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Resveratrol modulates expression of ABC transporters in non-small lung cancer cells: Molecular docking and gene expression studies

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Multidrug resistance (MDR) is one of the most common causes of relapse in cancer chemotherapy. Inhibition of ABC transporters to reverse MDR is a promising approach to enhance the efficacy of cancer chemotherapy. It was investigated the effect of Resveratrol (RSV) on the membrane transport function and the expression of proteins involved in the multidrug resistance in NCI-H460 cells. The membrane transport function was determined using Rhodamine 123 staining. The mRNA expression level of *MDR1*, *LRP*, *MRP2*, *ABCC1*, *ABCC2* and *ABCC3* genes were detected by qRT-PCR and P-glycoprotein (P-gp) expression was detected by western blot analysis. In silico docking studies revealed that RSV possesses greater binding affinity with TMD region of P-gp. In this study, RSV pretreatment significantly enhanced Paclitaxel (PTX) antiproliferative effect in NCI-H460 cells. The Rhodamine 123 drug efflux studies revealed that there was a significant transport function inhibition by RSV treatment and moderate transport function inhibition by PTX. Further, RSV treatment significantly decreased the mRNA expression levels of various ABC transporters genes. Furthermore, expression of P-gp was found to be down regulated during RSV treatment. It was also found that this enhanced anticancer efficacy of RSV was associated with PTX-induced cell arrest in the G2/M phase of cell cycle. Interestingly, significantly enhanced antiproliferative effect, transport function inhibition and down regulation of ABC transporters in RSV-PTX combination group was observed. This might be due to additive or synergistic effect of RSV with PTX in NCI-H460 cells. Thus, the present findings illustrate the modulatory role of RSV on PTX sensitization in resistant NCI-H460 cells.

Biography

S Karthikeyan has completed his PhD in Biochemistry from Annamalai University, Chidambaram and is currently working as ICMR-Post-Doctoral Fellow at Regional Medical Research Centre, Belgaum, India. He has published all his research findings in reputed journals and has served as a resource person in two National level workshops. He is currently looking at the effect of phytochemicals on chemosensitization in cancer cells and is his prime research interest. He is actively involved in the identification of MDR modulators from natural sources and will pursue the long term goal of development of effective chemomodifier to be applicable in health care and clinical oncology.

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