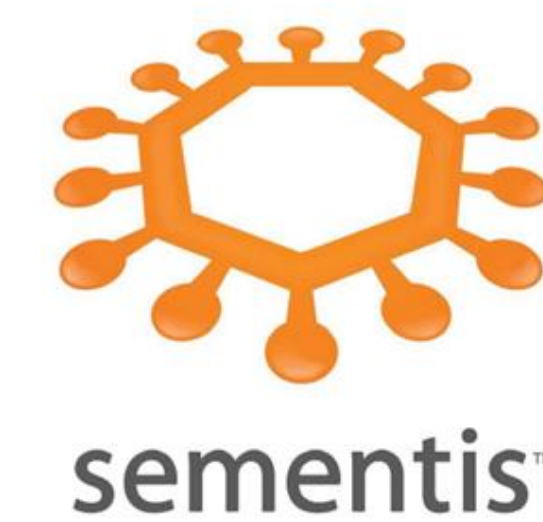


# Pre-clinical development of a new multiplication-defective, vaccinia-derived, CHO-manufactured, vaccine vector system (SCV) against Chikungunya and Zika virus infection



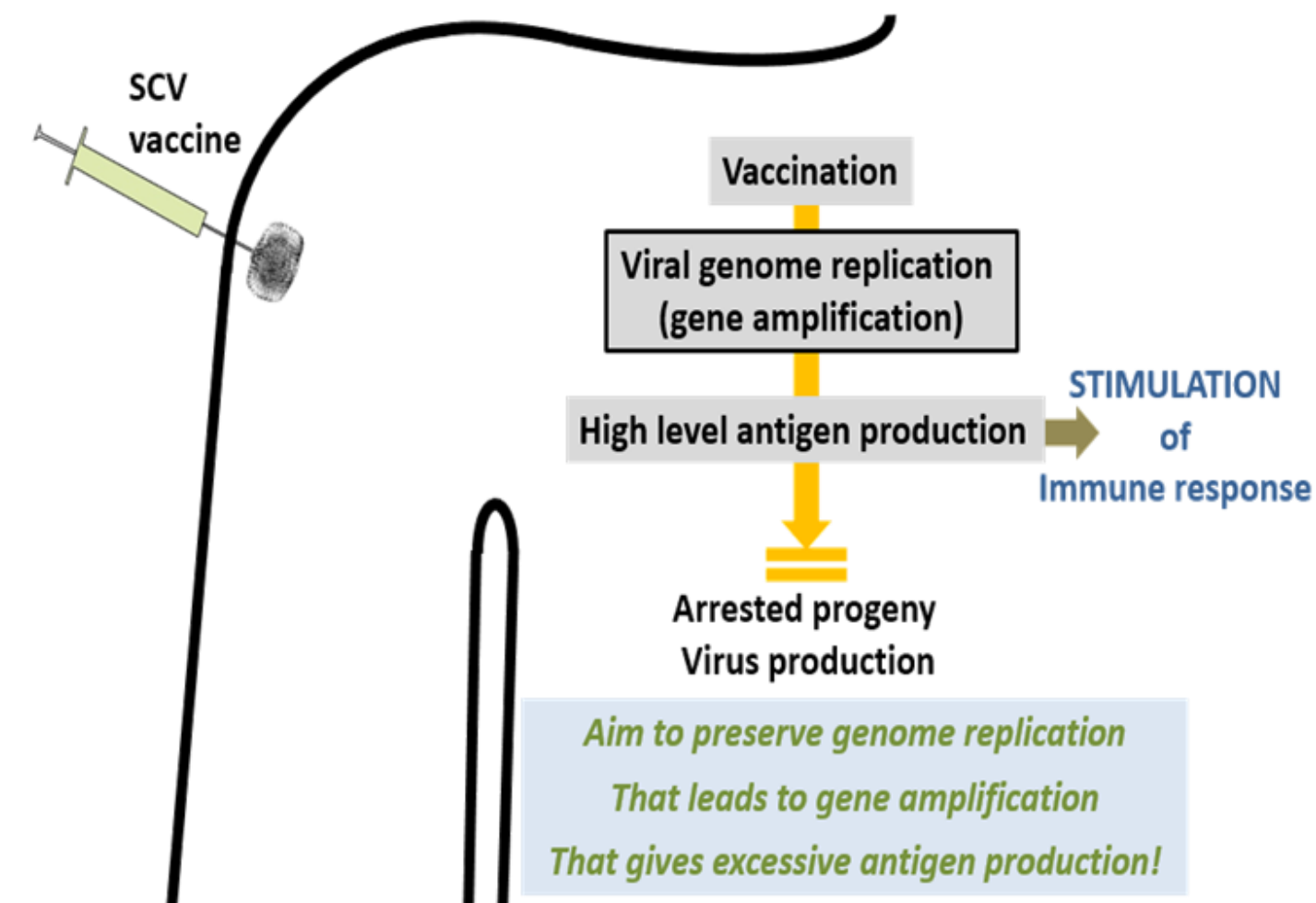
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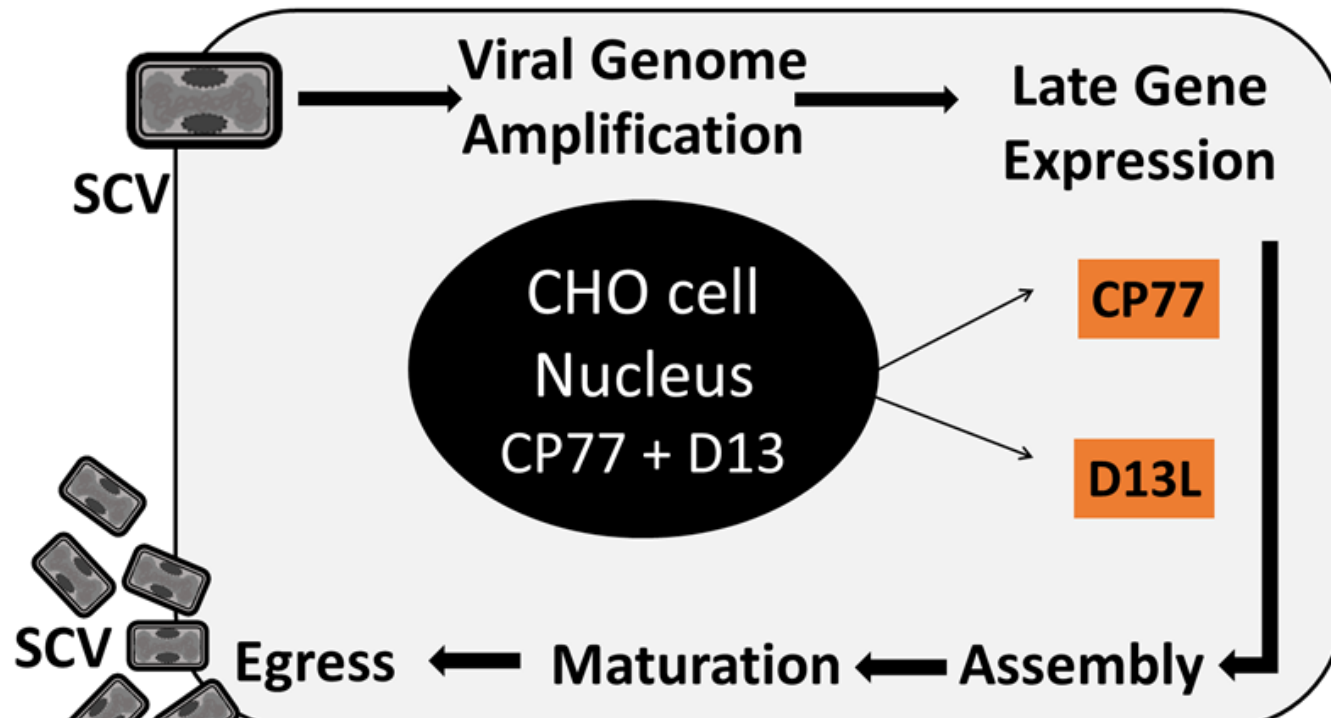
## What is the SCV vaccine platform technology?

