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RELEVANCE OF THE VARIABILITY OF THE FELINE IMMUNODEFICIENCY VIRUS IN REGARD TO PATHOGENICITY AND VACCINATION IN NEW ZEALAND

A thesis presented in partial fulfilment of the requirements for the degree of

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Abstract

Cats infected with the feline immunodeficiency virus (FIV) show a range of clinical signs. Given the variability of the FIV genome, it is possible that there is variation in certain biological characteristics of FIV, such as pathogenicity. This may also be relevant to vaccination against FIV, as an effective vaccine would have to result in the generation of T cells that recognise a range of different variants in the field. The Fel-O-Vax® FIV vaccine has been available to veterinarians in New Zealand (NZ) for the past 12 years. Despite this, there is a paucity of studies investigating the cross-reactivity of the vaccine-induced immune response against different variants of FIV, and no studies investigating the efficacy of the vaccine in NZ.

The overall aim of the research in this thesis was to determine the relevance of the variability of FIV, in regard to pathogenicity and vaccination in NZ. Firstly, 2 separate assays were designed to assess variation in the ability of different isolates of FIV to induce apoptosis or inhibit mitogen-induced proliferation in lymphoid cells in vitro. Results showed that variation in FIV-apoptosis did occur, supporting the argument that FIV variants may also differ in pathogenicity. Secondly, the cross-reactivity of the vaccine-induced immune response was assessed in vitro and in vivo, by measuring antigen-specific cellular activation and a delayed type hypersensitivity (DTH) response in vaccinated cats following inoculation with NZ field isolates of FIV. Results showed that the response was at least partially cross-reactive, however quantitative differences were detected in the response to each isolate of FIV tested. Finally, efficacy of the Fel-O-Vax® FIV vaccine under NZ conditions was investigated by comparing the prevalence of FIV in vaccinated and unvaccinated cats in the field. Results showed that there was no effect of vaccination on FIV prevalence, suggesting poor efficacy of the Fel-O-Vax® FIV vaccine in NZ.

Results described in this thesis support the argument that there is variation among FIV in NZ, and that this may affect pathogenicity and vaccine efficacy in this country. The evidence presented did not support use of the Fel-O-Vax® FIV vaccine in NZ.
Acknowledgements

To the many people who have helped me on this journey, I am sincerely grateful. Firstly, to my supervisors; Associate Professor Nicholas Cave, Dr. Magda Dunowska and Dr. Anthony Pernthaner. Thank you Tony for taking the time to explain even the most basic concepts in flow cytometry, and for your patience in answering all my questions. I would like to express my gratitude to Magda for her friendship and support, especially in the laboratory. I have come a long way with her guidance, and appreciate all that she has taught me. I am especially grateful to Nick, who taught me to question everything and inspired me to embark on this journey. Thank you Nick for all the emotional support, your friendship and mentorship, and your understanding of the challenges that I faced throughout this adventure.

