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ACCEPTED MANUSCRIPT

Epithelial-mesenchymal crosstalk influences cellular behavior in a 3D alveolusfibroblast model system

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Keywords: Alveolar epithelium, Fibroblast, Co-culture, Hydrogel, Cancer, Matrix metalloproteinases

Abstract

Interactions between lung epithelium and interstitial fibroblasts are increasingly recognized as playing a major role in the progression of several lung pathologies, including cancer. Three-dimensional *in vitro* co-culture systems offer tissue-relevant platforms to study the signaling interplay between diseased and healthy cell types. Such systems provide a controlled environment in which to probe the mechanisms involved in epithelial-mesenchymal crosstalk. To recapitulate the native alveolar tissue architecture, we employed a cyst templating technique to culture alveolar epithelial cells on photodegradable microspheres and subsequently encapsulated the cell-laden spheres within poly(ethylene glycol) (PEG) hydrogels containing dispersed pulmonary fibroblasts. A fibroblast cell line (CCL-210) was co-cultured with either healthy mouse alveolar epithelial primary cells or a cancerous alveolar epithelial cell line (A549) to probe the influence of tumor-stromal interactions on proliferation, migration, and matrix

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