- 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.
  - Titres to high levels.
- SCV was rendered multiplication-defective by the targeted deletion of the 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.

### SCV Vaccination:

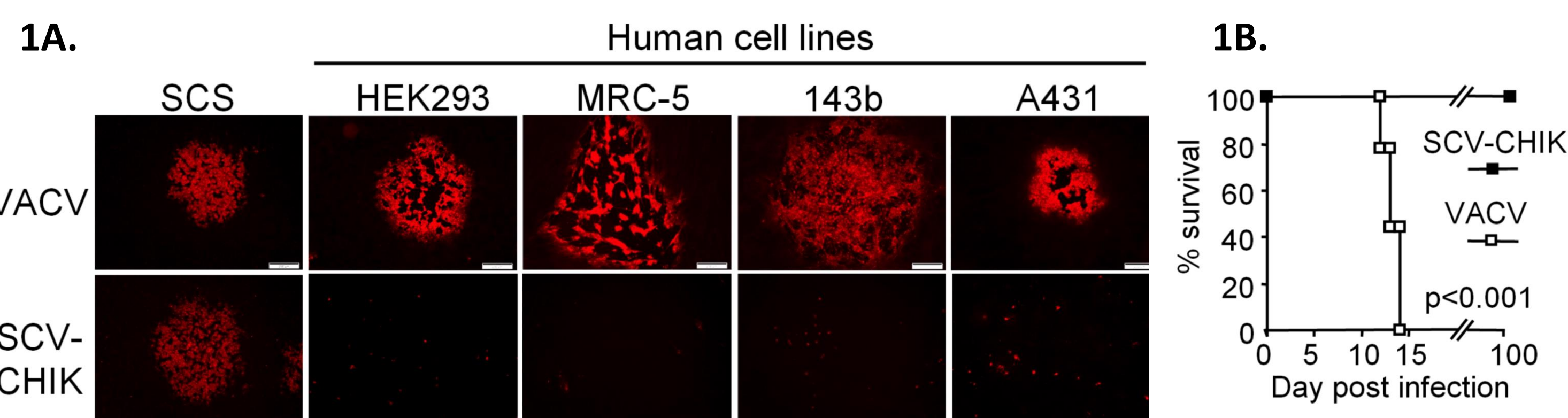


### SCV Cell Substrate:



Schematic of SCV vaccination depicting the production of heterologous antigens 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 (Fig. 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 an anti viral immune response *in vivo*, SCV is not pathogenic (Fig. 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.

