The role of phospholipid flippase in myotube formation

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Myoblast fusion and subsequent establishment of cell polarity in myotubes are fundamental steps to build skeletal muscle fibres. Distribution of phospholipids is thought to be tightly controlled during myoblast fusion events, despite dramatic alterations in the membrane structure. However, it is obscure how changes in phospholipid distribution govern the processes involved in myotube formation. Here we show that one of phospholipid flippases which catalyze translocation of phospholipids from the outer to the inner leaflets of the plasma membrane, is crucial for determination of the morphology in myotube formation. Deficiency in the genes encoding the main as well as the auxiliary subunits of phospholipid flippases caused formation of aberrantly enlarged myotubes, owing to uncontrolled myoblast fusions and impaired actomyosin assemblies underneath the plasma membrane. Mechanistically, we found that the phospholipid flippase was required for activation of one of mechanosensitive ion channels, thereby augmenting accumulation of phosphorylated myosin regulatory light chain underneath the plasma membrane. Thus, we propose a novel mechanism: phospholipids' distribution *via* phospholipid flippase positively regulates the mechanosensing machinery that is required for morphogenesis during myotube formation.