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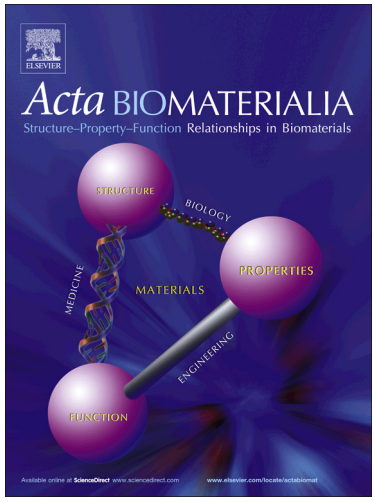

Review article

Engineering Cell Aggregates through Incorporated Polymeric Microparticles

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Engineering Cell Aggregates through Incorporated Polymeric Microparticles

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Abstract: *Ex vivo* cell aggregates must overcome significant limitations in the transport of nutrients, drugs, and signaling proteins compared to vascularized native tissue. Further, engineered extracellular environments often fail to sufficiently replicate tethered signaling cues and the complex architecture of native tissue. Co-cultures of cells with microparticles (MPs) is a growing field directed towards overcoming many of these challenges by providing local and controlled presentation of both soluble and tethered proteins and small molecules. Further, co-cultured MPs offer a mechanism to better control aggregate architecture and even to report key characteristics of the local microenvironment such as pH or oxygen levels. Herein, we provide a brief introduction to established and developing strategies for MP production including the choice of MP materials, fabrication techniques, and techniques for incorporating additional functionality. In all cases, we emphasize the specific utility of each approach to form MPs useful for applications in cell aggregate co-culture. We review established techniques to integrate cells and MPs. We highlight those strategies that promote targeted heterogeneity or homogeneity, and we describe approaches to engineer cell-particle and particle-particle interactions that enhance aggregate stability and biological response. Finally, we review advances in key application areas of MP aggregates and future areas of development.