ABSTRACT

Up-regulation of the Mps one binder proteins-2 (mob2) gene enhances human fibrosarcoma cells migration by increasing matrix metalloproteinases expression

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Background: Fibrosarcoma (fibroblastic sarcoma) is a malignant mesenchymal tumor. Tumor malignancy is associated with several cellular properties including proliferation and ability to metastasize. Mps one binder (mob) proteins are important components to control cellular processes, such as cell proliferation, cell migration, morphogenesis, and apoptosis. In present study, we found overexpression of mob2 in fibrosarcoma (HT-1080 cells) increased migration and expression of matrix metalloproteinase (MMP)-2 and MMP-9.

Materials and Methods: Mob2-mediated MMP-2 and MMP-9 expression was assessed by qPCR and Western blot analysis. The mechanisms of action of mob-2 in different signaling pathways were studied using Western blotting. Knockdown of proteins was achieved by transfection with siRNA.

Results: Mob2-mediated cell migration and MMPs expression were reduced by pretreatment with inhibitors of phosphatidylinositol 3-kinase (PI3K) and AKT, as well as the NFκB inhibitor and the IκB protease inhibitor. In addition, mob-2 induced phosphorylation of PI3K/AKT and resulted in increased NFκB-luciferase activity.

Discussion: These results suggest that mob2 activated PI3K/AKT, which in turn activated IκKα/β and NFκB, resulting in increased MMP-2 and MMP-9 expression and migration in human fibrosarcoma cells.