ACL repair (BE-repair) and bio-enhanced ACL reconstruction (BE-ACLR) is improved when compared to traditional ACL reconstruction (ACLR) or ACL transection with no treatment (ACLT).

Methods: With IACUC approval, 31 adolescent minipigs underwent surgical ACL transection in one knee followed by BE-repair (n=8), BE-ACLR (n=8), ACLR (n=8), and no treatment (ACLT; n=7). After 12 months of healing, the articulating surfaces of the surgically treated and contralateral ACL intact knees were macroscopically graded following application of India ink using a five point scale: 0=no changes; 1= intact surface with color changes; 2=surface fibrillation; 3=exposed bone10%. The surface areas of all lesions were determined using calipers and an elliptical fit. A mixed linear model was used to make comparisons between treatments (BE-repair, BE-ACLR, ACLR, and ACLT) and compartments (medial femoral condyle, lateral femoral condyle, medial tibial plateau, and lateral tibial plateau). Similar analyses were performed to compare the lesion areas within each compartment. All statistical analyses were done on the difference between the surgical and contralateral ACL-intact knee within each animal.

Results: We found significant mean differences in cartilage scores between treatments (p<0.05) and compartments (p<0.01). The mean difference ± confidence interval for BE-repair, BE-ACLR, ACLR and ACLT (pooled across compartments) were 0.2±0.193, 0.16±0.241, 0.48±0.181, and 0.66±0.392, respectively. Only the knees treated with BE-ACLR did not have increased chondral injury on the surgical side. For the lesion area measurements, the treatment effect was statistically significant in the medial femoral condyle (p=0.012). The mean difference ± confidence interval between the surgical and contralateral ACL-intact knees for BE-repair, BE-ACLR, ACLR and ACLT were 5±17.8mm², -19.1±23.1mm², and 5.7±31.9mm², and 57±51.5mm², respectively. Both the BE-repair and BE-ACLR procedures resulted in mean differences between the operative and non-operative side that were not significantly different from zero. It should also be noted that there were no lesions in either the surgical or contralateral ACL intact knee in the lateral femoral condyle or medial tibial plateau for any animal undergoing BE-repair.

Conclusions: ACL transection and ACL reconstruction both resulted in increased chondral damage of the knee at one year after surgery as noted in humans. In contrast, treatment of the ACL transection with either bio-enhanced repair with CPC or ACL reconstruction augmented with CPC prevented this increased chondral damage. These data suggest that the intra-articular application of CPC may be chondroprotective.

124 CHRONICITY PRODUCES DIFFERENTIAL ALTERATIONS IN PAIN BEHAVIORS IN MURINE OSTEARTHROSIS

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Purpose: Osteoarthritis pain is a growing problem due to an expanding elderly population and lack of safe and effective therapies. Understanding the origins and pathogenesis of chronic arthritis pain is important for developing effective therapies. Osteoarthritic pain does not correlate well with radiographic severity, and loss of function in patients with osteoarthrosis may result from pain, from altered biomechanics or from toxicity of analgesics. In order to better understand the relationship between osteoarthrosis, pain, and function, we measured different types of pain behaviors in mice with osteoarthrosis as a function of age, duration of arthritis and in response to different analgesic treatments.

Methods: Collagenase (10 IU) in 10 μl was given by intra-articular (IA) injection into the left knee of 4-week-old C57Bl6 male mice. This produced osteoarthritis that was identifiable histologically after 4 weeks. Arthritic mice were compared to uninjected naïve mice of the same age at 4 weeks and 6 weeks after collagenase injection and to arthritic mice treated with IA analgesics. Analgesics tested were IA morphine sulfate (0.7 mg/kg in 5 μl) or IA Botulinum toxin type A (BoNT/A) (0.02 IU given 3 d before testing). Pain behavior measures included evoked pain response to repetitive firm palpation of the knee for 1 minute, voluntary, spontaneous nocturnal wheel-running, mechanical withdrawal thresholds by Von Frey filament testing and digitized video gait analysis using DigiGait™ (Mouse Specifics, Inc, Quincy, MA). The nonarthritic knee was the internal nonpainful control.

Results: At both 4 and 6 weeks after collagenase injection, evoked pain responses in arthritic knees were increased, but this response was 65% greater at 4 weeks than at 6 weeks. Arthritis caused an increased swing/strike ratio measured by gait analysis and increased mechanical allodynia in the arthritic limb by Von Frey filament testing at both 4 and 6 weeks. Von Frey testing in the normal right limb revealed allodynia at 4 weeks but an increased pain threshold at 6 weeks. Spontaneous nocturnal wheel-running was reduced in both the 4 and 6 week arthritic groups, as well as in 6 week naïve mice. Both BoNT/A and Morphine were effective analgesics at 4 and 6 weeks as measured by evoked pain but did not normalize gait function at either time point. Only morphine normalized the threshold for mechanical allodynia to Von Frey filament testing at 4 weeks, but IA BoNT/A was more effective at 6 weeks.

Conclusions: IA injection of collagenase in mouse knees produces arthritis pain that can be measured by various methods at 4 weeks and persists to 6 weeks. Both opioids and BoNT/A given IA are effective analgesics when pain is measured by evoked pain behavior. Changes in functional measures such as gait analysis do reflect the development of arthritis pain but are not clearly normalized by analgesia and may be due not only to pain but to biomechanical changes in the joints. Chronic osteoarthritis pain produces mechanical allodynia, one indication of peripheral sensitization. Mechanical allodynia may be decreased by opioids if arthritis pain is not longstanding but IA BoNT/A may be more effective for sensitization due to arthritis that is more chronic. More work needs to be done to determine which pain behaviors best measure chronic pain in murine arthritis and are sensitive for detecting analgesia in order to use preclinical models for testing potential new analgesics.

125 LDL RECEPTOR DEFICIENCY RESULTS IN INCREASED OSTEOPHYTE FORMATION DURING EXPERIMENTAL OSTEARTHROSIS BOTH UNDER LOW AND HIGH CHOLESTEROL CONDITIONS


Purpose: Synovial macrophages have previously shown to be involved in joint destruction during experimental collagenase-induced osteoarthritis (OA). The low density lipoprotein (LDL) receptor expressed by synovial macrophages is involved in transport of cholesterol, carrying lipoprotein particles into cells, thereby regulating cholesterol homeostasis. In the present study we investigated whether the LDL receptor is involved in joint destruction during experimental osteoarthritis both under normal and high cholesterol conditions.

Material and Methods: LDL receptor deficient (LDLR⁻/⁻) mice and their wild type (WT) controls received either a high cholesterol or control diet for 120 days. Experimental osteoarthritis was induced by injection of collagenase into the mice’s knee joints on day 84 and 86. Paraffin sections of total knee joints were stained with safranin-o or haematoxylin-eosin to determine OA development. Synovial activation (1.4 ± 0.2) and cartilage destruction when compared to WT controls. In contrast, mean osteophyte formation was tremendously increased by 345% suggesting that the absence of the LDL receptor induces osteophyte formation in the OA knee joint.