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From single molecule to single tubules

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Biological systems often make decisions upon conformational changes and assembly of single molecules. *In vivo*, epithelial cells (such as the mammary gland cells) can respond to extracellular matrix (ECM) molecules, type I collagen (COL), and switch their morphology from a lobular lumen (100-200 micron) to a tubular lumen (1mm-1cm). However, how cells make such a morphogenetic decision through interactions with each other and with COL is unclear. Using a temporal control of cell-ECM interaction, we find that epithelial cells, in response to a fine-tuned percentage of type I collagen (COL) in ECM, develop various linear patterns. Remarkably, these patterns allow cells to self-assemble into a tubule of length $\sim$ 1cm and diameter $\sim$ 400 micron in the liquid phase (i.e., scaffold-free conditions). In contrast with conventional thought, the linear patterns arise through bi-directional transmission of traction force, but not through diffusible biochemical factors secreted by cells. In turn, the transmission of force evokes a long-range ($\sim$ 600 micron) intercellular mechanical interaction. A feedback effect is encountered when the mechanical interaction modifies cell positioning and COL alignment. Micro-patterning experiments further reveal that such a feedback is a novel cell-number-dependent, rich-get-richer process, which allows cells to integrate mechanical interactions into long-range ($>$ 1mm) linear coordination. Our results suggest a mechanism cells can use to form and coordinate long-range tubular patterns, independent of those controlled by diffusible biochemical factors, and provide a new strategy to engineer/regenerate epithelial organs using scaffold-free self-assembly methods.