Low doses of Paclitaxel repress breast cancer invasion through DJ₁/KLF 17 signalling pathway

Ismail Ahmed Ismail, Gamal H El-Sokkary, Saber H Saber

Abstract:

Paclitaxel (taxol) is an important agent against many tumours, including breast cancer. Ample data documents that paclitaxel inhibits breast cancer metastasis while others prove that paclitaxel enhances breast cancer metastasis. The mechanisms by which paclitaxel exerts its action are not well established. This study focuses on the effect of paclitaxel, particularly the low doses on breast cancer metastasis and the mechanisms that regulate it. Current results show that, paclitaxel exerts significant cytotoxicity even at low doses in both MCF-7 and MDA-MB-231 cells. Interestingly, paclitaxel significantly inhibits cell invasion and migration, decreases Snail and increases Ecadherin mRNA expression levels at the indicated low doses. Furthermore, paclitaxel inhibiting breast cancer metastasis is associated with downregulation of DJ₁ and ID₁ mRNA expression level with a concurrent increase in KLF17 expression. Under the same experimental conditions, paclitaxel induces KLF17 and concurrently represses ID₁ protein levels. Our results show for the first time that paclitaxel inhibits breast cancer metastasis through regulating DJ₁/KLF17/ID₁ signalling pathway; repressed DJ₁ and ID₁ and enhanced KLF17 expression.

Keywords:

breast cancer metastasis - DJ₁ - KLF17 - paclitaxel

Published In:

Clinical and Experimental Pharmacology and Physiology, Vol.45, PP.961-968