

**P026** Functional Differences between the Isoforms of Rho with Respect to Epithelial–Mesenchymal Transition and Proliferation of Proximal Tubule Epithelial Cells.  
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Increasing evidence suggests that the interstitial fibroblasts responsible for Renal Fibrosis are derived from tubular epithelium by the process of epithelial to mesenchymal transition (EMT). We have developed a model of EMT in order to delineate the relative contributions of the functionally distinct Rho (A, B and C) isoforms to this process.

In the human proximal tubule cell line HKC8, transforming growth factor-beta (TGF-beta) is responsible for the relocalization of filamentous actin from the cell cortex to striated structures identified as stress fibres, resulting in a more mesenchymal phenotype. Specifically silencing RhoC, but not RhoA or RhoB, with short interfering RNA (siRNA) inhibits the dissolution of cortical F-actin and subsequent stress fibre formation. However, concomitant to the reorganization of the cytoskeleton, RhoB knock-down reduces cell-cell contact.

Furthermore, we find that specifically ablating RhoC with siRNA reduces the rate of proliferation in HKC8 by 30% ( $p < 0.01$ , ANOVA). The silencing of RhoA and RhoB also reduces growth, but to a lesser extent (15% and 23% respectively). Renal fibrosis is a proliferative disease, and as such Ras-related proteins such as Rho are likely to be of paramount importance in its pathogenesis.