An Analysis of *Bovine immunodeficiency virus* and *Jembrana disease virus* Infections in *Bos javanicus*

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BSc (Hons)

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Abstract

Two closely related bovine lentiviruses have been described, *Jembrana disease virus* (JDV) and *Bovine immunodeficiency virus* (BIV), that produce very different clinical manifestations in infected cattle. JDV causes an acute disease with a case fatality rate of about 21% in *Bos javanicus* (Bali cattle) and is endemic in the cattle population of parts of Indonesia. BIV produces a subclinical infection in *Bos taurus* and buffalo and serological evidence has shown that this virus has a worldwide distribution, possibly including Indonesia.

Attempts were made to confirm a previous report that BIV was present in the *B. javanicus* population in Indonesia. BIV proviral DNA was not detected in any of the animals although JDV proviral DNA was detected in 12 of 171 animals, only one of which was seropositive.

To define the kinetics of BIV infection in *B. javanicus* and determine the optimal time for sampling to detect BIV infection, 13 animals were experimentally infected with the R29 strain of BIV. No clinical effects were detected but proviral DNA was detected from 4-60 days post-infection (dpi) with peak titres 20 days dpi, and a transient viraemia from 4 to 14 dpi. An antibody response to TM was detected 12 dpi but an anti-capsid (CA) antibody response was detected in one animal only and not until 34 dpi. The results indicated that detection of BIV in infected Bali cattle using PCR would have a greater chance of success soon after infection and prior to the onset of a CA antibody response.

To determine the effect of BIV infection on subsequent JDV infection in *B. javanicus*, 15 cattle were infected with BIV-R29 and 9 of these were subsequently infected 42 days later with JDV. The response to BIV was typical of that observed
previously but BIV infection did not markedly modify the response to subsequent infection with JDV. In response to JDV infection, all cattle previously infected with BIV still developed an acute disease process typical of Jembrana disease. The results suggested that despite the close genetic and antigenic relationship between BIV and JDV, BIV infection does not confer protection against subsequent JDV infection.

The close antigenic relationship between BIV and JDV is a problem in the development of specific serological tests and immunosurveillance of JDV infection. To develop reagents capable of differentiating between antibody to BIV and JDV infections, peptide mapping was used to define linear B cell epitopes on the matrix (MA), CA and surface unit (SU) proteins of JDV. Short overlapping peptides that spanned these regions were synthesised and used in an ELISA format to screen their reactivity with a panel of bovine sera from animals experimentally infected with JDV\textsubscript{Tab87}, JDV\textsubscript{Pul01} or BIV-R29. Peptides representing potential immunoreactive epitopes were identified that appeared to offer promise in the development of JDV-specific serological tests and need to be tested further with a panel of sera taken from naturally infected cattle.
Declaration

I declare that this thesis is my own account of my research and contains as its main content work which has not previously been submitted for a degree at any tertiary education institution.

