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**Epidemiological, pathological and
metabolomic characterisation of
an acquired myopathy of dogs
in New Zealand**

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requirements for the degree of

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Abstract

'Go Slow' myopathy (GSM) is an idiopathic myopathy in dogs in New Zealand, characterised by an acute onset of trembling, weakness and collapse, followed by a prolonged period of exercise intolerance. In the first part of this thesis, the epidemiology of the disease was investigated using a telephone survey to obtain information regarding the diet, exercise, and health of affected dogs. Eighty-six confirmed cases were included in this study, and ingestion of wild pig in the week prior to the onset of clinical signs was a consistent finding (76/86 dogs; 88%; 95% confidence interval = 82 – 95%). Cases occurred most commonly in the upper North Island, particularly in Northland.

The aim of the second part of this thesis was to characterise the pathology of GSM in the same 86 dogs included in the epidemiological study, using serum biochemistry (78 dogs), histology (20 dogs), and electron microscopy (4 dogs). Acutely, affected dogs had increased serum creatine kinase and aspartate aminotransferase activities, corresponding with the histological finding of skeletal muscle degeneration in the absence of inflammation. Ultrastructural changes in skeletal muscle included mitochondrial hypertrophy, intramitochondrial inclusions and increased sarcoplasmic glycogen. Similar lesions were observed in the skeletal muscle of wild pigs from areas where GSM occurred in dogs. Affected dogs also had increased serum alanine aminotransferase activities due to accumulation of lipid and glycogen in hepatocytes. Overall, the microscopic findings were consistent with a toxic myopathy.

To further investigate the pathogenesis of the disease, liver samples were collected from 15 affected dogs and 24 clinically normal dogs for untargeted metabolic profiling using liquid chromatography-mass spectrometry. Comparison of spectra between affected and normal dogs revealed a widespread decrease in phospholipids, and increases in selected dicarboxylic acids and N-acetylated branch chain amino acids in affected dogs. No causative compounds were identified although several candidate mass spectrometric features were identified for future investigation.

Taken together, the results of these studies suggest that 'Go Slow' myopathy is a toxic mitochondrial myopathy in dogs that is associated with the ingestion of wild pork. The findings reported aid in the prevention, diagnosis, and management of cases, with the primary suggestion being that owners avoid feeding wild pork in areas where the myopathy occurs. Further work is required to elucidate the cause of this disease.

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Abbreviations

AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
ALP	Alkaline phosphatase
ChE	Cholesteryl ester
Cer	Ceramide
CK	Creatine kinase
cf-DNA	Cell-free DNA
DG	Diglyceride
EM	Electron microscopy
EMG	Electromyography
FC	Fold change
FDR	False discovery rate
GRMD	Golden Retriever muscular dystrophy
GPx	Glutathione peroxidase
HE	Haematoxylin and eosin stain
LC	Liquid chromatography
miRNA	Micro-RNA
MPI	Ministry for Primary Industries
MRI	Magnetic resonance imaging
neg	Negative ionisation mode
NMR	Nuclear magnetic resonance spectroscopy
MS	Mass spectrometry
PA	Phosphatidic acid
PC	Phosphatidylcholine
PG	Phosphatidylglycerol
PE	Phosphatidylethanolamine
PI	Phosphatidylinositol
pos	Positive ionisation mode
PS	Phosphatidylserine
SM	Sphingomyelin
TG	Triglyceride
m/z	Mass to charge ratio
rt	Retention time

