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Sensing Traction Force Induces Cell-Cell Distant Communications for the Rapid Network Assembly of Airway Smooth Muscle Cells

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Abstract: The collective functions at cell population level rely on cell-cell communications with or without direct contacts [1-3]. The long-range biomechanical force propagating across certain scales far beyond single cell size may reserve the capability to trigger coordinative biological responses within cell population [3-5]. Whether and how cells communicate with each other mechanically in a distant manner remains largely to be explored. Airway smooth muscle (ASM) cells are one crucial component in providing mechanical support and contraction force for the bronchial tubes in respiratory system, whereas the mechanical property of ASM is also associated with asthma attack, and during airway hyper-responsiveness, ASM cells maintain prolonged contraction force to prevent air flow through the bronchial tubes [6]. In this work, we found that ASM cells can rapidly self-assemble into a well-constructed network incorporating nearly all the cells on the culturing surface of 3D matrigel mixed with type I collagen (COL I), which requires the collective functions and coordination of thousands of cells completed within 12-16 hours. This process requires the long-range mechanical forces across the extracellular matrix (ECM) to direct cell-cell distant interactions. We further found that single ASM cells can rapidly initiate multiple buds accurately pointing to neighbor cells in distance, which relies on cell traction force and force-transmission across ECM. Beads tracking assay also demonstrates the long-range transmission of cellular traction force to distant locations on the matrix. Cells are able to sense each other in distance to move directionally on both non-fiber matrigel and in a much more efficient way on matrigel mixed with COL I. Though cells can't form stable network on matrigel only, we found that cells are able to recruit COL I from the hydrogel to build nearly identical COL I fiber network to stabilize the cell network. Our results revealed that ASM cells can sense the traction force transmitted through ECM to initiate distant communications and rapidly coordinate the network self-assembly at the population level. As an interesting phenomenon, cells sound able to 'make phone call' via the role of mechanical force.

Keywords: Long-range biomechanical force; extracellular matrix; cell-cell distant communication; airway smooth muscle cells; traction force sensing

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