Editorial

Vascularization, Regeneration and Tissue Engineering

Highly organized microvascular networks, consisting of arterioles, capillaries, and venules, are fundamental elements of living tissues. They are essential for the transport of oxygen, nutrients, and metabolic waste products and, thus, for the maintenance of physiological tissue homeostasis. Accordingly, angiogenesis, i.e., the development of new blood vessels from pre-existing ones, is crucially involved in regenerative processes, such as wound healing and the engraftment of transplanted skin. In addition, restitution of nutritive perfusion and prevention of ischemia-associated complications are major prerequisites for the survival of surgical flaps. An adequate vascularization further determines the success of modern tissue engineering approaches. Hence, sophisticated strategies are currently under investigation to ensure a rapid and sufficient blood supply to bioengineered tissue substitutes. These strategies include the stimulation of blood vessel formation by pro-angiogenic factors as well as the generation of preformed microvascular networks within tissue constructs, which can be connected to blood vessels of the host tissue by means of inosculation or surgical anastomosis.

This special topic issue of *European Surgical Research* highlights the importance of vascularization for different processes and approaches in the field of regenerative medicine and tissue engineering. Sorg et al. describe angiogenesis as a major hallmark of wound healing and emphasize the fact that it can be divided into a pro-angiogenic phase with excessive formation of poorly differentiated microvessels and an anti-angiogenic phase, which is characterized by vessel maturation and regression. The deep understanding of the underlying mechanisms regulating these phases may contribute to the development of novel concepts in wound treatment and the prevention of wound healing disorders. Frueh et al. review the dynamic process of skin graft vascularization from the clinician's perspective. They further introduce promising adipose tissue-based approaches to enhance the vascularization of dermal substitutes and finally address the importance of a functional lymphatic drainage for the successful engraftment of skin substitutes. Schmauss et al. present the most common flap models in rodents with a detailed description of their surgical preparation and a balanced

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discussion of their advantages and disadvantages in flap research. Although these models may not perfectly mimic the clinical situation in humans due to species-specific discrepancies in vascular anatomy, they provide valuable insights into flap physiology and contribute to the establishment of treatment strategies for the protection of flaps from critical ischemia and ischemia-reperfusion injury. Lang et al. focus on the application of platelet-rich plasma and associated products as autologous cell culture supplements or as a rich source of pro-angiogenic and regenerative growth factors for tissue engineering. Besides the many advantages for clinical practice, the authors also address important critical issues regarding the routine use of platelet-derived preparations, such as the lack of standardized preparation methods and the large variability of growth factor concentrations in individual samples. Komae et al. report on a highly sophisticated scaffold-free approach for the fabrication of vascularized myocardial tissue. By combining cell sheet technology, microfluidics, and induced pluripotent stem cells, they are successful in generating pulsating human myocardial tissue, indicating that even the engineering of complex organs, such as the heart, may become a reality in the future. Finally, Weigand et al. provide an in-depth overview of the arteriovenous loop technique for the engineering of axially vascularized tissue. They not only describe the principal method and mechanisms behind axial vascularization, but also the multiple experimental and clinical applications of this promising vascularization approach.

Taken together, the contributions to this special topic issue impressively demonstrate the rapid progress in regenerative medicine and tissue engineering. Continuous research on basic mechanisms of blood vessel formation and further development of innovative vascularization strategies pave the way for novel therapies that will be beneficial for many patients.

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