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For the Health and Well-being of All Cats

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EXPLORING DEGENERATIVE JOINT DISEASE PAIN AND HYPERSENSITIVITY IN CATS

PROJECT STUDY: Master regulator of DJD associated pain and hypersensitivity in felines

Principal Investigator: Drs. Santosh Mishra and Duncan Lascelles; North Carolina State University

Final report summary, W18-028

Degenerative joint disease (DJD) associated pain in cats is a poorly understood disease and cats with DJD-pain have trouble moving, trouble performing activities of daily living. Cats with widespread sensitivity to stimuli is hallmark of arthritis and DJD-associated pain in cats, and contributes to the pain condition. Very little is known about the underlying mechanisms that drive pain in cats, and untreated pain results in increased sensitivity and more debilitating pain conditions. In last few decades, research has demonstrated better understanding of cells and molecules, which plays an important role in pain in rodents, but the relevance of these players in disease-associated pain remains unclear. Artemin, a neurotrophic factor, and its receptor, glial-derived neurotrophic factor (GDNF) family receptor alpha-3 (GFRα3), have been identified as involved in pain in rodents. In addition, these investigators have compelling evidence that the artemin/GFRα3 signaling pathway may be important in OA pain in dogs. Here, they teamed up again to identify mechanisms involved in this debilitating pain condition in felines, thus identifying therapeutic targets reflective of the true disease state. They found that artemin is significantly increased in the blood of cats with DJD, and pain associated with the DJD. This finding was so striking, that they may have identified a useful biomarker of DJD pain in cats, which would be very helpful given how difficult it is to diagnose chronic pain in cats. They also confirmed the presence of GFRA3 and downstream receptors in the sensory nerves of cats, and found some indication of increased gene expression in cats with DJD. Other findings indicate a change in the pattern of expression of GFRA3. Overall, their findings strongly implicate the artemin/GFRA3 signaling axis in chronic DJD pain in cats. ***The potential impact of their work is high, as it is focused on targeting the neurobiological aspects of the naturally occurring pain state in cats.***
Future work will repeat the measurement of serum artemin in cats with chronic DJD pain, and relate this to measures of sensitivity, and also explore the idea of using this as an additional biomarker of pain. Although they did not find increased GFRα3 gene expression, it may be that the gene is being transcribed to a greater level in cats with DJD, as suggested by some of their results. Therefore, future work will also examine the expression of GFRα3 and TRP channel expression in DRG tissues using in situ hybridization and multi-channel imaging. They have been developing an in situ hybridization technique to simultaneously look at 4 receptors. This has been successful in mice, and they are now moving on to explore this in dogs and then cats.

Publications: The investigators are currently working on writing the manuscript for publication.
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