The effect of mechanical conditioning on the production of collagen degradation enzyme MMP-2

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Introduction

Collagen remodeling (e.g. changes in net turnover, fiber orientation, fiber thickness and length) is an equilibrium of collagen synthesis and degradation, strongly influenced by mechanical straining. In addition, this equilibrium is affected by degradation enzymes, e.g. matrix metalloproteinases (MMPs) and their inhibitors (TIMPs) (figure 1).

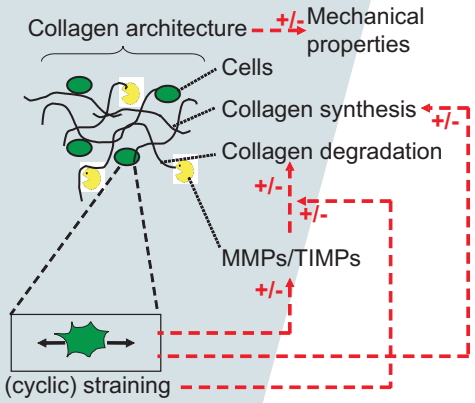

Figure 1 *Strain induced collagen synthesis and degradation by MMPs. Mechanical load also influences the production of MMPs.*

However, no quantitative relationships for collagen remodeling are available. Therefore, the objective of this PhD study is to investigate the relation between mechanical conditioning, the amount and activity of MMPs, collagen architecture and mechanical properties:

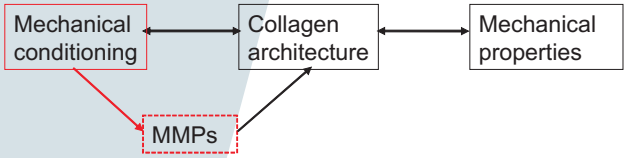

Figure 2 *This poster focusses on the effect of mechanical conditioning on the production of MMP-2.*

Of all MMPs, especially MMP-2 seems to play a key role in the degradation of soft connective tissues [1]. Furthermore, the role of MMP-2 appears to be two fold [2]:

- MMP-2 facilitates a remodeling response associated with cyclic straining
- MMP-2 accumulation contributes to the overal deterioration in mechanical integrity of the constructs when presented in large amounts

Objective

The objective of this study is to investigate the relationship between time, strain and the production of MMP-2. This relationship will be used to optimize conditioning strategies to improve mechanical properties of tissue engineered heart valves.

Material and methods

Human vena saphena cells were seeded on a PGA-P4HB scaffold and mechanically strained for 27 days in a FlexCell setup (figure 3).

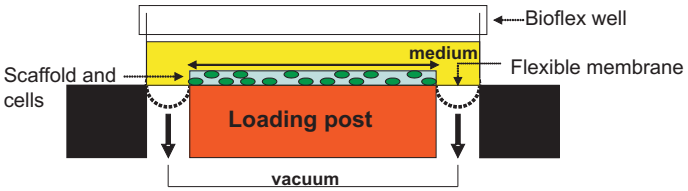

Figure 3 *By applying vacuum, flexible membranes with constructs are sucked inwards and stretched over a loading post.*

The concentrations of MMP-2 in culture media of unattached, attached and 4% dynamically strained constructs were determined after 9, 18 and 27 days by ELISA.

Results

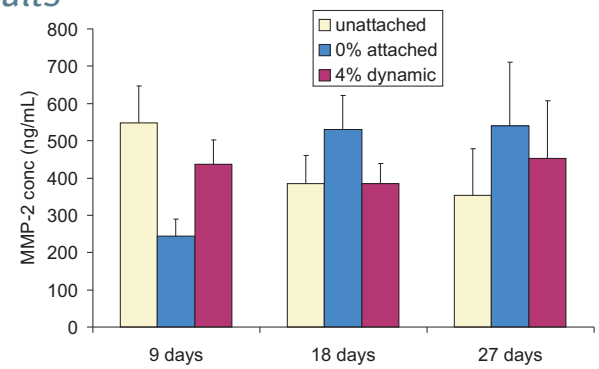

Figure 4 *Concentrations of MMP-2 in culture media of unattached, attached and 4% dynamically strained constructs after 9, 18 and 27 days. No significant changes are observed.*

Conclusion

- No significant changes in MMP-2 concentrations in culture medium were observed in time and upon mechanical loading
- Concentrations and activities of MMPs must also be determined in constructs

Future work

- Optimization of MMP protocols to determine the activity of MMPs in culture medium and in constructs
- Quantification of the relation between time, strain, mechanical properties and MMP activities
- Investigation of the effect of adding a MMP inhibitor on the collagen architecture and mechanical properties

References:

[1] Kerkvliet et al., Matrix Biol. 1999; 18: 373-380
[2] Seliktar et al., Tissue Eng. 2003; 9: 657-666