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Different effect of tunicamycin on expression of proteins involved in cell cycle regulation in relation to P-glycoprotein presence in L1210 cells

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The development of multidrug resistance (MDR) is a real problem in the treatment of leukemia. Cells with developed MDR phenotype are resistant to a wide variety of drugs, which differ in structure and mechanism of action. One of the most often occured resistance mechanisms represents expression/efflux activity of P-glycoprotein (P-gp). Expression of P-gp in L1210 cells, besides its efflux activity, leads to changes in some metabolic and regulatory pathways homeostasis. We focused on changes in expression of selected proteins, known as cell cycle regulators, after culturing P-gp negative S- and P-gp positive R- and T-variants of L1210 cells in medium containing tunicamycin (Tun). Tun induced an increase in the proportion of S cells in the G1 phase of the cell cycle. In contrast similar behaviors were not detected either in R or in T cells. Moreover, both resistant cell variants exerted elevated levels of cyclin D1 and E1 when compared with S cells. In contrast, expression of p53 on mRNA levels is less pronounced in R and T cells than in S cells. We did not detect p53 at the protein level in both resistant cell variant. While S cells express common variant of mRNA for p21, this protein is expressed in R and T cells from a differently spliced form. However, further study is needed to to understand in details the processes involved in the differences in response of S and R/T) cells induced by tun.

Keywords: multidrug resistance, P-glycoprotein, cell cycle, p53 and p21

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