



RESEARCH PROGRESS REPORT SUMMARY

Grant 02610-A: The Role of Motilin Signaling in Canine Osteoarthritis

Principal Investigator: Li Zeng, PhD
Research Institution: Tufts University
Grant Amount: \$15,000
Start Date: 3/1/2019 **End Date:** 2/28/2021
Progress Report: Mid-Year 2
Report Due: 8/31/2020 **Report Received:** 9/29/2020

(The content of this report is not confidential and may be used in communications with your organization.)

Original Project Description:

Osteoarthritis is a devastating disease characterized by joint pain and immobility and while it is highly prevalent in dogs, there is no optimal treatment for this disease. The goal of this study is to design strategies to prevent osteoarthritis progression and improve the quality of life for dogs. A central feature for osteoarthritis is the destruction of joint cartilage, a tissue that normally serves as a cushion between bones. Without this cushion, there is increased friction at the joint, causing mechanical stress and accelerating joint degeneration. One treatment strategy is to combat inflammation, because inflammation results in joint cartilage loss and is a key component in the pathogenesis of osteoarthritis. In preliminary studies, the investigators found that the hormone motilin has an anti-inflammatory activity that has not been previously reported. Their hypothesis is that motilin protects the canine joint against inflammation and improves the health of the cartilage in osteoarthritis. Outcomes of this research may benefit both dogs and humans suffering from osteoarthritis.

Publications: None at this time.

Presentations:

We presented part of the data (whole joint culture) in a local symposium (Center for Skeletal Research, MGH, in May 2019).



Report to Grant Sponsor from Investigator:

Osteoarthritis causes severe immobility in dogs, especially in certain large breeds, suggestive of an underlying genetic mechanism. In addition to the genetic component, repeated use causes mechanical stress which further results in chronic joint inflammation and articular cartilage degeneration. This creates a significant emotional and economic burden to the society. Thus, there is an urgent need to find a therapy to halt osteoarthritis progression.

We have been investigating the role of motilin on canine cartilage degeneration to understand the genetic regulation of joint stability and in search of a potential treatment option for osteoarthritis. Motilin, a hormone that enhances GI movement, has been shown to have anti-inflammatory activity. With the support of this grant, we have established two systems in the lab to analyze canine cartilage, including the culture conditions that enable the survival of cells in the joint. Our data suggests a reduction of motilin receptor in cartilage from osteoarthritis dogs, and an effect of motilin to modify chondrocytes' response to inflammation, which may be unique to canines, pointing to the importance of studying osteoarthritis and inflammation specifically in dogs, rather than adopting treatments from human and mouse studies.