RHO protein GDP dissociation inhibitor

RHO protein GDP dissociation inhibitor of Rho proteins (rho GDI), regulates GDP/GTP exchange.

The protein plays an important role in the activation of the oxygen superoxide-generating NADPH oxidase of phagocytes.

Glioma stem cells (GSCs) are a subset of tumor cells that drive glioma initiation and progression. The molecular mechanisms underlying the maintenance of glioma stem cells are still poorly understood.

Wu et al., investigated the role of Rho GDP dissociation inhibitor α (RhoGDIα) in GSCs. RhoGDIα was down-regulated in glioma stem cells. Over-expression of RhoGDIα suppressed the self-renewal and tumorigenesis of GSCs. Further data showed that RhoGDIα inhibited the transcription activity of stem cell marker Oct4. Moreover, inactivation of ROCK1, a downstream effector of RhoGDIα, also decreased the self-renewal and Oct4 transcription activity, and rescued the effects caused by RhoGDIα knockdown. The results indicate that RhoGDIα is involved in the maintenance of GSC [1)].

Rho GDP dissociation inhibitor α (ARHGDIA) as a target mRNA that binds to PCBP2, and we uncovered the role of ARHGDIA as a putative metastasis suppressor through analyses of in vitro and in vivo models of EMT and metastasis. Furthermore, we demonstrated that ARHGDIA is a potential target of miR-151-5p and miR-16 in gliomas. The interaction between PCBP2 and the 3'UTR of the ARHGDIA mRNA may induce a local change in RNA structure that favors subsequent binding of miR-151-5p and miR-16, thus leading to the suppression of ARHGDIA expression. PCBP2 may facilitate miR-151-5p and miR-16 promotion of glioma cell migration and invasion through mitigating the function of ARHGDIA. [2)].

β8 integrin and PTP-PEST form protein complexes at the leading edge of migrating cells and balance patterns of Rac1 and Cdc42 signaling by controlling the subcellular localization and phosphorylation status of Rho GDP dissociation inhibitor 1 (RhoGDI1). Translocation of Src-phosphorylated RhoGDI1 to the cell's leading edge promotes local activation of Rac1 and Cdc42, whereas dephosphorylation of RhoGDI1 by integrin-bound PTP-PEST promotes RhoGDI1 release from the membrane and sequestration of inactive Rac1/Cdc42 in the cytoplasm. Collectively, these data reveal a finely tuned regulatory mechanism for controlling signaling events at the leading edge of directionally migrating cells [3)].

Silencing β8 integrin in human GBM cells leads to impaired tumor cell invasion due to hyperactivation of the Rho GTPases Rac1 and Cdc42. β8 integrin coimmunoprecipitates with Rho-GDP dissociation inhibitor 1 (RhoGDI1), an intracellular signaling effector that sequesters Rho GTPases in their inactive GDP-bound states. Silencing RhoGDI1 expression or uncoupling integrin αvβ8-RhoGDI1 protein interactions blocks GBM cell invasion due to Rho GTPase hyperactivation. These data reveal for the first time that αvβ8 integrin, via interactions with RhoGDI1, regulates activation of Rho proteins to promote GBM cell invasiveness. Hence targeting the αvβ8 integrin-RhoGDI1 signaling axis might be an effective strategy for blocking GBM cell invasion [4)].

Abnormal expression of peroxiredoxin 6 and rho GDP dissociation inhibitor alpha may be associated with malignant transformation in oligodendroglioma and these proteins might be candidates of molecular predictive factors [5].

1)
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