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A one-step approach for \textit{in situ} cardiovascular tissue engineering

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\textbf{Introduction}

Cardiovascular tissue engineering continues to evolve with the growing global need for appropriate prosthetic cardiac valves and blood vessels. The classic tissue engineering paradigm (fig. 1A) has inherent logistic and economic limitations because of the long throughput time for cell expansion and \textit{in vitro} conditioning [1]. To create a clinically more attractive alternative with off-the-shelf availability, a novel approach of ‘guided tissue regeneration’ is suggested.

With this model system it should be possible to subject small samples to physiological cues, such as pressure, flow, strain and biochemical factors, and to evaluate the individual or combined effects of these cues on cell capture and retention, cell-matrix interactions, cell behavior (viability, proliferation, differentiation) and tissue formation (fig. 4).

\textbf{Aim}

The aim is to develop instructive, synthetic scaffolds for the \textit{in vivo} repopulation by circulating endogenous progenitor cells for heart valves and small diameter arteries, conform a one-step \textit{in situ} tissue engineering approach (fig. 1B).

Primary goal of this study is to explore cell-scaffold interactions under bio-mimicking conditions.

\textbf{Study approach}

\textbf{Model system}

A model system will be developed to investigate the one-step approach \textit{in vitro} using simple tissue geometries (fig. 2). The model system should allow for high-throughput, relatively simple, reproducible experiments on a variety of (bioactive) scaffold materials (fig. 3).

\textbf{Thrombogenicity}

Flow chamber experiments will be performed to evaluate platelet activation on a range of scaffold materials. Platelet activation will be used as an important measure, since this is considered to be the first instigator of the foreign body reaction and thrombogenic cascade [4]. Short-term implantation of scaffold patches in an animal model will be performed to form a first indicative onset towards preclinical testing.

\textbf{References}


\textbf{Figure 1:} The classic tissue engineering paradigm (A) versus the novel one-step approach (B).

\textbf{Figure 2:} Strip of P4HB-coated PGA scaffold seeded with ovine saphenous vein derived myofibroblasts with fibrin as a cell carrier.

\textbf{Figure 3:} Schematic representation of a supramolecular polymer with incorporated bioactive moieties [2]. ‘Smart’ functionalized biomaterials can be synthesized using an elegant method based on non-covalent hydrogen bonds via so-called UPy-units, allowing for tunable material properties [3].

\textbf{Figure 4:} Schematic representation of the model system. Small strips of scaffold material are subjected to a pulsatile medium flow (Q) containing progenitor cells. A pressure difference (\(\Delta p\)) can be applied over the scaffold to mimic the diastolic phase. The setup is mounted on a confocal microscope for imaging analyses.