Synopsis of Original Research Paper

Role of phospholipid translocases in skin repair

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Membrane repair is the fundamental process that is essential for maintaining the homeostasis of live cells. Phospholipids' distribution has been thought to be dramatically changed during membrane repair, but the detailed mechanisms underlying the membrane repair is still elusive. To elucidate the role of phospholipids' distribution in membrane repair, we have focused on phospholipid flippase that can translocate specific phospholipids from the outer to the inner leaflets of biological membranes, thus generating asymmetric distribution of phospholipids. We first established cell lines lacking phospholipid flippase by the CRISPR/Cas9 system, and performed membrane damage assays using a membrane-impermeable dye (FM1-43) or GFP-tagged membrane repair proteins expressed in the phospholipid flippase-deficient cell lines. Phospholipid probes were also utilized to elucidate the role of phospholipids' localization in membrane repair. Our results revealed that continuous influx of FM1-43 was observed in phospholipid flippase-deficient lines after introduction of membrane damages. Accumulation of one of membrane repair-related proteins to damaged sites was affected in the flippase-deficient cells, suggesting that the membrane repair was affected by deficiency in the phospholipid flippase. Moreover, during the course of this project, we identified PIEZO1, a mechanosensitive cation channel that is activated by membrane tension, as a downstream target of phospholipid flippase-dependent phopsholipids' localization. Our results indicate that phospholipid flippase plays a role in the membrane repair system, thus providing the therapeutic strategies for a variety of diseases including skin diseases.