

Seroprevalence of neutralising antibodies in an HTLV-1c+ First Nations cohort from central Australia.

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Background:

HTLV-1 subtype A is the globally dominant strain that is associated with adult T-cell lymphoma and inflammatory diseases such as myelopathy and bronchiectasis. Subtype C is endemic in Melanesia and First Nations communities of remote Central Australia where the adult prevalence around 40% is thought to contribute to the decreased life expectancy of Indigenous Australians. There are currently no vaccines or approved therapeutics for prevention or treatment of HTLV-1 infection. Here, we assessed the prevalence of anti-Envelope (Env) antibodies in a cohort of Aboriginal Australian patients from Central Australia and investigated the capability of these immunoglobulins to neutralise HTLV-1 subtype C infection.

Methods:

Plasma was isolated from HTLV-1c+ individuals (n=46) admitted to the Alice Springs Hospital. Neutralising activity was assessed using a pseudovirus (PSV) reporter assay, proviral load (PVL) measurements of integrated viral genome were quantified by droplet digital PCR (ddPCR) and binding epitopes were mapped using a peptide ELISA.

Results:

Of the 46 HTLV-1c+ plasma samples tested, 87% demonstrated the ability to neutralise HTLV-1c PSV infection with ID50 values as high as 39,125 compared to HTLV-1c- samples (ID50 <40). PVL, a predictor of disease outcome, positively associates with neutralising titres. Mapping of these binding epitopes suggests that a well-conserved region of the proline rich repeat region (PRR) from amino acids 191 – 196 is an important contributing factor to this anti-Env response.

Conclusion:

Our data indicate that antibodies capable of binding Env and neutralising infection commonly arise over the long course of HTLV-1c infection, with a high proportion targeting the PRR. This first study frequently finding an effective neutralising antibody response in an Australian First Nations cohort has important implications for future vaccine and therapeutics development.

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Nothing to disclose.

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