CD154 induces p73 to overcome the resistance to apoptosis of chronic lymphocytic leukemia cells lacking functional p53.

Based on immunoregulatory properties of CD40 and CD40 ligand (CD154), CD40 stimulation is being investigated as an active therapy for hematologic malignancies, such as chronic lymphocytic leukemia (CLL)(1). Transduction of CLL cells with CD154 by virus vectors can upregulate costimulatory adhesion molecules, restore antigen-presenting capacity, and induce an antigen-specific T-cell response (2, 3). Furthermore, CLL patients who had received adenovirus-CD154 gene therapy showed rapid reduction in leukemia cell counts and lymph node size (4). In accordance with the kinetics of leukemia-cell clearance and expression of death receptors on CLL cells transduced with CD154 (4), Dicker et al (5) hypothesized that this treatment sensitized CLL cells to death-receptors-mediated apoptosis. By examining apoptotic mechanisms following CD154 stimulation, they found that CD154 could induce activation of p73. As a member of the p53 family, p73 restored the sensitivity of p53-deficient CLL cells to drug-induced apoptosis.

References:


