

P032 Effects of serum-deprivation, PI3-kinase inhibition and cisplatin exposure on P-PKB, Puma and Bcl-X_L expression in malignant mesothelioma cells

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PI3-kinase and protein kinase B (PKB) activation is involved in chemotherapy resistance of malignant mesothelioma. Phosphorylated PKB (P-PKB) can inhibit apoptosis via regulation of Bcl-2-family proteins. We examined the effect of serum deprivation, PI3-kinase-inhibition with LY294002 (LY), and cisplatin exposure on cell survival and expression of P-PKB and the Bcl-2 family proteins Puma (pro-apoptosis) and Bcl-X_L (pro-survival) in a human malignant mesothelioma cell line (P31wt) and its cisplatin-resistant sub-line (P31res1.2). Protein expression was determined with Western blotting, and apoptosis induction with TUNEL-staining.

After 72 h exposure, only cisplatin reduced cell viability and induced apoptosis. Serum deprivation inhibited P-PKB up to 6 h in P31wt, but not in P31res1.2. Expression of Puma was inhibited, and Bcl-X_L was reduced in both cell lines. A 50 μM LY exposure inhibited P-PKB in P31wt, but only up to 2 h in P31res1.2. However, after 6 h both Puma and Bcl-X_L expression was reduced in both cell lines. Cisplatin reduced expression of the proteins in both cell lines.

Conclusively, it was difficult to inhibit P-PKB in P31wt, and more so in P31res1.2. Low levels of P-PKB seemed sufficient for cell survival, and could explain the observed down-regulation of Puma.