Differentiation-inducing factor-1 attenuated cellular motility of BRAF^V600E mutation bearing malignant melanoma cells via altering mesenchymal features

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We reported that differentiation-inducing factor-1 (DIF-1) inhibited the proliferation of various cancer cells including malignant melanoma and that DIF-1 prevented lung colony formation in a mouse model of metastatic melanoma. However, the mechanisms of this action remain to be elucidated. In the present study, we investigated the anti-metastatic effects of DIF-1 in human BRAF^V600E mutation bearing malignant melanoma A2058 cells. Activities of cell migration and invasion were measured by the wound healing assay and cell invasion assay, respectively. Activities of cell adhesion to extracellular matrix (ECM) were measured by using ECM-coated plate. Expression levels of signaling molecules were measured by Western blotting. DIF-1 suppressed the phosphorylation levels of signal transducer and activator of transcription 3 and subsequently reduced a variety of genes related to mesenchymal features such as matrix metalloproteinase-2, vimentin, N-cadherin and twist. DIF-1 also suppressed a variety of genes related to cell-matrix adhesion such as focal adhesion kinase, Src, paxillin. Consequently, DIF-1 inhibited cell migration, invasion and adhesion to ECM. These results suggested the possibility that DIF-1 suppresses the detachment of malignant melanoma cells from the primary tumor by inhibiting mesenchymal features which exhibit aggressive and metastatic phenotypes.