CELL CYCLE MODULATES PGP EXPRESSION IN L EUKEMIA CELLS

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P-Glycoprotein (Pgp) is an ATP-dependent efflux pump that, owing to a loss of regulatory mechanisms, is overexpressed in resistant tumor cells, characterizing the Multidrug Resistance (MDR) phenotype. In tumor cells Pgp is upregulated during G0/G1 arrest, moreover Pgp expression is also negatively regulated by fast cell division velocity. The aim of this work was to analyse Pgp expression, in a time dependent manner, trying to establish a correlation between cell cycle and Pgp expression in three distinct tumor cell lines, resistant or sensitive to chemotherapic drugs. Using flow cytometry, the cell lines K562, and the K562-derived cell lines Lucena-1 and FEPS (both overexpressing Pgp) were stained with an anti-Pgp antibody. Additionally, cell cycle analysis were performed via the quantification of nuclear DNA, as well as cell duplication time. Pgp expression and activity was negative in K562, while Lucena-1 and FEPS cell lines showed a high activity and expression of this protein (the later showing a two-fold increase over the cell line Lucena-1). Furthermore, analysing the speed of cell cycle, we observed that Lucena-1 displayed a faster cycle than FEPS. These results suggest a correlation between the speed and phase of cell cycle and Pgp expression, possibly denoting a regulation of Pgp by cell cycle in leukemic cells.

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