WINN FELINE FOUNDATION
For the Health and Well-being of All Cats

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ARE POLYMORPHISMS A RISK FACTOR IN FIP DEVELOPMENT?

PROJECT STUDY: Are interferon-gamma polymorphisms a risk factor in FIP development – a large cohort study.

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Final report summary, W18-010

Feline infectious peritonitis (FIP) is a common infectious cause of death in cats. Increased incidence of FIP within particular breeds, or lines of breeds, is suggestive of inherited genetic risk factors. For other genetic diseases, out-crossing with non-pedigree cats has been suggested to increase genetic diversity and reduce risk of various genetic diseases in those breeds of particularly high risk.

The inflammatory protein, interferon-gamma, has been strongly implicated in the development of FIP. Previous sequencing of fragments of the feline interferon-gamma gene in a mixed population of cats found an *increased* risk of FIP associated with the target sequence at two positions. As a result, commercial tests are available, based on the sequence of the interferon-gamma gene and other genes, to indicate genetic risk of FIP.

The aims of the present study were to i) determine the interferon-gamma gene target sequence within a population of non-pedigree cats confirmed as having FIP; ii) determine the interferon-gamma gene target sequence within the "general non-pedigree cat population" as represented by a large cohort of prospectively-sampled cats recruited into a lifetime longitudinal study for which epidemiological data are available (i.e. Bristol Cats study); iii) determine the relative risk conferred by specific interferon-gamma gene sequences in the development of FIP. Non-pedigree cats were selected, in part for their genetic heterogeneity (i.e. to minimize breed bias) and because they represent over 80% of the cats with FIP.

A novel assay was designed for this purpose. DNA was purified from 264 buccal swab samples collected from non-pedigree cats from the Bristol Cats study, and from 59 samples of tissue or effusion (i.e. FIP-associated fluid) from cats with FIP from the Bristol FIP Biobank and Veterinary Laboratory Services, University of Liverpool. Partial sequencing of the interferon-gamma gene was possible for nearly all samples.

There was a statistically significant association between FIP status and genetic variants of the interferon-gamma gene, with a *reduced* risk of developing FIP in cats with one form of the gene. However, as this form was present in 16% of cats with FIP and absent in 66% of cats in the general population, and as the previously reported associations between genotype and risk at these positions were not detected in this population, the clinical application of characterization of these genetic markers, both on an individual risk basis and to guide breeding programs, cannot be recommended at this time.

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In conclusion, these results indicated that, although *fIFNG* variants may be associated with altered risk of FIP disease, the prevalence of both interferon-gamma gene sequences within both populations severely limits their use to inform breeding programs to reduce the incidence of FIP.

Publications:

Barker, E.N., Lait, P., Ressel, L., Blackwell, E.-J., Tasker, S., Helps, C.R. (2020) Evaluation of interferon-gamma polymorphisms as a risk factor in feline infectious peritonitis development in non-pedigree cats – a large cohort study *Pathogens* **9**: 535 DOI:10.3390/pathogens9070535