Results demonstrated that for the collagens, MCL scar demonstrated increased mRNA levels for type I, III, and V collagen consistent with previous results [4]. Surprising, the LCL and AM band of the ACL also demonstrated similar changes. The collagen mRNA levels in the PCL did not change significantly.

Fig 2. MMP-13:TIMP-1 Ratio Of Various Ligaments Following MCL/Partial ACL Transection

Uninjured
Injured
*p<0.04

MCL
LCL
AM-ACL
PCL

The RT-PCR results for the collagen types is summarized in figure 1. Results demonstrated that for the collagens, MCL scar demonstrated increased

References:

Introduction: Following injury, ligaments heal through a process similar to that of healing in skin [1]. Although the molecular changes within healing ligaments are well described [2-4], changes within the other periarticular ligamentous structures is not. Indeed for the most part, these ligaments have been largely ignored and have been assumed to remain unaltered. The purpose of this study was to characterize the molecular changes of the ligaments of the knee following medial collateral ligament (MCL) and partial anterior cruciate ligament (ACL) transection. Methods: Five skeletally mature, female suffix/suffix-cross sheep were utilized for the study. The right leg was used as the experimental limb and the left leg as contralateral uninjured control. Through a mid-line incision the MCL was transected at the joint line and the ACL approached through a parapatellar arthrotomy utilizing the same skin incision. The two bands of the ACL (posterolateral (PL), anteromedial (AM)) were identified. The PL band of the ACL was then transected in the midsubstance and allowed to retract. The anteromedial (AM) band and posterior cruciate ligament were left undisturbed. A partial ACL injury was chosen to model a non-destabilizing ACL injury while minimizing the biomechanical effects of a complete ACL injury. The MCL was injured to create an internal control representing extrarticular scar tissue. Following transection there was no evidence of gross instability. Standard closure was performed and the animals were allowed to recover with unrestricted activities. Six weeks following initial surgery the animals were sacrificed with an overdose of Euthynol (MTC Pharmaceuticals: Cambridge, ON). The midsubstance of the MCL scar, lateral collateral ligament (LCL), AM band of the ACL (AM-ACL) and the posterior cruciate ligament (PCL) were harvested and snap frozen in liquid nitrogen. Reverse transcriptase polymerase chain reaction (RT-PCR) was performed as previously described [5] for type I, III, and V collagen, matrix metalloproteinase-13 (MMP-13) and normalized to the housekeeping gene GAPDH using sheep-specific primer sets. Paired t-tests were used to determine differences between injured and uninjured control legs. The ethics review board from our institution approved the study. Results: All animals recovered with no gait disturbance detected after 1 week. At time of sacrifice all MCL’s had healed and there was no evidence of overt injury to the AM-ACL, PCL, or LCL. There was no evidence of cartilage degeneration.

Fig 1. Collagen mRNA Levels For Various Ligaments Following MCL/Partial ACL Transection

Uninjured
Injured
*p<0.05

Col I Col IIICol ICol IIICol ICol IIICol ICol IIICol IVCol ICol IIICol IV

MCL
LCL
AM-ACL
PCL

Discussion: Following ligamentous injury to the knee, the response to injury occurs not only in the injured tissue, but throughout the entire joint. Previous studies on the vascular response to injury have demonstrated increased vascularity of neighboring periarticular tissues (ACL, PCL, LCL, menisci) even following isolated MCL injury [6]. In this study we used a non-destabilizing partial ACL injury model to determine the response of the other ligamentous tissues to a ligament injury. Although the biomechanical influence of this injury cannot be eliminated, we hoped to minimize it by creating a partial injury. As expected, the collagen I, III and V mRNA levels in the MCL increased following injury [4]. However, increased collagen I, III and V mRNA levels in other uninjured ligaments suggests that the knee undergoes a wider response following injury and that there is significant matrix remodelling occurring in tissues other than those directly injured. Indeed the findings are consistent with an anabolic response in uninjured periarticular tissues.

Interestingly, the MMP-13:TIMP-1 ratio was also significantly increased in the AM band of the ACL but not the other ligamentous tissues. With the known action of MMP-13 in collagen degradation [7], increases in this ratio is suggestive of matrix degradation in the remaining portion of the ACL. Thus these findings may provide a mechanism whereby long-term clinical follow-up of partial ACL injuries has demonstrated that 42% of patients develop complete ACL insufficiency [8].

Conclusions: MCL/partial ACL injury to the ovine knee leads to specific changes in type I, III, and V collagen, MMP-13 and TIMP-1 mRNA levels in periarticular ligaments not directly injured. This suggests a wider response to injury even in non-destabilizing injuries and may have implications in the treatment of partial ACL injuries.