MONASH University

MONASH INNOVATION

MICROCUBE VACCINE: A PLATFORM FOR COMPLEX ANTIGENS

MicroCubes that can accommodate diverse antigens and elicit strong T-cell responses. They distinguish themselves by a unique crystalline organisation, resulting in slow-release of the antigen and self-adjuvanted stimulation of both arms of the immune system.

- **Versatile vaccine platform to deliver a wide range of antigens.**
- **Induce strong antigen-specific cellular and humoral immune responses without additional adjuvant**
- **Heat, freeze, and protease-resistance facilitates vaccine storage**
- **Second generation 'PH-MicroCube' can accommodate full-length, functional membrane proteins with native structure**

THE CHALLENGE

Traditionally vaccines have been developed from attenuated or killed viruses because they induce strong T-cell responses. Unfortunately, these vaccines can only be extended to a few pathogens and may be associated with significant side effects. DNA vaccines or recombinant viruses have been investigated over the past decade and but have fallen short of their initial promise.

Many alternative antigen delivery systems have been actively investigated for greater efficacy, safety and ease of production. One successful system uses virus-like particles (VLPs) to self-assemble the viral structural proteins and this is the basis of recent successes such as anti-HBV, anti-HPV and malaria vaccine candidates.

Many pathogens do not produce self-assembling particles and there are limitations to the size of the antigens that can be incorporated onto heterologous VLP scaffolds. Consequently, there remains a need for a versatile vaccine platform able to deliver antigens of various natures and sizes, inducing robust humoral and cellular responses.

THE TECHNOLOGY

A team of Monash University researchers, led by Assoc. Prof. Fasséli Coulibaly, has developed the MicroCube vaccine platform from polyhedrin protein crystals produced by insect viruses.

The remarkable capacity of MicroCubes to accommodate cargoes of different sizes and natures is unique and offers advantages to that of VLPs. The ease of design and versatility of MicroCubes supports their use as a potential generic platform for vaccines against infectious diseases.

Recent murine immunisation studies showed no toxic effect of MicroCubes. Mice immunized with non-adjuvanted HIV-1 Gag MicroCubes mounted an immune response characterized by Gag-specific IFNγ- and IL2-producing T cells and high titers of anti-Gag antibodies.

Researchers have also engineered second generation 'PH-MicroCubes', allowing the incorporation of full-length membrane proteins into crystals of the cypovirus polyhedrin protein. Studies demonstrated that PH-MicroCubes can present the HIV Env protein on their surface in a functional state and with native-like structure (*Fig 1.* and *Fig 2.*). Importantly, Env PH-MicroCubes present multiple epitopes relevant to human vaccination and present more efficiently the membrane proximal external region (MPER) of Env with better exposure of 10E8 (*Fig 2.*). The 'PH-MicroCube' technology has also demonstrated promising results when applied to the HA hemagglutinin antigen in a murine challenge model of influenza (*Fig 3.*).

Together, these data support the notion that the MicroCube technology can be applied to a range of antigens and viruses. We are working to develop the technology for a range of flaviviruses and alphaviruses.

Intellectual property: National phase applications (US, CA, EP, AU and JP) for PCT/AU2011/000763 and PCT/AU2015/050408.

THE OPPORTUNITY

Monash seeks a partner to optimise and adapt the system for application.

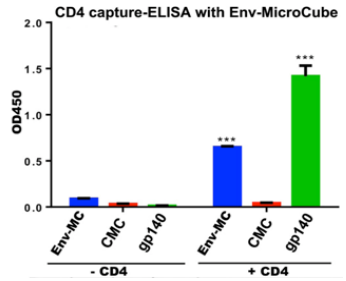

Figure 1. Binding of CD4 implies the presentation of native-like Env on the surface of PH-MicroCubes (Env-MC).

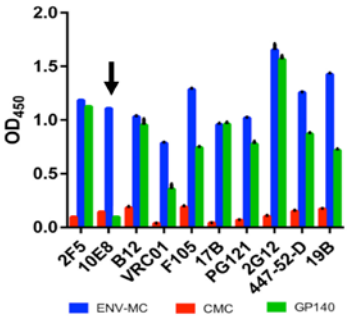

Figure 2. Recognition of Env epitopes on the surface of PH-Microcubes (ENV-MC) by a panel of conformational antibodies. Arrow highlights efficient presentation of the membrane proximal external region (MPER) with better exposure to antibody 10E8.

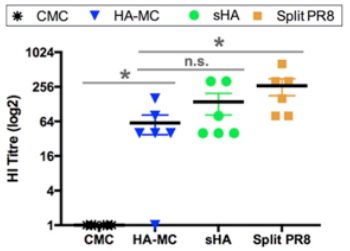

Figure 3. HA PH-MicroCube immunisation produces antibodies with hemagglutination inhibition titers comparable to commercial influenza vaccines in a murine challenge model of influenza.

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Produced by Monash Innovation: June 2017