Piezo1 is essential for cell remodeling on micropatterns

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Adherent cells are able to integrate the mechanical input from the substrate, such as patterns, features and stiffness, to modify their shape, movement, and cytoskeletal tension. We have previously shown that HEK293 cells grown on microprinted fibronectin stripes developed elongated shape. We speculated that Piezo1 could be the key element that detects the confinement at the substrate and facilitate cells' remodeling. We tested Piezo1 knockout HEK cells (P1KO) on the same patterns, and found that P1KO cells were not able to stretch to the full extent on the stripes compared with wild-type. By following GFP-tagged Piezo1 in permanently transfected HEK cells during their stretching, we found that the substrate confinement promoted punctuate Piezo1 plaques to translocate to the extrusion edges in a cell during cell expansion. In comparison, Piezo1 were mostly located on the nuclear envelope in non-stretching cells. To access whether Piezo1 functions as Ca^{2+} permeable ion channels, we inhibited Piezo1 channels using specific and non-specific MSC inhibitors, GsMTx4 and Gd^{3+}, and both inhibited cells' expansion on the pattern, suggesting Piezo1 channels are activated during cell spreading. These results demonstrate that Piezo1 plays an essential role in cells' response to the mechanical inputs from the local environments.