

P019 PI3K/AKT-dependent activation of cAMP-response element binding (CREB) protein in Jurkat T leukaemula cells treated with TRAIL

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We recently demonstrated the paradoxical activation of PI3K/AKT survival pathway in Jurkat T leukaemula cells known for their sensitivity to the cytotoxic action of TNF-Related Apoptosis Inducing Ligand (TRAIL)/Apo2L. The present investigation was done to elucidate the role of cAMP-response element binding (CREB) protein in this system. **Jurkat T cells were treated** with 100-1000 ng/ml TRAIL for time intervals up to 24 h in the presence or absence of selective pharmacologic inhibitors of PI3K/AKT (LY294002) or p38/MAPK (SB253580) pathways. Upon TRAIL treatment, a dose-dependent increase in the percentage of apoptotic cells as well as in caspase-3 activity was observed. Western blot analysis showed an early (1 h) increase in CREB phosphorylation at Ser¹³³ which was reduced upon pre-treatment with LY294002 or SB253580, demonstrating the PI3K/AKT- and p38/MAPK-dependency of this effect. The parallel analysis in immunofluorescence demonstrated the nuclear translocation of the phosphorylated form upon treatment with 100 ng/ml TRAIL, whereas the immune labelling was mainly detectable in the cytoplasm compartment upon the higher more cytotoxic dose. These results let us hypothesize that a failure in CREB activation can be a player in the complex crosstalk among pro- and anti-apoptotic pathways in this peculiar cell model.