Research internship in the field of skin regeneration (6 months minimum, MSc student):

Developing signaling scaffolds to combat skin fibrosis after full thickness skin injury in burn wounds

The lab of Willeke Daamen (Radboudumc, RIMLS, Dept. of Biochemistry) is currently investigating type I collagen scaffolds functionalized with anti-fibrotic agents. The goal of these bioactive scaffolds is preventing a fibrotic response after full-thickness skin injuries, e.g. burn wounds, thereby promoting skin regeneration. The internship will focus on the development and *in vitro* characterization of these biofunctionalized collagen scaffolds.

In general terms fibrosis is hallmarked by excessive deposition of matrix, leading to destruction of tissue architecture and thereby compromising normal tissue function. Skin fibrosis may develop after the occurrence of a full-thickness skin injury, when both the epidermis and dermis are damaged. Without clinical intervention, the healing process will result in a fibrotic scar. The key players in the fibrotic response are myofibroblasts, which become trapped in a self-amplifying activation loop (Figure 1). Their activation is mainly controlled by the transforming growth factor beta (TGFβ) pathway. By functionalizing type I collagen scaffolds with growth factors the fibrotic response may be controlled (Figure 2).

This internship will focus on the development and *in vitro* characterization of type I collagen scaffolds functionalized with heparan sulfate mimetics and growth factors. Heparan sulfate (HS) is a major component of the ECM and acts as a protective reservoir for growth factors. HS mimetics have the added benefit of degradation resistance, offering prolonged growth factor protection. The student will produce, characterize and optimize the collagen-HS mimetic scaffolds using various techniques. Several growth factors will be applied to the scaffolds and the ability of these functionalized scaffolds to reduce the fibrotic response *in vitro* will be evaluated.

During the internship the following techniques will be used:

- Production and functionalization of the collagen scaffolds using lyophilization
- Characterization of collagen scaffolds: dot blotting, Alcian Blue staining, SDS-PAGE and Western blotting, immunohistochemistry, scanning electron microscopy
- Quantification of the anti-fibrotic response *in vitro*: culturing of cell lines and primary cells, proliferation assays, SDS-PAGE and Western blotting, immunohistochemistry, gene expression analysis (RT-qPCR), contraction assays

We are looking for a motivated student with a special interest in tissue engineering and preferably with previous internship experiences. Daily supervision will be provided by a PhD candidate, interested candidates are invited to sent a motivation letter and CV to Merel Gansevoort (merel.gansevoort@radboudumc.nl). The intended starting date of the internship is October/November 2022.

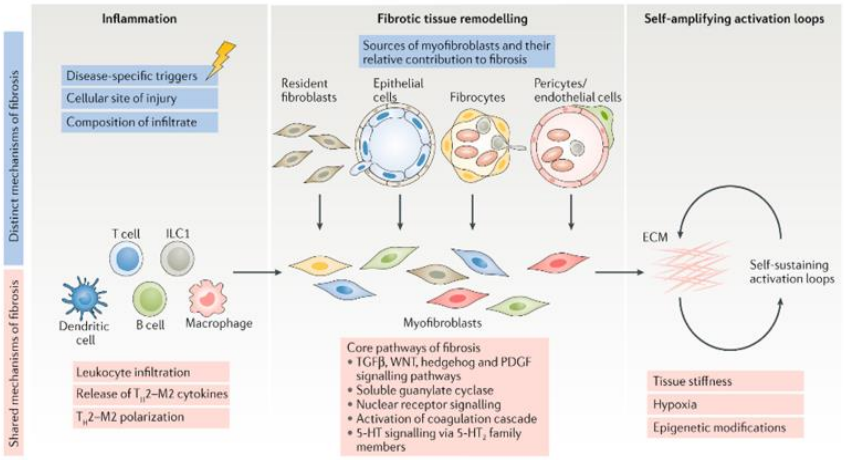

Figure 1. The common mechanism of fibrosis. Distler, J.H.W. (2019). Nat Rev Rheumatol

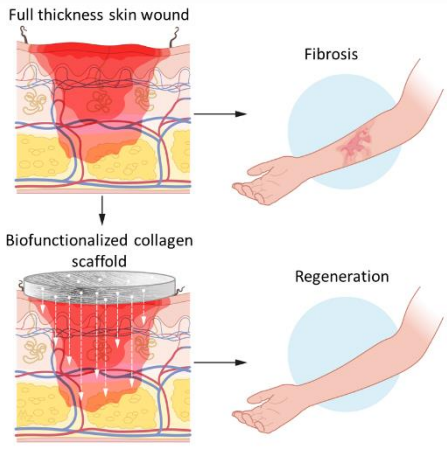

Figure 2. Promoting skin regeneration with biofunctionalized collagen scaffolds. Copyright: Manon Zuurmond, LUMC