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My research interest is mainly in the field of vascularization of tissue engineered constructs employing hydrogels for the self-assembly of endothelial and mural cells. Results of this research will be translated mainly to cardiac tissue generation. In addition, decellularization of native tissues e.g. small vessels, and characterization of retrieved matrices is another area of research.

## "Cardiovascular tissue engineering based on natural matrices"

As the shortage of human donor organs and tissues for transplantations will persist or even increase in future, research on alternatives is pursued. Tissue engineering (TE) offers a possible solution by generating functional tissue *in vitro* for the reconstruction of failing organs. TE is based on three columns: (1) cells, which fulfill the actual function of the desired tissue, (2) matrices, which offer a 3-dimensional scaffold, and (3) growth factors, which mimic a natural environment and support cell survival and function.

Applied matrices need to comply with basic requirements, such as: (1) biocompatibility, (2) biodegradability, (3) support of cell adhesion, proliferation, migration, survival and differentiation (4) mimicking the extracellular tissue matrix (ECM) of the desired tissue (i.e. mechanical properties, fiber alignment, etc.)

The tissue engineering group in the LEBAO focuses on the use of biological (collagen, fibrin) and decellularized tissue matrices (small intestinal submucosa (SIS), vessels, heart valves) for cardiovascular tissue engineering.

One main research topic is the generation of cardiac tissue based on hydrogels made from human collagen or fibrin cast on decellularized SIS. In natural tissues, the nutrition of cells and removal of waste products is facilitated by a dense capillary network which is generated during development. This perfusion system is also indispensable for tissue formation *in vitro* to generate tissues of clinically relevant dimensions. Without a functional perfusion system, survival of the TE constructs relies solely on the slow process of diffusion. Therefore, rebuilding a perfusable, dense capillary network for the nourishment of metabolic highly active cardiomyocytes (or other target cells) will be mandatory for envisioned clinical application. In addition, sites for anastomosis to the host circulatory system for immediate perfusion with blood after transplantation need to be implemented.

The second topic comprises the generation of xenogeneic, decellularized heart valves for transplantation. Decellularized allogeneic heart valves, which are already investigated in extensive multi-centric clinical trials, seem to provide an optimal valve substitute, exhibiting long-lasting durability, physiologic hemodynamic properties, and the ability of adaptive growth processes. However, due to a substantial lack of human donor valves, alternatives have to be found. A simple transfer of decellularization protocols from the allogenic setting to xenogeneic matrices generated scaffolds, that failed in clinical studies. Failure is most likely attributed to an immune response to xeno-antigens still present on the matrix. Removal of these xeno-antigens will be mandatory for successful application of such matrices in the clinic.