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

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Evaluation of Inflammatory Mediator Profiles in Cats with Pain Associated with Naturally-Occurring Degenerative Joint Disease

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As a result of the funding received by the Winn Foundation, we have been able to characterize cytokine concentration profiles in 186 cats with and without degenerative joint disease (DJD) and associated pain. This is the first work of its kind, and is an area of research that puts us at the forefront of work being done in veterinary and human medicine to better understand the inflammatory component of chronic pain.

Serum samples used in this study were collected from cats presented to the Comparative Pain Research Laboratory for a number of analgesic trials aimed at evaluating treatments for cats with chronic pain. All cats were examined by a veterinarian and received a physical, orthopedic, and neurologic exam, followed by radiographs of each joint and spinal segment. During the orthopedic exam, each joint was evaluated for the presence of pain, and scored using a standardized pain scale. The results of the orthopedic and radiographic evaluations allowed us to generate orthopedic pain scores (the sum of scores for individual joints) and radiographic DJD scores (the sum of standardized scoring of each individual joint) and categorize cats as to the presence and severity of pain and radiographic DJD.

Samples were analyzed using a feline-specific multiplex magnetic bead assay of 19 different cytokines and chemokines. Samples were run in triplicate across eight plates, and concentrations of the cytokines and chemokines were analyzed for relationships with the total pain score, total DJD score, and presence or absence of chronic kidney disease. Cluster analysis was also performed to determine whether one or more cytokines/chemokines could reliably distinguish between cats with and without DJD and associated pain. We found that several cytokines were associated with orthopedic pain score and radiographic DJD score.

Specifically, TNF-α and IL-8 concentrations were increased with increasing orthopedic pain score, and IL-4 and IL-8 concentrations were increased with increasing radiographic DJD score. Concentration of IL-8 also increased with increasing age. As both radiographic DJD score and orthopedic pain score increase with age, this is a potential confounder in our findings with IL-8, and will be evaluated further. While many of the cytokine concentrations were below detectable levels for many of the cats, the number of samples above the lower limit of detection for the assay increased with increased total pain and total DJD score for several cytokines.
Cluster analysis did not find that any cytokines (alone, or as a group) were able to reliably distinguish between groups of cats (those with and without DJD). While we were hopeful that this analysis would be revealing, the findings were not entirely unexpected given the complexity of the interactions of the immune system and the local production and consumption of many cytokines. A different approach, allowing the

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cytokine concentrations to "drive" the clustering showed better separation of groups of cats, but the underlying similarities between the groups have not yet been determined.

This work has provided new knowledge on cytokine concentrations in cats with and without DJD and serves as a launching point for further research including verification of our findings with targeted ELISAs and comparison of serum findings with concentrations at the level of the joint.

Publications:

Publications resulting from this work include:

1. Gruen ME, Messenger KM, Thomson AE, Griffith EH, Paradise H, Vaden S, Lascelles BDX. A comparison of serum and plasma values using a multiplexed cytokine assay in cats. (In preparation for submission to Veterinary Immunology and Immunopathology).

2. Gruen ME, Griffith EH, Aldrich LA, Thomson AE, Vaden S, Messenger KM, Lascelles BDX. Evaluation of serum cytokines in cats with and without degenerative joint disease and associated pain. (In preparation for submission to Veterinary Immunology and Immunopathology).