Three-in-one Vaccine: A Single Recombinant Measles Virus Expressing Three Arbovirus Antigens

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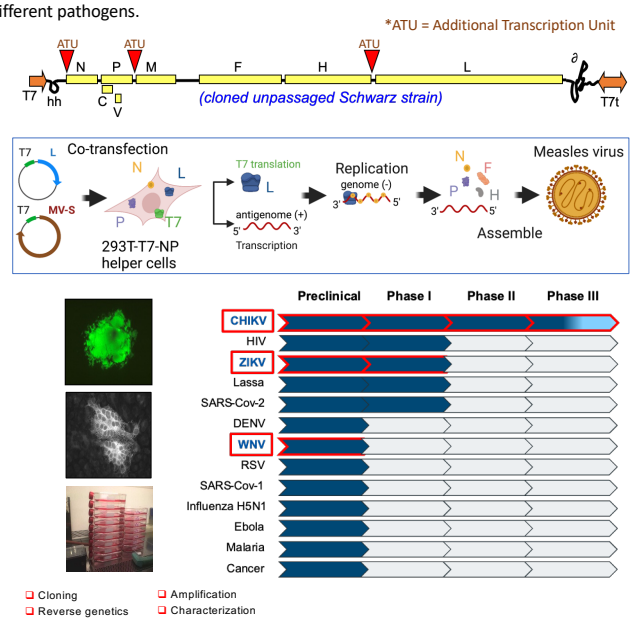
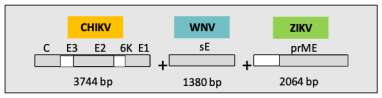
Recombinant measles vaccine platform

The measles vaccine (MV) delivery platform has undergone development from preclinical to clinical stages, demonstrating its ability to adapt rapidly and effectively to different pathogens.

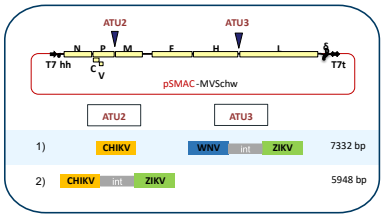


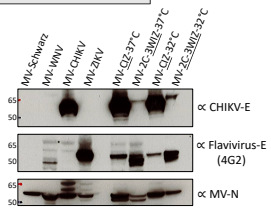
Three-in-one Vaccine Design

To enhance the capabilities of MV vector, we have engineered an improved MV vector using a bacterial artificial chromosome (BAC) plasmid. With the stability of BAC plasmids, this new MV vector can now accommodate and maintain the expression of more than 7 kb of additional heterologous gene/s within a single rescued recombinant MV. Our proof-of-concept demonstrated the successful construction of a combined MV vector that expresses three protective antigens derived from the Chikungunya virus (CHIKV), West Nile virus (WNV), and Zika virus (ZIKV), simultaneously.



MV-Construct Design

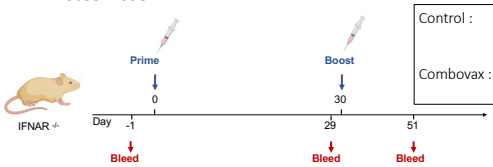




Western Blot Analysis confirming the antigen expression in Vero cells infected with recombinant Measles viruses.

Immunogenicity test

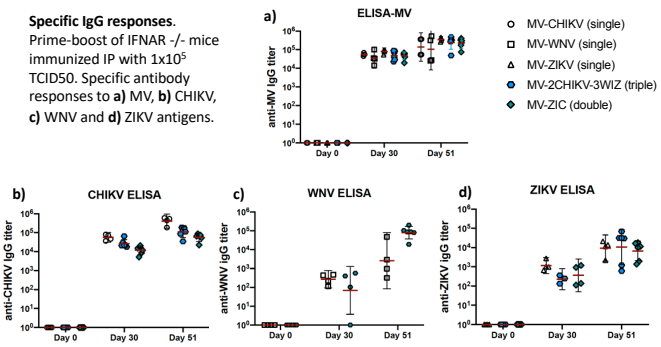
The immunogenicity of MV recombinant viruses was assessed using MV susceptible IFNAR$^{-/-}$ mouse model.



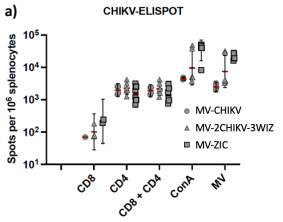
Control :	1. MV-CHIKV
	2. MV-WNV
	3. MV-ZIKV
Combovax :	1. MV-2CHIKV-3WIZ
	2. MV-ZIC

Humoral Responses

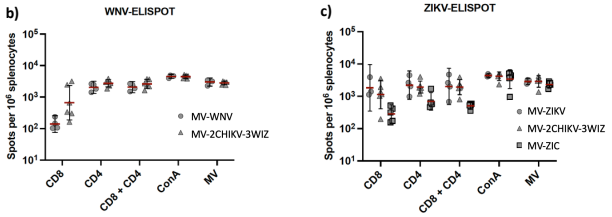
Specific IgG responses. Prime-boost of IFNAR -/- mice immunized IP with 1x10^5 TCID50. Specific antibody responses to **a)** MV, **b)** CHIKV, **c)** WNV and **d)** ZIKV antigens.



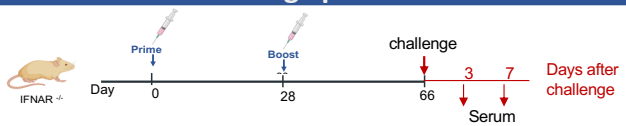
Cellular Responses

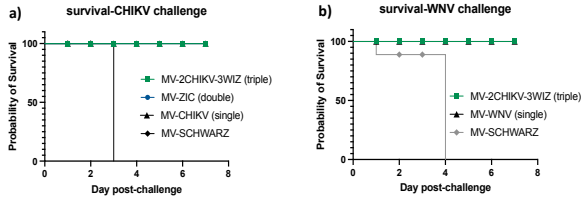


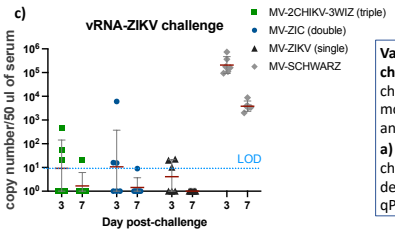
Induction of specific cellular responses by rMV vaccination. IFNAR-/- immunized by IP with 1x10^5 TCID50 of rMV. ELISPOT for IFNγ was performed on freshly extracted splenocytes. The data are shown as IFNγ-secreting cells or spot-forming cells (SFC) per 1x10^6 splenocytes detected after stimulating with **a)** CHIKV, **b)** WNV and **c)** ZIKV peptide pools specific to CD8+ or CD4+ T cells.



Challenge protection







Vaccine protection efficacy after challenge. Immunization and challenge schedule for mouse model. Survival curve of double and triple vaccine challenged with **a)** CHIKV or **b)** WNV and **c)** ZIKV challenge, viral RNA copies detected in mouse sera by RT-qPCR at 3 and 7 dpc.

Conclusions

In summary, we developed a new plasmid system for MV vector platform that can accommodate a very large heterologous gene/ genes insertion. The vector proves to generate a replicating MV vaccine candidate carrying 3 separate flavivirus antigens that elicits, in preclinical relevant rodent models, strong antibodies and T cell responses. The immune responses result in protection of animals from infectious challenge viruses. These promising pre-clinical data support the development of this 3 vaccines in a single vaccine candidate.

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