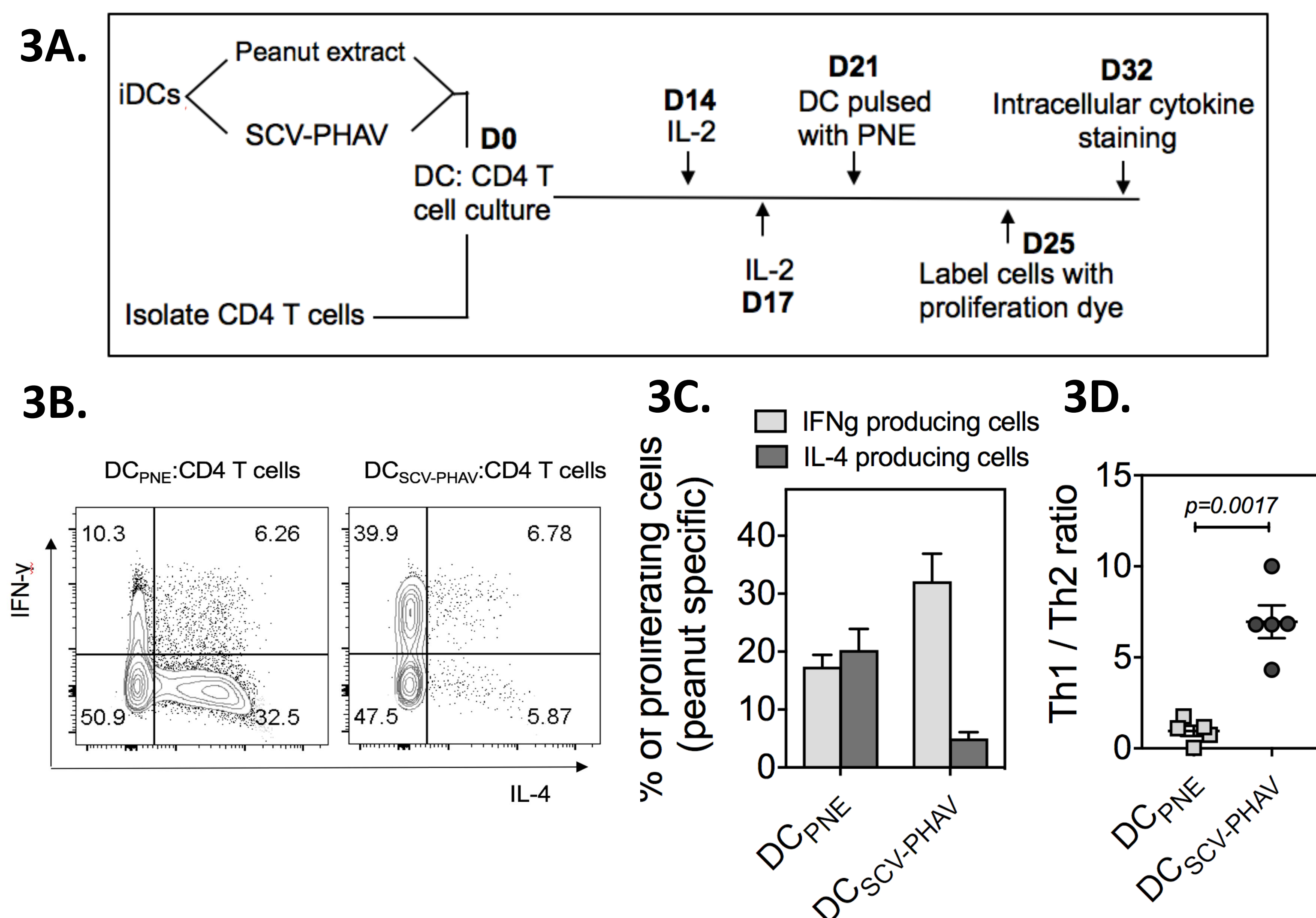
- Induces neutralising antibodies against Chikungunya virus (CHIKV; Figure 2A)
- Prevents viraemia (Figure 2B)
- Prevents foot swelling representative of arthritic symptoms caused by CHIKV infection (Figure 2C)



SCV-Zika/CHIK vaccination:

- A single vector, multi-pathogen vaccine
- Induces neutralising antibodies against CHIKV and Zika virus
- Prevents CHIKV viraemia and foot swelling
- Prevents Zika viraemia, foetal/placental and testes infection

Application of SCV as a hypoallergenic peanut vaccine



SCV-PHAV *ex vivo* vaccination of peanut allergic human cells:

- Peanut allergy is mediated by a pathogenic, allergen-specific, helper T cell-type 2 (Th2) biased CD4 T cell response.
- Dendritic cells vaccinated with SCV-PHAV (Figure 3A) mediated a switch in the CD4 T cell response to peanut extract (PNE) from Th2 (IL-4) to Th1 (IFN γ) biased, shown by flow cytometric intracellular cytokine analysis (Figure 3B)
- This shift from a pro-allergic Th2 bias to a Th1-biased profile with potential to alleviate allergic symptoms was demonstrated in 5 peanut-allergic individuals (Figure 3C and D)

Conclusion

SCV is a novel platform technology designed for transition into a biopharmaceutical manufacturing process. A single vector, targeting multiple diseases is a new approach to addressing public health concerns and reducing “shot burden” for co-circulating viruses. The flexibility and immunogenicity of the SCV technology also provides opportunity to address complex immunological conditions such as peanut allergy.