Single cell chirality regulated by alpha-actinin-1

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Abstract

The establishment of a left-right axis during development is essential for the left-right patterning of our internal organs. A strong association between chirality and cytoskeleton dynamics has been observed. Alpha-actinin-1 is an actin-binding protein that forms an antiparallel homodimer capable of crosslinking F-actin filaments. Here, we demonstrate the development of actomyosin chirality during actin cytoskeleton self-organization within cells grown on circular fibronectin islands. This chiral pattern is characterized by the unidirectional tilting of symmetrical radial actin fibers that are polymerized by formin from focal adhesions. The subsequent centripetal movement of contractile transverse actin fibers along the radial fibers acquires a tangential component that resembles a swirling motion. Remarkably, the chiral pattern exhibited a defined handedness. This handedness could be reversed by overexpressing full-length alpha-actinin-1. Overexpression of a truncated alpha-actinin-1 mutant, where the actin binding domain was deleted, failed to reverse this chirality. This suggests that the F-actin-crosslinking function of alpha-actinin-1 is essential to reverse chirality. We propose a model whereby the handedness of the chiral pattern depends on the intrinsic helical symmetry of actin filaments and filament polarity. In this case, the filament barbed ends are capped by formins immobilized at peripheral focal adhesions. As F-actin polymerization progresses, the filaments rotate unidirectionally, relative to the formins. This rotation translated to a counter-clockwise swirling of the transverse fibers. Increased F-actin crosslinking by alpha-actinin-1 inhibits filament rotation, resulting in an accumulation of torsional strain. A periodic rotation of the filaments in the opposite direction to the rotation of unconstrained filaments may relax this strain, thereby promoting clock-wise swirling. Our results suggest a scenario whereby alpha-actinin-1 can regulate single cell chirality by varying the degree of F-actin-crosslinking.