Bioprinting of spheroid-based cartilage constructs

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Valorization

The valorization potential of this research can be analyzed regarding the clinical and potential commercial relevance. First, the concepts described in the present thesis are of great significance to be also applied in the clinical environment. Analyzing the use of uniform spheroids produced by a robust microwell array insert (Chapter 2), the clinical relevance should be emphasized not only to be employed to develop tissue engineering and regenerative medicine strategies, but also to other fields. 3D cell culture has tremendous advantages to mimic the microenvironment of healthy tissues and organs, as well as pathological tissues such as solid tumors [43, 44]. These can be used for drug screening, efficacy, and cytotoxicity trials of tumor models [45–47]. Besides cancer research, other examples of clinical relevance are to elucidate mechanisms related to congenital and infectious diseases [48–50] and to reproduce the human system on a miniaturized scale [51] combining or not high-throughput platforms [52] or microfluidic techniques [53], among others.

In addition, analyzing the use of tissue-like constructs (Chapter 3), clinical relevance regards also the possibility of generating more realistic implants, when compared to cell monolayers or single cells suspended in hydrogels, to be applied on translational medicine. Interesting studies already demonstrated the production of bioprinted spheroid-loaded constructs focused on clinical research [13, 15]. Employing the extrusion bioprinting process with spheroid-loaded bioinks, constructs with intended homo- or heterogeneity spheroid architectural distribution can be obtained. In addition, this approach allows to reproduce specific tissues and biological microenvironments with refined control and reproducibility, which are crucial to be applied on clinical trials and translational medicine both in healthy [54] and disease [28] conditions.

The lack of reproducibility of experimental models can reflect variations of performance in clinical trials. Indeed, mouse-based models are still among the most currently used because they are highly standardized [55]. Thus, the research focused on the development of more realistic and reproducible 3D tissue-like constructs using the techniques demonstrated in the present thesis aim to help in the translation from the bench to the bedside [14, 34, 56, 57]. In addition, these approaches are in accordance with the principle of replacing and reducing the use of animals in pre-clinical research, which has been strongly recommended by regulatory agencies worldwide [58].
Finally, the commercial relevance of the present thesis is demonstrated in Chapter 5, in which we present an analysis comparing the implementation of four types of microwell array inserts to obtain spheroids (three commercial systems, and our proprietary device developed in-house, presented in Chapter 2). Through a bioprocess economics perspective, the results demonstrated the flexibility and affordability of the microwell array devices, in terms of reaching high yields of spheroids with high control of diameter and shape. The resulting case study provided evidence of the attractiveness of the use of the developed in-house device in cell culture laboratories, small companies, and start-ups considering both qualitative parameters and detailed cost analysis.

References


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