Summary

When surgical intervention is needed to reconstruct a ruptured anterior cruciate ligament (ACL), the hamstring tendons are often harvested and subsequently used as autograft. The harvested hamstring tendons have the potential to regenerate. The main of this thesis was therefore to improve the clinical outcome following harvest of the hamstring tendons through a better understanding of the process of hamstring tendon regeneration.

Chapter 2 summarized the available literature on hamstring tendon regeneration and showed that 70% of the patients have the potential to regenerate their harvested tendons. However, the included studies assessed hamstring tendon regeneration dichotomously, used multiple definitions for tendon regeneration and only evaluated regeneration at a single follow-up period. Therefore, **Chapter 3** evaluated hamstring tendon regeneration rates both 1 and 2 years after harvest using magnetic resonance (MR) imaging. We found that the semitendinosus tendons regenerated in 65.7% and that the gracilis tendons regenerated in 82.9% of the cases. In addition, regenerated hamstring tendons were found to have significantly increased cross-sectional areas and lengths compared to the original tendons. Failure to regenerate and the altered morphological properties might cause clinical symptoms such as posterior thigh pain, cramping and weakness. In this light, it might be interesting to preoperatively identify individuals with poor chances of complete regeneration of the hamstring tendons. **Chapter 4** revealed that aging and smoking were negatively associated with regeneration chances. In addition, it revealed that patients without regeneration reported higher pain scores compared to those with regenerated tendons.

Another well-known factor involved in tissue repair processes is inflammation. **Chapter 5** revealed that polymorphisms within genes encoding inflammatory proteins such as *IL6* and *IL1B* affect the production of structural and fibril-associated extracellular matrix components in a risk-dependent manner. In addition, it was found that these polymorphisms contribute to risk of ACL injuries. Taken this together, these results suggest that *IL6* and *IL1B* might be important factors during the process of hamstring tendon regeneration. In order to direct the inflammatory process, **Chapter 6** focused on the modulation of inflammation using activated STAT-signaling pathways in macrophages. Specific inhibition of activated STAT proteins modulated the inflammatory phenotype, potentially via modulating macrophage phenotypes.

CONCLUDING REMARKS

To conclude, the work in this thesis described the regenerative capacity of hamstring tendons following harvesting procedures. In the future, clinicians should preoperatively inform patients about tendon regeneration, its clinical consequences and possibly alter the choice of graft. Furthermore, this thesis identified potential targets to improve tendon