Differentiation-inducing factor-1 exhibits anti-metastatic effects by inhibiting cellular motility and adhesion in malignant melanoma cells

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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 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) and vascular endothelial cells were measured by using ECM-coated plate and human umbilical vein endothelial cells (HUVECs). Expression levels of signaling molecules were measured by Western blotting. DIF-1 suppressed the phosphorylation levels of signal transducer and activator of transcription 3 (STAT3) and subsequently reduced a variety of genes related to cell migration and invasion such as matrix metalloproteinase-2, vimentin, N-cadherin and twist, resulting in the inhibition of cell migration and invasion. Further, DIF-1 inhibited the melanoma cell adhesion to ECM and HUVECs. These results suggested that DIF-1 suppresses the detachment of cancer cells from the primary tumor by inhibiting cell migration and invasion, and also prevents circulating cancer cells from adhering to vascular endothelial cells. Therefore, DIF-1 may have potential to be a lead chemical compound for developing a novel anti-metastatic agent against malignant melanoma.