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Delivering life's blood: emerging technologies, current opportunities and challenges

Editorial overview - Biological engineering

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Engineering functional tissue constructs with clinically relevant dimensions faces a fundamental challenge of exchanging nutrients and oxygen to satisfy their metabolic needs. A viable strategy for vascularization is critical for engineering viable tissues and organs [1]. Vascularization also plays an important role in the initiation and progression of many pathologies such as cancer [2] and cardiovascular disease [3]. Vascularization is an area where tissue engineering, an inherently multidisciplinary field, can greatly benefit from chemical engineering. The strength of chemical engineers in process design has led to the development of novel biomaterials that can be mechanically and chemically tailored to mimic the extracellular matrix in native tissues [4], and in some cases induce the formation of vascular network. Considerable amount of work has been devoted to the incorporation of growth factors within these biomaterials to induce angiogenesis, *in vitro* and following implantation. Incorporation of microcirculation within engineered tissues is another crucial parameter for establishing functional vascular supply of oxygen and nutrients [5]. The knowledge of bioreactor design offered by chemical engineers combined with the emergence of microtechnologies has enabled the fabrication of perfusable microscale conduits within biocompatible scaffolds. This strategy allows control of the architecture of the microvascular network and enables immediate perfusion of the scaffolds.

In keeping with the theme of this issue of *Current Opinion in Chemical Engineering*, we invited contributions on current approaches to engineering vasculature, *in vitro* and *in vivo*. The reviews we present to you cover two broad areas: (i) engineering approaches for inducing blood vessel formation and (ii) microfluidic strategies for *in vitro* vascularization.

Identifying suitable cell sources, designing scaffolds that mimic the arterial mechanical properties, and regulating the functional state of the cells of the vessel wall are among the current challenges in the creation of a functional vasculature. Truskey *et al.* discuss these challenges in the context of tissue-engineered blood vessels, in their critical review of the current approaches to the repair or replacement of injured blood vessels. Along the same direction, Gui and Niklason review state-of-the-art technologies that have been successfully implemented in clinical trials. They cover a range of novel approaches in creating perfusable vascular networks with emphasis on the use of stem cells in generating endothelial cells. They show that the use of stem cells combined with advanced biomaterials has a great potential to enhance the tissue regeneration [6]. Hutton and Grayson review stem cell-based methods for the formation of vascularized bone grafts, toward the development of effective and biomimetic approaches in bone regeneration.

Engineering and Medical Sciences at Columbia University. She directs the Laboratory for Stem Cells and Tissue Engineering. She serves as a scientific director of the Columbia University Stem Cell Core, Craniofacial Regeneration Center, and Stem Cell Imaging Core. Gordana obtained a PhD in chemical engineering at the University of Belgrade in Serbia where she stayed on faculty and became Full Professor in 1993. After 12 years at MIT, she joined Columbia University in 2005. She has been a visiting professor in Israel, Netherlands, Serbia and several universities in the USA, adjunct professor at Tufts University, and a visiting scientist at MIT. The focus of her research is on engineering functional human tissues for regenerative medicine and study of development and disease. She is a Fellow of the American Institute for Medical and Biological Engineering, a Fellow of the Biomedical Engineering Society, a founding Fellow of the Tissue Engineering and Regenerative Medicine Society, and a member of the Women in Technology International Hall of Fame, New York Academy of Science, Academia Europaea, Serbian Academy of Sciences and Arts, and the National Academy of Engineering.

Blood vessel maturation, which involves proper interaction of endothelial cells with vascular smooth muscle cells (pericytes), is another crucial factor for creating tissue constructs for clinical applications. Proper understanding of the cellular and molecular basis of vessel maturation is essential for the life cycle of blood vessels. Blinder *et al.* focus on the role of novel biomaterials and microtechnologies in producing functional, perfusable vascular networks *in vitro*. The insight gained from these studies is not only applicable to tissue engineering, but also paves the path toward developing effective strategies for pro-angiogenic and anti-angiogenic therapies.

The survival of any engineered tissue highly depends on its microcirculation and the capacity of the construct to integrate with the existing recipient circulation. Moya and George discuss current advances in the formation of functional microvessel networks *in vitro*. They discuss organ-specific functional and structural characteristics of vasculature for four distinctly different organs: lung, brain, liver, and muscle.

The emergence of microscale and nanoscale technologies is now facilitating the development of innovative platforms for tissue engineering applications. Biomimetic microsystem with the ability to reconstitute the functionality of organs has been demonstrated as powerful and low-cost alternatives to animal models for drug screening and toxicology applications [7]. The application of microfluidic systems to study the effect of physiochemical cues on the vascular formation and function has recently drawn tremendous attention. Smith and Gerecht review innovative fabrication techniques utilized for studying spatiotemporal dynamics of vascular cell behavior, providing biomimetic data on the effect of oxygen and shear stress levels on the sprouting of microvessels into the matrix.

Tien discusses the physical principles enabling the formation of stable vasculature using microfluidic systems. He also provides an overview of existing computational models that have been developed for the design and optimization of microfluidic vascular systems. Within the same theme but on another topic, Santoro *et al.* explain the use of microfluidic systems to study the effect of fluid flow on cancer progression, by monitoring biological processes with high spatiotemporal resolution and improving our understanding of tumor microenvironment.

References

1. Bae H *et al.*: **Building vascular networks**. *Sci Transl Med* 2012, **4**:160ps23.
2. Hanahan D, Weinberg RA: **The hallmarks of cancer**. *Cell* 2000, **100**:57-70.
3. Battegay E: **Angiogenesis: mechanistic insights, neovascular diseases, and therapeutic prospects**. *J Mol Med* 1995, **73**:333-346.
4. Annabi N *et al.*: **25th anniversary article: rational design and applications of hydrogels in regenerative medicine**. *Adv Mater* 2013, **26**:85-124.
5. Koike N *et al.*: **Tissue engineering: creation of long-lasting blood vessels**. *Nature* 2004, **428**:138-139.
6. Bianco P, Robey PG: **Stem cells in tissue engineering**. *Nature* 2001, **414**:118-121.
7. Huh D *et al.*: **Reconstituting organ-level lung functions on a chip**. *Science* 2010, **328**:1662-1668.