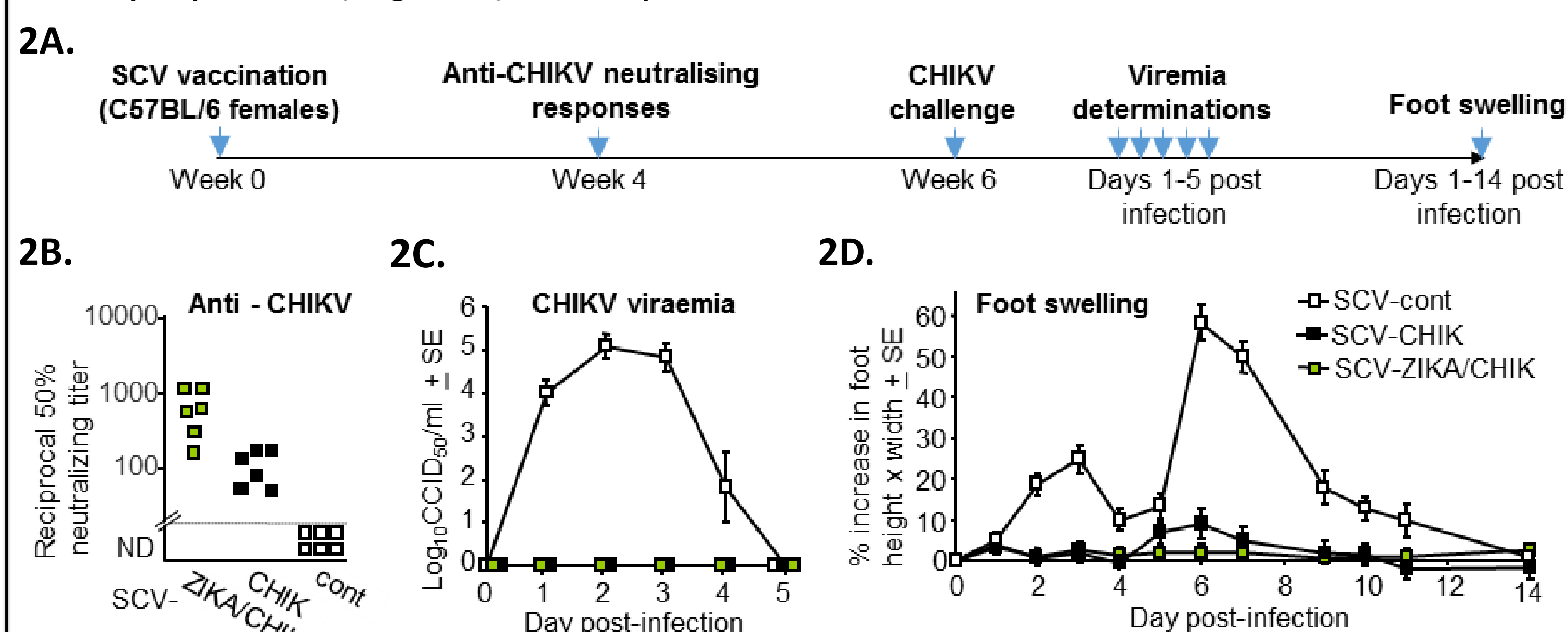


## Pre-clinical development as a single vector, multi-pathogen vaccine against Chikungunya (CHIKV) & Zika



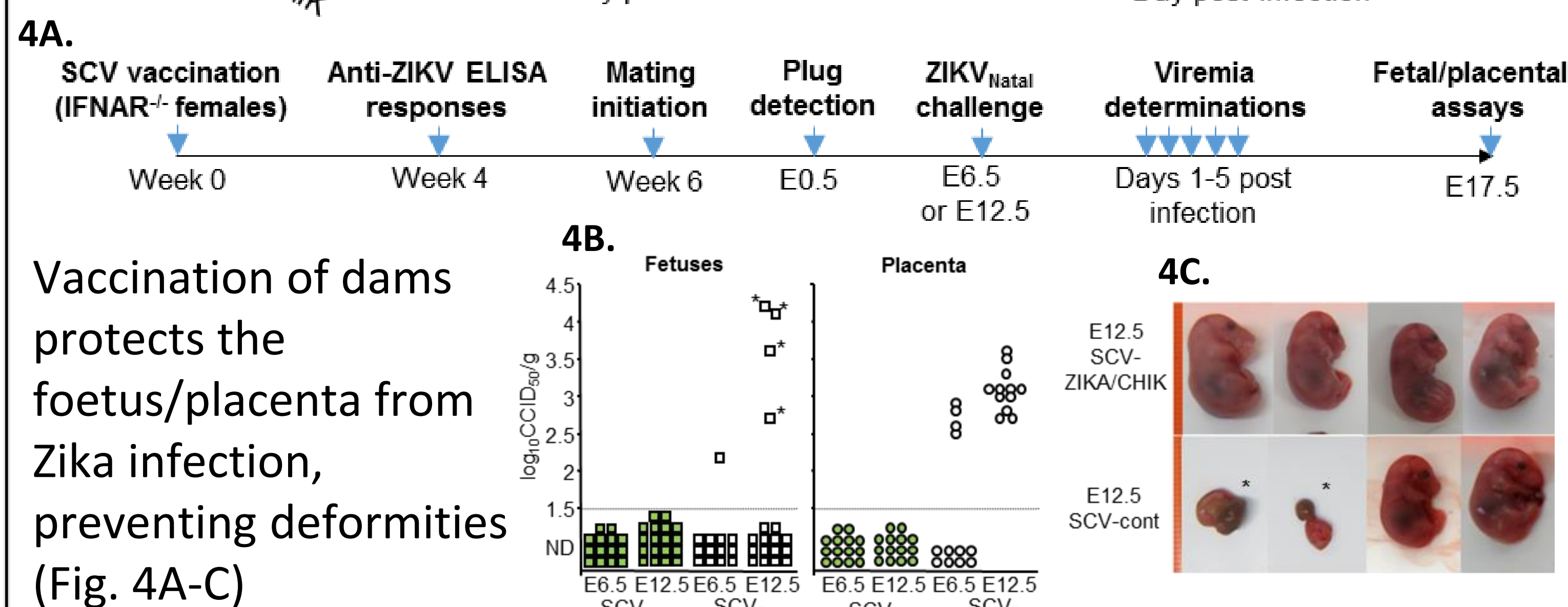
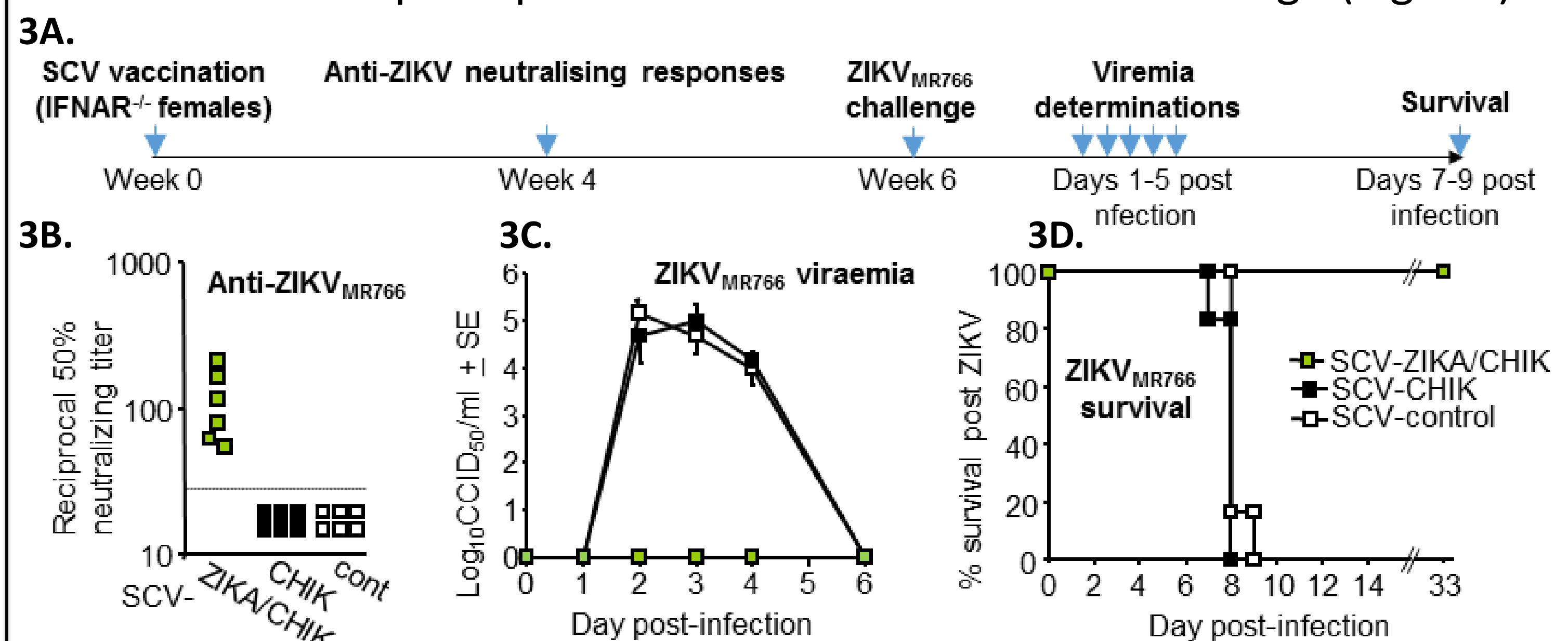
**SCV-Zika/CHIK vaccination (Fig 2A) protected mice from CHIKV.**

- Neutralising antibodies against CHIKV were induced (Fig. 2B)
- CHIKV viraemia (Fig. 2C) and foot swelling representative of arthritic symptoms (Fig. 2D) were prevented.

