Novel constructs for flavivirus vaccines and diagnostics

KEY FEATURES

- Chimeras combining an insect-specific flavivirus (ISF) genomic backbone with specific antigenic elements of a vertebrate-infecting flavivirus (VIF)
- ISF chimeras replicate only in mosquito cells, are expected to be safe to administer to humans and can be prepared with minimal biocontainment
- Data show diagnostic and vaccine applications with strong antigenic authenticity
- ISF chimeras successfully designed to display the antigens from a range of flavivirus pathogens

Background

Researchers at The University of Queensland have developed a new chimeric virus platform suitable for use in flavivirus vaccine and diagnostic applications. Flaviviruses are predominantly carried and transmitted by mosquitoes and often infect humans, causing widespread morbidity and mortality. Common clinically-relevant flavivirus diseases include Zika, dengue fever, West Nile fever, yellow fever and Japanese encephalitis.

The new chimeric viruses are formed by splicing the genes that code for the specific antigenic elements of a vertebrate-infecting flavivirus (VIF) into the genome backbone of an insect-specific flavivirus (ISF). ISFs are specialised viruses that can only replicate and survive in mosquito cells, therefore forming chimeras based on the ISF genome prevents the constructs from replicating in vertebrate cells. ISF-VIF chimeras for West Nile Virus, dengue and Zika have been generated and shown to replicate in mosquito, but not vertebrate cell lines.

Several novel Australian ISFs have been identified and characterised, with selected ISFs demonstrating potential as high-performing chimeric backbones.

Vaccine

As a vaccine vehicle, the ISF genome structure provides a genetic scaffold similar to a VIF, allowing the immunogenic epitopes from VIFs to be presented in their native form. The antigens presented to the human immune system are therefore in authentic conformation and expected to induce a good protective immune response. The ISF-based chimeras are highly versatile and can be designed to present the immunogenic epitopes of the virion proteins (prM & E) from a range of flavivirus pathogens including Zika virus, dengue viruses, West Nile virus, yellow fever virus and Japanese encephalitis virus. Our data has shown ISF-based chimeras displaying the prM & E proteins of Zika virus or West Nile virus are antigenically indistinguishable from the wild type pathogens.

The inability of the chimeras to replicate in mammalian cells also makes them safe to prepare and administer.

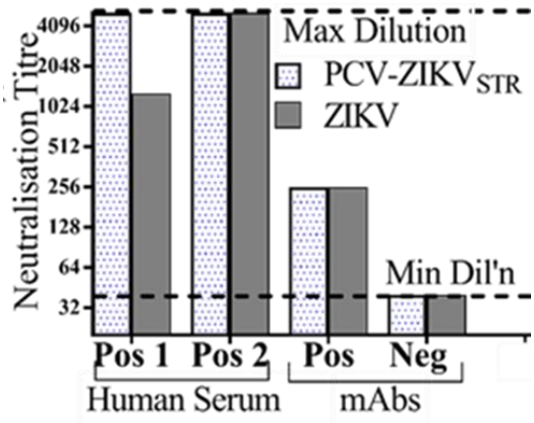

Figure 1. ZIKA-immune human sera and ZIKA-specific mAbs neutralise both an ISF-ZIKV chimera (PCV-ZIKV) and wild type ZIKV in a virus neutralisation assay with similar efficiency. The graph represents the highest reciprocal dilution of serum that completely neutralised/prevented virus replication. PCV (Palm Creek Virus) is a novel Australian ISF

Diagnostic

For diagnostic applications, the pathogen epitopes presented on the ISF chimeras are specifically recognised by antibodies in sera from patients infected with that pathogen. Studies have demonstrated the accurate diagnosis of West Nile virus (Figure 2) and Zika virus infection in sera of humans and animals.

The authenticity of the pathogenic flavivirus antigens presented on the ISF chimeric particles is ensured through their assembly on a native viral scaffold. Production of these chimeric antigens can also be safely scaled up. These are key features of the ISF chimeric platform.

The materials are expected to be amenable to a point of care diagnostic format as well as laboratory-based diagnostic testing.

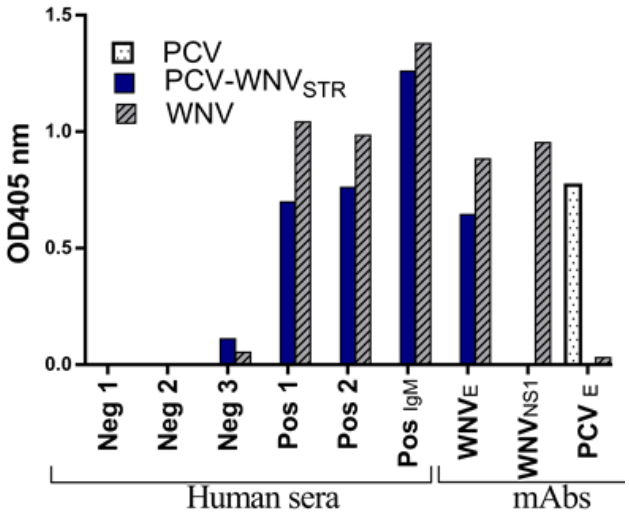

Figure 2: Evidence for the utility of ISF-VIF chimeras in diagnostic assays is demonstrated by the specific recognition of PCV-WNV chimeric antigens by WNV-immune human sera (Pos) in ELISA. There was negligible reactivity of naïve sera (Neg). PCV (Palm Creek virus) is a novel Australian ISF.

These constructs represent a new approach to developing efficacious and safe vaccines or diagnostics with anticipated high specificity for a range of flaviviruses, many of which are currently underserved in key markets.

Intellectual property

The invention is the subject of an PCT application covering chimeric ISFs for expressing proteins useful for the production of vaccines and diagnostics.

Commercialisation opportunity

UniQuest is seeking licensing, collaborative or investment partners to commercialise the technology.

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RESEARCH LEADERS

Prof Roy Hall is a specialist in vector-borne virology. His research explores emerging mosquito-borne viruses with a focus on their pathogenesis and the development of novel vaccine and diagnostic platforms.

His work has led to the design and development of novel diagnostic assays and vaccine candidates and the discovery of several new mosquito-borne viruses.

Dr Jody Hobson-Peters is a virologist specialising in mosquito-borne virus discovery and the development of novel diagnostic assays. Following almost a decade working in industry in the development and commercialisation of rapid point-of-care assays, her most recent research interests have culminated in a greater understanding of the mosquito virome, producing an extensive suite of monoclonal antibodies to novel mosquito-borne viruses and the optimisation of safe and authentic viral protein production for next-generation mosquito-borne virus vaccines and diagnostics.

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CONTACT

George Adamson
UniQuest Pty Limited
Phone: +61 (0)402 284 340
E-mail: g.adamson@uniquest.com.au