Fluid Shear Stress Alters Primary Renal Tubule Epithelial Cell Phenotype

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Background:

Primary cells cultured *in vitro* gradually lose features characteristic to the *in vivo* cell type, variously termed "senescence" or "culture stress". Culture conditions that help maintain cell-specific phenotype are advantageous. Here we evaluated the impact of applying apical fluid shear stress on the phenotype of primary kidney tubule epithelial cells.

Methods:

Renal tubule epithelial cells were isolated from donor kidneys not suitable for transplant. Cells were cultured on Transwell inserts under static conditions or on an orbital shaker at a rotation frequency producing fluid shear stresses of 2 dyn/cm^2. Transepithelial resistance was measured daily. After 2 weeks in culture, expression of tubule-specific markers was measured by PCR and western blot. Mitochondria were counted in TEM sections.

Results:

Shear stress significantly increased steady state transepithelial resistance from 284±23 to 477±20 Ω-cm^2 ($p<0.001$) and resulted in significantly increased gene expression of tubule epithelial cell-specific markers (GGT1, COL4A1, COL4A2, ITCH, and PEX14) with fold increases in expression of 4.9±0.2, 5.6±0.6, 3.4±0.2, 2.6±0.6, and 2.3±0.4, respectively. Cells grown under shear also showed increased protein expression of gamma glutamyl transpeptidase.

Discussion:

Primary cells grown under physiologic levels of fluid shear stress appear to express proximal tubule markers more than cells grown in static conditions. This may be due to increased nutrient delivery and waste removal with improved mixing at the apical brush border, or due to specific gene regulation related to mechanotransduction. Further mechanistic insight may allow investigators to develop more accurate *in vitro* models of disease.