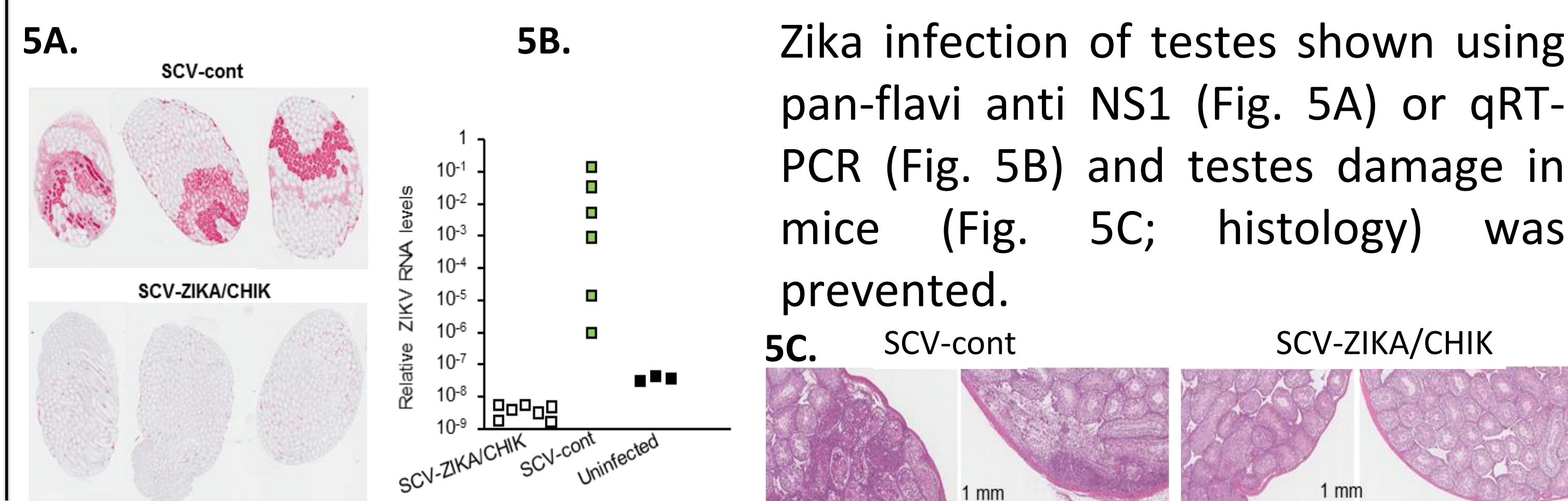


**SCV-Zika/CHIK vaccination (Fig. 3A) protected mice from Zika.**

- Neutralising antibodies against Zika were induced (Fig. 3B)
- Vaccination prevented viraemia (Fig. 3C) and
- Provided complete protection from a lethal Zika challenge (Fig. 3D)



Vaccination of dams protects the foetus/placenta from Zika infection, preventing deformities (Fig. 4A-C)



Zika infection of testes shown using pan-flavi anti NS1 (Fig. 5A) or qRT-PCR (Fig. 5B) and testes damage in mice (Fig. 5C; histology) was prevented.

## Conclusion

A single vectored, multi-pathogen vaccine provides complete protective immune responses against Chikungunya and Zika virus infection in mice (Prow et al 2018, Nature Communications) using a safe, flexible SCV vaccine platform with manufacturing advantages (Eldi et al 2017, Molecular Therapy).