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Transcriptome Analysis of Doxorubicin Resistance in Cancer Cell Lines: Breast Cancer (MCF7), Osteosarcoma (SaOS-2) and Neuroblastoma (SKN-SH390).

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Introduction

Tumor adaptation to biological responses of chemotherapy causes failure of treatment which subsequently leads to tumor relapse. Thus, acquisition of multidrug resistance for several anticancer agents that are structurally and mechanistically unrelated is one of the major obstacles in chemotherapy and is described as “the single most common reason for discontinuation of a drug". For each anticancer agent, more than one mechanism of resistance have been suggested in available evidence.

Objective

This study aimed to identify common pathways of resistance among different tumor cell lines toward single anticancer agent, which is Doxorubicin.

Methods

The resistant Breast cancer (MCF7), Osteosarcoma (SaOS-2) and Neuroblastoma (SKN-SH390) cell lines were developed by stepwise increase of Doxorubicin concentrations over a period of 12 months. The alterations in genes expression obtained from Affymetrix microarrays and were subjected to Ingenuity pathway analysis (IPA).

Results

Findings showed distinct alterations at the genetic level in some central cancer pathways like the tumor suppressor pathway PTEN. Some biological functions exhibited molecular shifts as well like downregulation of cell to cell signaling pathway molecules.

Conclusion

We conclude that inhibition of PTEN pathway is suggested to be associated with doxorubicin resistance. Thus, pharmacological agents could be used to selectively target PTEN affected genes. Further investigations on the upstream regulator molecules and their target genes could serve as new treatment targets that circumvent doxorubicin resistance.

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