Study 2405: Inhibition of Collagenolysis in Canine Cranial Cruciate Ligament During Rupture

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Breed(s): All (non-specified), Great Pyrenees, Mastiff, Miniature Poodle, Newfoundland, Standard Poodle, Toy Poodle

Abstract:

The long-range goal of this work is to study tissue repair in the canine cruciate ligament and to determine what causes cruciate rupture. Our objective is to determine whether the presence of two enzymes, tartrate-resistant acid phosphatase and cathepsin K, causes excessive breakdown of collagen within the cruciate ligament, and weakening of the ligament. It is currently believed that excessive expression of this type of enzyme is an important factor causing cruciate rupture. Having determined whether these enzymes cause breakdown of collagen within the cruciate ligament, this knowledge will offer new insight into cruciate rupture in dogs and facilitate development of new treatments. To accomplish the objective of this application, we will determine whether these enzymes are released into the knee joint fluid in dogs with cruciate rupture. Using a tissue culture technique with pieces of ruptured ligament collected from surgical patients, we will also determine whether treatment of the ligament with enzyme inhibitors prevents excessive breakdown of ligament collagen.

Upon completion of this work, we expect to have gained a detailed understanding of the role of these ligament-dissolving enzymes in cruciate rupture. We also expect that the results will lead to development of new medical treatments for cruciate rupture.

Animals—30 dogs with ruptured CCL, 8 aged dogs without ruptured CCL, and 9 young dogs without ruptured CCL.

Procedure—The CCL was examined histologically and cells containing TRAP and cathepsin K were identified histochemically and immunohistochemically, respectively.

Results—Cathepsin K and TRAP were detected within the same cells, principally within the epiligamentous region and to a lesser extent in the core region of ruptured CCL. Numbers of cells containing TRAP and cathepsin K were significantly greater in ruptured CCL, compared with CCL from young or aged dogs, and numbers of such cells were greater in CCL from aged dogs, compared with those of young dogs. In aged dogs, small numbers of cells containing TRAP and cathepsin K were seen in intact CCL associated with ligament fascicles in which there was chondroid transformation of ligament fibroblasts and disruption of the extracellular matrix.

Conclusion and Clinical Relevance—Ruptured CCL contain greater numbers of cells with the proteinases TRAP and cathepsin K than CCL from healthy, young, or aged dogs. Results suggest that cell-signaling pathways that regulate expression of these proteinases may form part of the mechanism that leads to upregulation of collagenolytic ligament remodeling and progressive structural failure of the CCL over time. (*Am J Vet Res* 2002;63:1279–1284).