

# ACL Healing and Regeneration

L. Yang<sup>1</sup> and K. L. Paul Sung<sup>1</sup>

## 1 Introduction

It is well known that the medial collateral ligament (MCL) has a considerably high healing capacity even without operative repair. Conversely it has been reported that the anterior cruciate ligament (ACL) has a limited healing capacity, in both clinical and animal experimental studies. After ligament-knee injured, the matrix metalloproteinases (MMPs) are heavily involved in processes such as degradation, repair and remodeling of the extracellular matrix (ECM). Our previous studies have shown that the excessive MMPs are involved in the injury and remodeling processes of ACL. Those excessive MMPs will disrupt the delicate neo-tissue process necessary for the ACL repair. To choose the appropriate MMPs inhibitors and evaluate other factor's roles in injured ACL are essential to rescue the injured ACL. Our final goal is to develop a new method to promote healing processes during ACL injury.

## 2 Materials and Methods

In order to find a way to eliminate the MMPs detrimental effects, the following research was designed on the ACL ligament. (A) Two *in vitro* experiments were done to evaluate cellular phenomena: 1) The MMPs activities in constant ACL fibroblast stretch injury. 2) The effect of different signal pathway inhibitors on the MMPs expression. (B) Multiple groups in *in vivo* studies have been designed and performed on 77 Wistar rats by using different combinations of MMPs inhibitors and inflammatory regulators cocktails together with primary suture application.

## 3 Results

The results from our animal studies are very

encouraging and clearly show that our proposed cocktail strategy worked out very well. Our rat study indicated that compared with the normal rat ACL with an average tensile strength of 35 Newton (N), the primary suture (PS) of the injured rat ACL only restored 14% of the normal tensile strength. Administration of MMP inhibitors further restored the tensile strength up to 43%. Administration of specific inflammatory and MMP inhibitors (RXT, RXA, etc) together with PS to the injured rat ACL restored up to 48% of the normal tensile strength. Furthermore, application of growth factors (GFs) with PS and MMP inhibitors restored as high as 84.3% of the normal tensile strength. This indicates that the future cocktail recipe should contain PS, various MMP inhibitors and certain GFs. Our most recent data, by application of higher dosages of GF, the tensile strength of injured ACL is weaker than that of the ACL applied with regular dosage of GF. Besides, more scar tissues were formed around the injured ACL after application of over dosages of GF.

## 4 Discussion

Most clinicians agree that patients with reconstructed ACL or PCL do not possess normal knee functions. With understanding the molecular events involved in the ligament injury, there would be a chance to find a cocktail medicine to help the injured ligament in its healing process, reducing the need of ACL or PCL reconstructions.

---

<sup>1</sup>Departments of Orthopaedics and Bioengineering, University of California at San Diego, La Jolla, CA 92093 USA

