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

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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.

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2-ME	2-Mercaptoethanol
7AAD	7 amino actinomycin D
AB	Annexin binding buffer
AICD	Activation induced cell death
AIDS	Acquired immunodeficiency syndrome
ANOVA	Analysis of variance
CD	Cluster of differentiation
cDNA	Complementary DNA
CFGS	Chronic feline gingivostomatitis syndrome
ConA	Concanavalin A
CPM	Counts per minute
CPT	Cell preparation tube
Cq	Quantification cycle
CRD1	First cysteine rich domain of the CD134 molecule
CRD2	Second cysteine rich domain of the CD134 molecule
CRFK	Crandell-Reese Feline Kidney
CTLA-4	Cytotoxic T lymphocyte antigen 4 (CD152)
DC-SIGN	Dendritic Cell-Specific Intercellular adhesion molecule-3-Grabbing Non-integrin
DMEM	Dulbecco's Modified Eagle Medium
DNA	Deoxyribonucleic acid
DTH	Delayed-type hypersensitivity
EDTA	Ethylenediaminetetraacetic acid
env	Envelope
FBS	Foetal bovine serum
FHV-1	Feline herpesvirus 1
FITC	Fluorescein isothiocyanate
FIV	Feline immunodeficiency virus
FMO	Fluorescence minus one
FSC	Forward scatter
gag	Group-specific antigen
GM	Growth medium
gp100	Surface unit of the FIV envelope glycoprotein
gp35	Transmembrane unit of the FIV envelope glycoprotein
HIV	Human immunodeficiency virus
IFN	Interferon
IL	Interleukin
MEM	Minimum essential medium
MFI	Mean fluorescence intensity (geometric)
MHC	Major histocompatibility complex
MOI	Multiplicity of infection
mRNA	Messenger RNA
MUAEC	Massey university animal ethics committee
MUFNU	Massey university feline nutrition unit
MUVTH	Massey university veterinary teaching hopsital
NaCl	Sodium chloride

NEAA	Non-essential amino acids
NK	Natural killer
NZ	New Zealand
OD	Opitcal 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