Transport by Renal Tubule Cell Bioreactor Is Dependent on Extracellular Matrix Choice

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Background:
Renal tubule cell bioreactors are of interest for in vitro disease models, high-throughput drug and toxicity testing, and renal replacement therapy. The parameter space to be exploited in optimizing in vitro cell phenotype is extensive. There are several commercially available extracellular matrix preparations available to facilitate cell-scaffold attachment, leading to the question of whether any one matrix was associated with particular phenotypic features.

Methods:
Primary human renal tubule cells (HRTC) were grown to confluence on Transwell inserts preincubated with Collagen IV, Collagen I, Laminin, Matrigel, or fibronectin, with and without 50 uM ascorbic acid. TEER and inulin leak rates were measured to verify confluence. Apicobasal volume transport was measured in the presence and absence of ouabain, an inhibitor of basolateral sodium-potassium ATPase.

Results:
HRTC grew to confluence on all substrates. Inulin leak rates were not different from a control well bearing an impermeable substrate. Transport rates were different in the presence and absence of ouabain ($p = 5.6 \times 10^{-10}$ by ttest). Transport rates differed between matrices ($p=0.006$ by one-way ANOVA). Fibronectin and laminin displayed highest volume transport. When cells were cultured in the presence of ascorbic acid, transport was not significantly different between substrates ($p > 0.08$ by one-way ANOVA).

Conclusions:
Choice of extracellular matrix substrates influences apicobasal transport in bioreactors, but adding cofactors for basement membrane synthesis to the culture medium abolishes differences arising from initial matrix choice.