Shell engineering in soft alginate-based capsules for culturing liver spheroids

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Authors

Xuan Peng Željko Janićijević Sandy Lemm Markus Laube **Jens Pietzsch** Michael Bachmann Larysa Baraban

Abstract

Functional interaction between cancer cells and the surrounding microenvironment is still not sufficiently understood, which motivates the tremendous interest for the development of numerous in vitro tumor models. Diverse parameters, for example, transport of nutrients and metabolites, availability of space in the confinement, etc. make an impact on the size, shape, and metabolism of the tumoroids. We demonstrate the fluidics-based low-cost methodology to reproducibly generate the alginate and alginate-chitosan microcapsules and apply it to grow human hepatoma (HepG2) spheroids of different dimensions and geometries. Focusing specifically on the composition and thickness of the hydrogel shell, permeability of the microcapsules was selectively tuned. The diffusion of the selected benchmark molecules through the shell has been systematically investigated using both, experiments and simulations, which is essential to ensure efficient mass transfer and/or filtering of the biochemical species. Metabolic activity of spheroids in microcapsules was confirmed by tracking the turnover of testosterone to androstenedione with chromatography studies in a metabolic assay. Depending on available space, phenotypically different 3D cell assemblies have been observed inside the capsules, varying in the tightness of cell aggregations and their shapes. Conclusively, we believe that our system with the facile tuning of the shell thickness and permeability, represents a promising platform for studying the formation of cancer spheroids and their functional interaction with the surrounding microenvironment.