Cell Handedness in Development and Disease

Abstract: Cell chirality (also known as handedness and left-right (LR) asymmetry) is an intrinsic capability of the cell telling left from right. The development of the vertebrate body plan with left-right asymmetry requires the emerging chiral morphogenesis at multicellular levels at specific embryonic stages. Changes in orientation of the LR axis due to genetic or environmental factors can lead to malformations and disease. However, the concept of cell chirality has never studied in detail until the recent development of novel engineering tools. We demonstrate that the cultivation of cells on micropatterned 2D surfaces and in 3D graded hydrogels reveals an intrinsic cellular LR asymmetry, which is dependent of cell phenotype and actin cytoskeleton. With these new tools, we examine the role of cell chirality on the embryonic development of cardiac LR asymmetry as well as the barrier function of endothelium layers. We find that Protein Kinase C (PKC) activation reverses the inherent chirality from clockwise to counter clockwise in engineering systems. Interestingly, activation of PKC signaling reverses the directional bias of chick cardiac C-looping. Mediating endothelial cell chirality can regulate the permeability of endothelial layers. Overall, our results strongly suggest critical roles of cell chirality in cardiovascular development and disease.

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