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Protein phosphatase 1B dephosphorylates Rho guanine nucleotide dissociation inhibitor-1 and suppresses cancer cell migration and invasion

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Rho GTPases control a wide range of cellular processes and their deregulation is associated with promotion of an aggressive and metastatic tumor phenotype in human cancers. Rho guanine nucleotide dissociation inhibitor-1 (RhoGDI1) plays a key role in regulating the activity of Rho GTPases. However, the underlying mechanisms are still unclear. In this study, we showed that, protein phosphatase 1B (*PPM1B*) interacts with RhoGDI1 and functions as its phosphatase. Ectopic expression of *PPM1B* results in dephosphorylation of RhoGDI1 and thereby, abates the activation of RhoA, Rac1 and CDC42 by epidermal growth factor (EGF). *PPM1B* overexpression in Hs578T and SKBR3 human breast cancer cells increases their motility and invasiveness *in vitro* and cancer metastasis *in vivo*. In contrast, knockdown of *PPM1B* in MCF-7 and MDA-MB-468 human breast cancer cells that express endogenous *PPM1B* enhances EGF-induced RhoGDI1 phosphorylation, activation of Rho GTPases and cancer cell migration and invasion. Knockdown of RhoA or Rac1 by siRNA reverses the enhanced cell migration seen after *PPM1B* depletion. Collectively, these results indicate that *PPM1B* negatively regulates cancer cell motility and invasiveness through dephosphorylating RhoGDI1.

Biography

Hee Gu Lee has conducted an extensive research on production and application of antibodies for functional analysis of cancer related genes at the Immunotherapy Convergence Research Center of Korea Research Institute of Bioscience and Biotechnology, Daejeon, South Korea.

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