Introduction

Osteoarthritis (OA) is a degenerative joint disease that causes the breakdown of the joint’s cartilage. It is one of the oldest and most common types of arthritis affecting more than 20 million adults in the United States and is estimated by 2030 to affect 70 million Americans. The surgically induced animal model of osteoarthritis in rats is used to study the pathogenesis of cartilage degeneration and to evaluate potential anti-arthritis drugs for clinical use. Surgically creating a meniscal tear results in rapid and severe cartilage degeneration that resembles human OA, occurring in some stages of human osteoarthritis. The medial tibia is divided into 3 zones (inner, middle, outer), each zone is assigned a score ranging from 0 to 5% according to the severity of the degeneration that has resulted in the observed morphological changes. The knee joints are fixed in 10% Neutral Buffered Formalin for 48 hours and then placed into decalcification solution (5% formic acid) for 3-6 days. Once decalcified the knee joints are cut into approximately 2 equal halves, processed and embedded properly so that the subsequent levels demonstrate with consistency the lesion severity.

Materials & Methods

Animal Model

The surgically induced rat medial meniscal tear is performed on 300 - 400 gram rats. The medial collateral ligament is transected and the medial meniscus is reflected medially toward the femur with a 3.0 ligature. The patella is removed to allow proper fixation of the joint. The meniscus is reflected or the joint to avoid fragmentation of the joint. The joint is then placed in 10% Neutral Buffed Formalin (buffered) and allowed to assume a natural degree of flexion.

Histology

Histological evaluation is performed by analyzing the decalcified paraffin-embedded Toluidine Blue sections to determine the severity of cartilage degeneration, osteophyte formation and efficiency of the potential drug candidates.

Results

This knee joints were evaluated for severity of the medial femoral and medial tibial cartilage degeneration and osteophyte formation. The primary area that is evaluated for cartilage damage is the medial tibia. The medial tibia is divided into 3 zones (inner, middle, outer), each zone is assigned a score ranging from 0 to 5% according to the severity of the degeneration that has resulted in the observed morphological changes. The knee joints are processed for paraffin embedding and sectioned at 8um for toluidine blue staining.

Score

1=small up to 299um
2=moderate 300 - 399um
3=large 400 or greater um

Vehicle

Table 1. Individual Animal Histopathology Report. The table is created in Microsoft Excel to generate and tabulate the data taken from the joint sections.

<table>
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<th>Sex</th>
<th>Disposition</th>
<th>Study Information</th>
<th>Left Knee</th>
<th>Right Knee</th>
<th>Relative Depth - level 1</th>
<th>Total Width/Sig. Width (um) - Level 1</th>
<th>Relative Depth - level 2</th>
<th>Total Width/Sig. Width (um) - Level 2</th>
<th>Relative Depth - level 3</th>
<th>Total Width/Sig. Width (um) - Level 3</th>
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</table>

Conclusions

The information gleaned from the histopathology allows the evaluation of potential anti-arthritis drugs. The results support the animal model of disease show the effects of compounds on proteoglycan degradation and osteophyte formation. In addition it may detect efficacy of metalloproteinase inhibitors and other anti-arthritis compounds. This model mimics human trauma of cartilage since it results in morphological changes with comparative pathogenesis to human disease.

Since the data generated from the histology cannot be captured by any other means it is important that each specimen is handled appropriately. Great care must be taken to assure that the knee joint is handled properly. All specimens are processed and embedded properly so that the subsequent levels demonstrate with consistency the lesion severity.

References