DIFFERENTIAL RHOA ACTIVITY IN CHONDROCYTES UNDER FLOW

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Mechanical force environment is a major factor that influences cellular homeostasis and remodeling. The prevailing wisdom in this field demonstrated that a threshold of mechanical forces or deformation was required to affect cell signaling. However, we hypothesized that RhoA activities can be either elevated or reduced by selecting different levels of shear stress intensities. To test this hypothesis, a fluorescence resonance energy transfer (FRET)-based approach was used. The result revealed that C28/I2 chondrocytes exhibited an increase in RhoA activities in response to high shear stress (10 or 20 dyn/cm^2), while they showed a decrease in their RhoA activities to intermediate shear stress at 5 dyn/cm^2. No changes were observed under low shear stress (2 dyn/ cm^2). The observed two-level switch of RhoA activities was closely linked to the shear stress-induced alterations in actin cytoskeleton and traction forces. In the presence of constitutively active RhoA (RhoA-V14), intermediate shear stress suppressed RhoA activities, while high shear stress failed to activate them. Collectively, these results here suggest that intensities of shear stress are critical in differential activation and inhibition of RhoA activities in chondrocytes.