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Tegan Josephine McNab.
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To Bong for just being you.
**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>Acquired immunodeficiency syndrome</td>
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<tr>
<td>AGID</td>
<td>Agar gel immunodiffusion</td>
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<tr>
<td>APOBEC</td>
<td>Apolipoprotein B mRNA-editing enzyme-catalytic polypeptide-like</td>
</tr>
<tr>
<td>AUC</td>
<td>Area under the curve</td>
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<tr>
<td>BFL</td>
<td>Bovine foetal lung</td>
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<tr>
<td>BIV</td>
<td><strong>Bovine immunodeficiency virus</strong></td>
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<tr>
<td>BVDV</td>
<td><strong>Bovine viral diarrhoea virus</strong></td>
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<tr>
<td>CA</td>
<td>Capsid</td>
</tr>
<tr>
<td>CAEV</td>
<td>Caprine arthritis encephalitis virus</td>
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<tr>
<td>CE</td>
<td>Cell equivalents</td>
</tr>
<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>CCR5</td>
<td>C-C (beta) chemokine receptor 5</td>
</tr>
<tr>
<td>CD4</td>
<td>Cluster of differentiation 4</td>
</tr>
<tr>
<td>CD8</td>
<td>Cluster of differentiation 8</td>
</tr>
<tr>
<td>CTL</td>
<td>Cytotoxic T-lymphocyte</td>
</tr>
<tr>
<td>CXCR4</td>
<td>C-X-C (alpha) chemokine receptor 4</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>dNTP</td>
<td>Deoxynucleotide Triphosphate</td>
</tr>
<tr>
<td>DMSO</td>
<td>Dimethyl sulfoxide</td>
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<tr>
<td>dpi</td>
<td>Days post-infection</td>
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<tr>
<td>ELISA</td>
<td>Enzyme linked immunosorbent assay</td>
</tr>
<tr>
<td>EIAV</td>
<td><strong>Equine infectious anaemia virus</strong></td>
</tr>
<tr>
<td>EDTA</td>
<td>Ethylenediamine tetra-acetic acid</td>
</tr>
<tr>
<td>FIV</td>
<td><strong>Feline immunodeficiency virus</strong></td>
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<tr>
<td>GAPDH</td>
<td>Glyceraldehyde 3-phosphate dehydrogenase</td>
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<td>HRP</td>
<td>Horse radish peroxidase</td>
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<tr>
<td>HIV</td>
<td><strong>Human immunodeficiency virus</strong></td>
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<tr>
<td>HTLV-1</td>
<td><strong>Human T-cell lymphotropic virus type 1</strong></td>
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<tr>
<td>ID</td>
<td>Immunodominant</td>
</tr>
<tr>
<td>IgG</td>
<td>Immunoglobulin G</td>
</tr>
<tr>
<td>IR</td>
<td>Immunoreactive</td>
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<tr>
<td>IN</td>
<td>Integrase</td>
</tr>
<tr>
<td>JDV</td>
<td><strong>Jembrana disease virus</strong></td>
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<tr>
<td>LTR</td>
<td>Long terminal repeat</td>
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<tr>
<td>M-tropic</td>
<td>Macrophage tropic</td>
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<tr>
<td>VMV</td>
<td><strong>Visna maedi virus</strong></td>
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<tr>
<td>MHR</td>
<td>Major homology region</td>
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<tr>
<td>MA</td>
<td>Matrix</td>
</tr>
<tr>
<td>NC</td>
<td>Nucleocapsid</td>
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<tr>
<td>Nef</td>
<td>Negative factor</td>
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<tr>
<td>ORF</td>
<td>Open reading frame</td>
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<tr>
<td>PBMC</td>
<td>Peripheral blood mononuclear cells</td>
</tr>
<tr>
<td>PBS</td>
<td>Phosphate-buffered saline</td>
</tr>
<tr>
<td>PBS-T</td>
<td>Phosphate-buffered saline-Tween 20</td>
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<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
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<tr>
<td>pi</td>
<td>Post-infection</td>
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<tr>
<td>PR</td>
<td>Protease</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<td>--------------</td>
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<tr>
<td>qPCR</td>
<td>Quantitative polymerase chain reaction</td>
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<tr>
<td>qRT-PCR</td>
<td>Quantitative reverse transcriptase polymerase chain reaction</td>
</tr>
<tr>
<td>Rev</td>
<td>Regulator of expression of virion proteins</td>
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<tr>
<td>RT</td>
<td>Reverse transcriptase</td>
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<tr>
<td>RNA</td>
<td>Ribonucleic acid</td>
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<tr>
<td>RPMI</td>
<td>Roswell Park Memorial Institute</td>
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<tr>
<td>SIV</td>
<td>Simian immunodeficiency virus</td>
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<tr>
<td>SRLV</td>
<td>Small ruminant lentivirus</td>
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<tr>
<td>SU</td>
<td>Surface unit</td>
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<tr>
<td>T-tropic</td>
<td>T-lymphocyte-tropic</td>
</tr>
<tr>
<td>TCID&lt;sub&gt;50&lt;/sub&gt;</td>
<td>Median tissue culture infective dose</td>
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<tr>
<td>Tat</td>
<td>Trans-activator of transcription protein</td>
</tr>
<tr>
<td>TM</td>
<td>Transmembrane glycoprotein</td>
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<tr>
<td>U3</td>
<td>3' Untranslated region</td>
</tr>
<tr>
<td>U5</td>
<td>5' Untranslated region</td>
</tr>
<tr>
<td>Vif</td>
<td>Viral infectivity protein</td>
</tr>
<tr>
<td>VL</td>
<td>Viral load</td>
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<tr>
<td>Vpr</td>
<td>Viral protein R</td>
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<tr>
<td>Vpu</td>
<td>Viral protein U</td>
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<tr>
<td>Vpx</td>
<td>Viral protein X</td>
</tr>
<tr>
<td>WIB</td>
<td>Western immunoblotting</td>
</tr>
<tr>
<td>YT</td>
<td>Yeast tryptone broth</td>
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Publication and International Conference Presentations

Publications arising from this thesis


Manuscripts submitted for publication


Oral presentations

“Bovine immunodeficiency virus infection fails to provide protection against subsequent Jembrana disease virus infection” Presented at the European Society for Veterinary Virology Conference in Budapest, Hungary 2009.

Poster presentations