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**L-ASCORBIC ACID AND ARSENIC TRIOXIDE SYNERGISTICALLY  
REPRESS CONSTITUTIVE ACTIVATION OF NF- $\kappa$ B AND COX-2  
EXPRESSION IN HUMAN ACUTE PROMYELOCYTIC LEUKEMIA,  
HL-60**

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Eukaryotic nuclear transcription factor, NF- $\kappa$ B and cyclooxygenase-2 (COX-2) has been implicated in pathogenesis of many human diseases including tumor and are known to be activated by various external stimuli. Recently, increasing evidences have supported that L-ascorbic acid (LAA) is selectively toxic to some types of tumors at pharmacological concentrations as a prooxidant, rather than antioxidant. However, the molecular mechanisms by which LAA initiates cellular signaling toward cell death are still unclear. Therefore, the effects of LAA on eukaryotic transcription factor NF- $\kappa$ B and COX-2 expression were investigated. In the present study, LAA suppressed DNA binding activity of NF- $\kappa$ B composed of p65/p50 heterodimer through inhibition of degradation of I $\kappa$ B- $\alpha$  and preventing nuclear translocation of p65 subsequently, but not direct-interruption of DNA binding of NF- $\kappa$ B to their consensus sequences. Inhibitory effect of LAA on NF- $\kappa$ B DNA activity was dependent upon GSH level in HL-60 cells as well as H<sub>2</sub>O<sub>2</sub> generation but not superoxide anion. LAA also downregulated the expression of COX-2 which has NF- $\kappa$ B binding site on its promoter through

repressing the NF- $\kappa$ B DNA binding activity. Moreover, cotreatment of 1  $\mu$ M As<sub>2</sub>O<sub>3</sub> with various concentrations of LAA enhanced LAA induced-repression of NF-B activity and COX-2 expression. In conclusion, it is likely that LAA exerts its anti-tumor promotional effect through downregulation of NF- $\kappa$ B activity and COX-2 expression. Cotreatment of 1  $\mu$ M As<sub>2</sub>O<sub>3</sub> can synergistically enhance inhibitory effect of LAA suppressing NF- $\kappa$ B activity and COX-2 expression