Inhibition of Cell-Cell Adhesion Randomized Epithelial Chiral Morphogenesis on Micropatterned Surfaces

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The development of the vertebrate body plan with left-right (LR) asymmetry (also known as handedness and chirality) requires the emerging chiral morphogenesis of epithelial cells at specific embryonic stages. In this process, cell-cell adhesions coordinate cellular organization and collective cell migration, and are critical for the directional looping of developing embryonic organs such as chicken cardiac tubes. However, the underlying biophysical mechanism is not yet well understood. Here we modeled normal and delayed epithelial LR symmetry breaking with patterned epithelial chiral morphogenesis on microscale lines with various widths. The patterned cells exhibited biased migration wherein those on opposing boundaries migrated in different directions. Disrupting adherens junctions with ethylene glycol tetraacetic acid (EGTA) resulted in a decrease in velocity difference in opposing boundaries as well as the associated biased cell alignment, along with an increase in the overall random motion. Altering the distance between the opposing boundaries did not significantly alter alignment, but significantly disturbed the velocity profile of the cell migration field. The further examination of cell polarity indicated that disruption of adherens junctions did not affect cell polarization on the boundaries, but decreased the transmission of chiral bias into the interior region of the epithelial cell sheet. Overall, our results demonstrated the dependence of the scale of collective cell migration on the strength of cell-cell adhesion, and its effects on the chirality of a multicellular structure through mediating cell polarity in the vicinity of geometric boundaries. This study demonstrated that our 2D microscale system provides a simple yet effective tool for studying LR symmetry breaking, and possibly for fetal drug screening to prevent birth defects.