DJ 1 upregulates breast cancer cell invasion by repressing KLF17 expression

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Abstract:

Background: DJ 1 PARK7 was reported as an oncogene in a Ras-dependent manner. Recent studies have shown that DJ 1 stimulates cell proliferation, cell invasion, and cancer metastasis. However, the molecular mechanism by which DJ 1 induces cancer cell invasion and metastasis remains unclear. Methods: Breast cancer cells were transfected with DJ 1 siRNA or DJ 1 overexpression to investigate the effect of DJ 1 on KLF17 expression. ID 1 luciferase promoter assay was performed to evaluate DJ-1-dependent KLF17 expression changes. In addition, Epistasis analysis of DJ 1 and KLF17 was performed to evaluate their regulatory interactions. Ras inhibitors were pretreated to determine whether DJ 1 regulates cell invasion in a Ras-dependent manner. Results: In the present study, we found increased DJ 1 expression in highly invasive breast cancer cells as compared with nonmetastatic cells. Furthermore, DJ 1 promoted breast cancer cell invasion by downregulating E cadherin and increasing Snail expression. Interestingly, exogenous DJ 1 overexpression markedly decreased mRNA and protein expression of KLF17, the EMT negative regulator. These data were confirmed by ID 1 promoter activity, which is directly regulated by DJ-1-dependent KLF17 transcription factor. Epistasis analysis showed that KLF17 overexpression overcomes increased cell invasion by DJ 1, suggesting that KLF17 might be one of the downstream signalling molecules of DJ 1. Acceleration of cell invasion by DJ 1 was alleviated by Ras inhibitors, suggesting that DJ 1 cooperates with Ras to increase cell invasion.

Keywords:

DJ 1 PARK7, breast cancer cells, invasion, epithelial–mesenchymal transition (EMT), KLF17, ID-1, Ras

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