

Opportunity

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Broad and ultra-potent anti-HIV-1 antibodies

Broad and ultra-potent cross-clade neutralising HIV-1 monoclonal antibodies

The Technology

- Immunotherapy with anti-HIV-1 antibodies has the potential to suppress infection and increase the rate of clearance of infected cells.

Market Need

- HIV-1 infection remains a public health problem with no cure. Antiretroviral therapy (ART) is a lifelong treatment which requires diligent adherence and can be associated with toxicity and significant economic costs.

Technology Status

- Ultra-potent neutralising monoclonal antibodies targeting the key conserved sites on HIV-1 envelope. Isolated anti-HIV-1 bovine neutralising antibodies are broader and more potent than a majority of anti-HIV-1 human broadly neutralising antibodies.

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Market Need

There are no means to cure or prevent HIV infection. Approximately 38.4 million people were living with HIV at the end of 2021 with approximately 1.5 million people per year becoming newly infected with HIV globally.

Anti-retroviral therapy (ART) is effective but requires lifelong drug administration owing to a stable reservoir of latent proviruses integrated into the genome of CD4+ T cells. As a result, ART therapy is associated with significant economic costs (that can run anywhere between \$1,000 to \$2,700 each month during a person’s lifetime). ART can also be associated with toxicity and lead to various side effects. Long-term use of anti-retroviral drugs could also introduce drug-resistant escape mutants.

Solution

Prof Damian Purcell and his team at the Doherty Institute for Infection and Immunity have developed 10 novel anti-HIV-1 bovine antibodies that have target epitopes and antibody molecular features similar to human broadly neutralising antibodies (bNAbs). Unique features such as ultra-long CDRH3 or presence of certain amino acids that are similar to those playing roles in neutralisation by human bNAbs are expected to account for the ultra-potent neutralising response.

Key advantages of the Doherty Institute anti-HIV-1 bovine neutralising antibodies are:

- superior breadth of neutralising antibodies response;
- ultra-potent neutralisation of HIV viruses: MEL-1872 is 29-fold more potent than VRC01 against clade B viruses and is 21-fold more potent than CHO1-31 against tested clade A viruses;
- bovine bNAbs are not polyreactive (autoreactivity and polyreactivity were evaluated against several human autoantigens);
- opportunity for a platform technology for rapid discovery and testing of therapeutic antibodies.

Technology and IP Status

Comprehensive in vitro and structural characterisation data demonstrating broad ultra-potent neutralising response targeting the key conserved sites on HIV-1 envelope.

Superior breadth and potency of neutralising response in comparison to the clinical stage antibodies that bind to the HIV-1 CD4 binding site.

Further preclinical evaluation is currently underway.

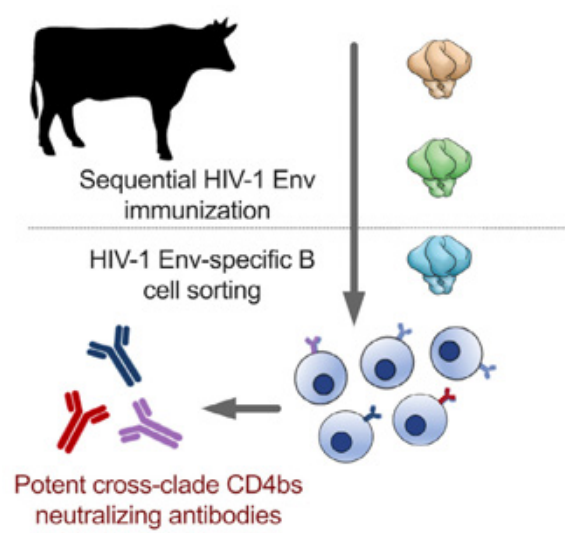


Figure 1. The process of cow immunisation with HIV-1 Env and isolation of bNAbs

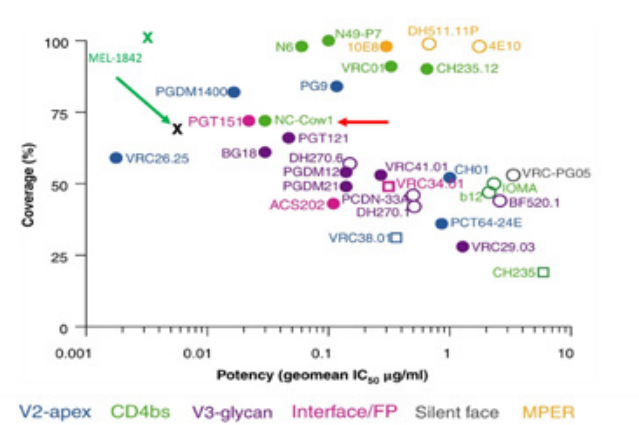


Figure 2. Comparison of potency and breadth of coverage for various classes of anti-HIV antibodies. Antibodies that target CD4bs are shown in green. This data demonstrates competitive advantages of the University’s MEL-1842 antibody as the most potent and broadestacting mAbs for HIV.

Tech name and number	2019-101 - HIV neutralising chimeric bovine-human mAb
Research Leads	Prof Damian Purcell, Dr. Behnaz Heydarchi
Publications	Heydarchi B. et al. Broad and ultra-potent cross-clade neutralization of HIV-1 by a vaccine- induced CD4 binding site bovine antibody. Cell Rep Med. 2022 May 17; 3(5):100635.
Patents	National phase patent applications in Australia, USA, Europe, China and Japan. International Publication NO.: WO2021/248198, earliest priority date 10 June 2020.
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