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Building Blocks for Biofabricated Models

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Biofabrication is a rapidly evolving field of research in which a broad range of automated manufacturing processes are implemented to either directly print cells and materials, or bio-assemble cell-containing building blocks, into three dimensional (3D) constructs.[1] Bioprinting inherently requires a bioink, which can be defined as "a formulation of cells suitable for processing by an automated biofabrication technology that may also contain biologically active components and biomaterials".[2] Materials that are suitable for bioprinting represent an important bottleneck of the field and have thus been a focus area of biofabrication research,[3] resulting in a growing variety of available bioink formulations applicable for different cell types and fabrication technologies. Biofabrication holds great promise for developing in vitro models or implantable constructs that mimic the complexity and functionality of native tissues and organs. It should, however, be noted that the field is maturing, and with the growing number of available materials and fabrication strategies, it is now entering the next level that focuses on the fabrication and evaluation of more complex cell-material constructs as stepping stone on the way to biologically functional tissue models.

This special issue on "Building Blocks for Biofabricated Models" has a focus on material and technological building blocks that are tailored for the fabrication of 3D tissue models. It contains 12 original and two review articles. To highlight the portfolio of different biofabrication technologies available to deposit cells and biomaterials as a toolbox to fabricate organised cell-laden structures, an overview is provided for the engineering of bone tissue. (See article number 1801048). Moreover, as bioreactors are an essential technological aspect of biofabrication to mature fabricated tissue constructs, this is reviewed for the field of cardiac tissue engineering (see article number 1701504).

The application oriented bioink development is exemplified by the study of Kelly et al., (see article number 1801501), who developed a bioink formulation based on decellularized cartilage extracellular matrix (ECM). Combining the deposition with a reinforcement strategy based on printed PCL fibers, constructs were generated that mimick cartilage both biochemically and mechanically. A similar strategy was followed by Yoo et al., (see article number 1800992) who developed a photo-crosslinkable kidney ECM-derived bioink and demonstrated that this material has beneficial effects on renal tissue formation. A new strategy for the biofabrication of bone tissue is presented by Gelinsky et al., (see article number 1801512) and involves the 3D plotting and functional release of growth factors. The same group employed an alginate/methylcellulose hydrogel-blend for the 3D bioprinting of functional islets of Langerhans (see article number 1801631).

A complementary technological building block was developed by Wallace et al., who present a novel co-axial printing platform that focuses on the fabrication of implantable islet-containing constructs (see article number 1801181). In general, the portfolio of different biofabrication technologies to deposit cells and biomaterials is rapidly expanding and providing us with a growing toolbox to fabricate organised cell-laden structures,

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(see article number 1801048). This does not only allow for the generation of specific tissues but also can address the tissue-interfaces (see article number 1800806). Additionally, the integration or convergency of biofabrication technologies with different resolutions/length scales into a single process, as shown by Malda et al. for hydrogel plotting and melt electrowriting, is extending the control over the design of the living 3D construct (see article number 1800418). As demonstrated by Dalton et al., high resolution-printed biomaterial scaffolds are also valuable building blocks for tissue models. In particularly as they can serve as a three-dimensional positioning guides during bioassembly of cell-containing building blocks (see article number 1801326). For specific the interaction of the scaffold structure with cells and cell containing building blocks, a permanent hydrophilization and surface bioactivation of such scaffolds is deemed to be an important aspect (see article number 1801544).

Bioreactors can facilitate the maturation of more complex tissues, as for example described for cardiac tissue (see article number 1701504). Moreover, mechanical stimulation can also be an important aspect for maturation, as is highlighted by Swieszkowski et al. for the evolution of stem cell-loaded hydrogel yarns towards tendon-like tissue (see article number 1801218). Generation of functional tissue structures is the next frontier in biofabrication and while the field is moving towards this goal, the application of specific tissue models is becoming a reality (see article number 1801019). Better mimicking the in vivo environment through the control over the fabricated structures, as well as the culture environment will further accelerate these developments. Clearly, there are already reports of the implantation of the first functional tissue structures (see article number 1800983).

Taken together, the studies presented in this Special Issue demonstrate that biofabrication is evolving from the development of material and technological building blocks towards the fabrication of more complex and functional 3D cell-material constructs. This underscores the growth of this young field and its potential impact on healthcare.

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