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Crosslinkable gelatins - From Innovative Chemistry and Valorization of Bioinks towards Human Trials: Utopia or Reality?

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Biofabrication is a specific area within the field of tissue engineering which takes advantage of rapid manufacturing (RM) techniques to generate 3D structures which mimic the natural extracellular matrix (ECM). A popular material in this respect is gelatin, as it is a cost-effective collagen derivative, which is the major constituent of the natural ECM. The material is characterized by an upper critical solution temperature making the material soluble at physiological conditions. To tackle this problem, covalent crosslinking is realized by functionalizing gelatin with (photo-)crosslinkable functionalities. In this respect, methacrylamide-functionalized gelatin (gel-MA/gel-MOD) currently is the gold standard. However, gel-MA poses some important limitations with regard to network homogeneity and processing capabilities exploiting laser-based additive manufacturing (AM). As a result, we have developed mono- and bifunctional (patented) crosslinkable gelatin derivatives which offer distinct advantages (e.g. solubility at room temperature) for various AM techniques. The hydrogels support processing with digital light projection, multiphoton lithography (2PP) and extrusion-based additive manufacturing. Furthermore, they are suited to encapsulate a.o. adipose tissue-derived stem cells and to support differentiation into different lineages (e.g. adipogenic and osteogenic). The gelatin derivatives offer a unique opportunity to serve a plethora of tissue engineering (TE) applications (including ocular, adipose, bone, etc.) and some gelatins are currently being valorized by a spin-off company as bioink constituents. In addition to their in vitro biocompatibility assessment, we also performed in vivo animal trials (mice) which indicated that the implanted constructs actively stimulate vascularization. Currently, the regulatory trajectory towards first in-human trials of an injectable crosslinked bifunctional gelatin to serve adipose tissue engineering applications is ongoing.

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