PTEN Regulates pMoesin and F-actin to Control Cellular Morphology

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Proper cellular morphology and plasma membrane structure during interphase are integral for proper mitosis and homeostasis. Tumor suppressor PTEN (Phosphatase and TENsin homologue deleted on chromosome 10) is involved in regulating genome stability and cell survival. Moesin is an ERM (Ezrin/Radixin/Moesin) protein that regulates the cell cortex and membrane structure via interaction with the F-actin cytoskeleton. PTEN is reported to suppress pMoe (phosphorylated Moesin) and impair plasma membrane/F-actin bridging: PTEN deficient cells exhibit Moe hyperphosphorylation and dislocation to the cell center and inversely lowered F-actin levels with peripheral fortification. Further investigation showed that the absence of PTEN is demonstrated to cause abnormal cell rounding and F-actin fortification at the cell cortex due to disorganization of the actin cytoskeleton. The mechanism of the atypical cell structure, F-actin fortification, and F-actin/pMoe mislocation is revealed to be cortical actin hyperpolymerization. Specifically, chemical inhibition of actin polymerization by actin blocker Cytochalasin-D restored pMoe and F-actin distribution and cell shape to a wild-type level. To explore the different manifestations of PTEN deficiency, different mutant cell lines were evaluated for protein expression of pMoe. The data revealed that specific genetic alterations of PTEN decrease pMoe expression while total PTEN knockout increases pMoe expression. The elucidation of a novel perspective of PTEN function in actin cortex remodeling and exploration of PTEN mutation variance unveils key mechanisms behind the cell microenvironment and provides insight that may inform precise therapeutic strategies against cancer.

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