Research internship (6 months minimum, MSc student):

Developing spatiotemporal signaling scaffolds with click-to-release chemistry to stimulate skin regeneration

The lab of Willeke Daamen (Matrix Biochemistry workgroup, Dept. of Medical BioSciences, Radboudumc) is currently investigating type I collagen scaffolds functionalized with a click-to-release agent that carries anti-fibrotic compounds. The goal of these 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 scaffolds.

Fibrosis is hallmarked by the excessive deposition of extracellular matrix, leading to the 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. Their activation is mainly controlled by the transforming growth factor beta (TGFβ) pathway. By functionalizing type I collagen scaffolds with anti-fibrotic compounds the fibrotic response may be controlled.

Anti-fibrotic compounds will be added to the collagen scaffolds using a click-to-release linker. Click-to-release chemistry is a relatively novel research field derived from the click-chemistry field, which was awarded the Nobel prize in Chemistry 2022. Click reactions are uniqely suited for use in living systems due to their specificity and rapid reaction rates. The click-to-release linker will release its anti-fibrotic compound only after the addition of an activator: the tetrazine molecule. Click-to-release chemistry allows control over the place (spatio) and time (temporal) of release of the anti-fibrotic compound. The student will produce, characterize and optimize the click-to-release collagen scaffolds. The ability of these functionalized scaffolds to reduce the fibrotic response will be evaluated using an *in vitro* fibrotic model.

During the internship the following techniques will be used:

- Production and functionalization of the collagen scaffolds using lyophilization and chemical conjugations
- Characterization of collagen scaffolds: scanning electron microscopy, high performance liquid chromatography (HPLC), biochemical assays
- Quantification of the anti-fibrotic response *in vitro*: culturing of cell lines and primary cells, proliferation assays, SDS-PAGE and Western blotting, cryosectioning, immunofluorescence assays, gene expression analysis (RT-qPCR).

We are looking for a motivated student with a special interest in chemistry and regenerative medicine/tissue engineering (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 2023.