Optogenetic Mechanostimulation of ER in Live Cells Reveals ER Mechanosensitivity

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The ability of cells to perceive and respond to mechanical cues is essential for numerous biological activities. Emerging evidence indicates important contributions of organelles to cellular mechanosensing and mechanotransduction. However, whether and how ER senses and reacts to mechanical forces remains elusive. To fill the knowledge gap, after developing an ER-specific optogenetic mechanostimulator, we reveal that mechanostimulation of ER elicits a transient and rapid efflux of Ca2+ from ER, which is dependent on the cation channels TRPV1 and PKD2. This mechanostimulation-induced ER Ca2+ release can be repeatedly stimulated, and can be tuned by varying the intensity and duration of force application. Moreover, mechanostimulation of ER inhibits ER-to-Golgi trafficking, and sustained mechanical stimuli on ER can induce ER stress. Our results provide direct evidence for ER mechanosensitivity and the tight mechanoregulation of ER functions.