



RECIPROCAL INDUCTION OF TUBULOGENESIS AND VASCULOGENESIS BY MOUSE EMBRYONIC KIDNEY MESENCHYMAL AND URETERIC BUD PROGENITOR CELLS IN 3-DIMENSIONAL CO-CULTURE.

Category: Differentiation of Stem Cells

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Kidney development is regulated by a coordinated reciprocal induction of metanephric mesenchymal (MM) and ureteric bud (UB) cells during organ development. In this study, isolated MM and UB progenitor cell lines were recombined in 3-dimensional Matrigel implants in SCID mice. Differentiation potential was examined for changes in phenotype, structural organization, and the presence of specialized marker proteins using bright-field, immunofluorescence, and electron microscopy. Both cell types, when grown in matrigel as homogenous populations were monodisperse throughout the matrix. Additionally, the UB cells formed infrequent 2-3 cell spheroids. When UB and MM cells were combined in implants, they organized into abundant well-defined cysts and tubuloid structures consisting of a polarized epithelium with lumens, frequently surrounded by peripheral "satellite" cells often in capillary-like structures. Tracker experiments using PKH fluorescent cell linkers indicated the tubuloid structures were derived primarily from UB cells and the satellite cells were derived from MM cells. The epithelial cells stained for pancytokeratin, the apical junctional complex protein- ZO-1, and the basement membrane protein collagen type IV, as well as for UB and collecting duct markers- RET, D. biflorus, EndoA cytokeratin, and Aquaporin 2. Satellite cells stained for α -smooth muscle actin, vimentin, WT1, and Aquaporin 1, an early marker of cell migration and vasculogenesis. By EM, the epithelium exhibited well-developed specialized features including apical vacuoles, microvilli, junctional complexes, and basement membranes. Satellite cells featured mesenchymal and endothelial phenotypes characterized by attenuated cytoplasm in frequent capillary-like structures showing lumens lined by endothelial-like cells and occasional pericytes. UB cells grown as homogenous populations underwent tubulogenesis in the presence of conditioned medium derived from MM cells. However, UB conditioned medium failed to induce MM differentiation. These studies indicate that tubulogenesis and vasculogenesis can be partially recapitulated *in situ* by recombining individual MM and UB cell lineages, providing an excellent model to conveniently study a variety of topics in renal development.

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