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<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-ME</td>
<td>2-Mercaptoethanol</td>
</tr>
<tr>
<td>7AAD</td>
<td>7 amino actinomycin D</td>
</tr>
<tr>
<td>AB</td>
<td>Annexin binding buffer</td>
</tr>
<tr>
<td>AICD</td>
<td>Activation induced cell death</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired immunodeficiency syndrome</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
</tr>
<tr>
<td>CD</td>
<td>Cluster of differentiation</td>
</tr>
<tr>
<td>cDNA</td>
<td>Complementary DNA</td>
</tr>
<tr>
<td>CFGS</td>
<td>Chronic feline gingivostomatitis syndrome</td>
</tr>
<tr>
<td>ConA</td>
<td>Concanavalin A</td>
</tr>
<tr>
<td>CPM</td>
<td>Counts per minute</td>
</tr>
<tr>
<td>CPT</td>
<td>Cell preparation tube</td>
</tr>
<tr>
<td>Cq</td>
<td>Quantification cycle</td>
</tr>
<tr>
<td>CRD1</td>
<td>First cysteine rich domain of the CD134 molecule</td>
</tr>
<tr>
<td>CRD2</td>
<td>Second cysteine rich domain of the CD134 molecule</td>
</tr>
<tr>
<td>CRFK</td>
<td>Crandell-Reese Feline Kidney</td>
</tr>
<tr>
<td>CTLA-4</td>
<td>Cytotoxic T lymphocyte antigen 4 (CD152)</td>
</tr>
<tr>
<td>DC-SIGN</td>
<td>Dendritic Cell-Specific Intercellular adhesion molecule-3-Grabbing Non-integrin</td>
</tr>
<tr>
<td>DMEM</td>
<td>Dulbecco’s Modified Eagle Medium</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>DTH</td>
<td>Delayed-type hypersensitivity</td>
</tr>
<tr>
<td>EDTA</td>
<td>Ethylenediaminetetraacetic acid</td>
</tr>
<tr>
<td>env</td>
<td>Envelope</td>
</tr>
<tr>
<td>FBS</td>
<td>Foetal bovine serum</td>
</tr>
<tr>
<td>FHV-1</td>
<td>Feline herpesvirus 1</td>
</tr>
<tr>
<td>FITC</td>
<td>Fluorescein isothiocyanate</td>
</tr>
<tr>
<td>FIV</td>
<td>Feline immunodeficiency virus</td>
</tr>
<tr>
<td>FMO</td>
<td>Fluorescence minus one</td>
</tr>
<tr>
<td>FSC</td>
<td>Forward scatter</td>
</tr>
<tr>
<td>gag</td>
<td>Group-specific antigen</td>
</tr>
<tr>
<td>GM</td>
<td>Growth medium</td>
</tr>
<tr>
<td>gp100</td>
<td>Surface unit of the FIV envelope glycoprotein</td>
</tr>
<tr>
<td>gp35</td>
<td>Transmembrane unit of the FIV envelope glycoprotein</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>IFN</td>
<td>Interferon</td>
</tr>
<tr>
<td>IL</td>
<td>Interleukin</td>
</tr>
<tr>
<td>MEM</td>
<td>Minimum essential medium</td>
</tr>
<tr>
<td>MFI</td>
<td>Mean fluorescence intensity (geometric)</td>
</tr>
<tr>
<td>MHC</td>
<td>Major histocompatibility complex</td>
</tr>
<tr>
<td>MOI</td>
<td>Multiplicity of infection</td>
</tr>
<tr>
<td>mRNA</td>
<td>Messenger RNA</td>
</tr>
<tr>
<td>MUAEC</td>
<td>Massey university animal ethics committee</td>
</tr>
<tr>
<td>MUFNU</td>
<td>Massey university feline nutrition unit</td>
</tr>
<tr>
<td>MUVTH</td>
<td>Massey university veterinary teaching hopsital</td>
</tr>
<tr>
<td>NaCl</td>
<td>Sodium chloride</td>
</tr>
</tbody>
</table>
NEAA  Non-essential amino acids
NK   Natural killer
NZ   New Zealand
OD   Optical density
ORF  Open reading frame
p24  Capsid peptide of the FIV gag protein
PBMC Peripheral blood mononuclear cells
PBS  Phosphate buffered saline (pH 7.2)
PCR  Polymerase chain reaction
PD-1 Programmed death receptor 1
PF   Preventable fraction
PI   Post inoculation
pol  Polymerase
PS   Phosphatidylserine
qPCR Quantitative PCR
RNA  Ribonucleic acid
RPMI Roswell park memorial institute (medium)
rRNA Ribosomal RNA
RT   Reverse transcriptase
SI   Stimulation index
SSC  Side scatter
SU   Surface unit of the FIV envelope glycoprotein (gp100)
TCID_{50} Median tissue culture infectious dose
TH1/2 T helper 1/2 cells
TM   Transmembrane unit of the FIV envelope glycoprotein (gp35)
TNF  Tumour necrosis factor
UV   Ultraviolet
V1-V9 Hypervariable regions (1-9) of the FIV envelope gene
vif  Viral infectivity factor
VNA  Virus neutralising antibodies