

Oligonucleotide IMT504 induces an immunogenic phenotype and apoptosis in chronic lymphocytic leukemia cells.

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Oligonucleotides (ODNs) of the PyNTTTTGT class directly stimulate B lymphocytes and plasmacytoid dendritic cells of the immune system of primates. Here we investigated the ability of the PyNTTTTGT ODN prototype IMT504 to regulate the expression of surface molecules and apoptosis in human B-chronic lymphocytic leukemia (CLL) cells. The surface molecules CD25, CD40, CD80 and CD86 were up-regulated upon incubation of the B-CLL cells with IMT504. Co-stimulation with IL-2 resulted in further up-regulation. IMT504-activated B-CLL cells were also good stimulators of T cells in allogeneic mixed lymphocyte reactions and co-stimulation with IL-2 improved this stimulation capacity. Apoptosis of the B-CLL cells in vitro was also stimulated by incubation with IMT504. In this case, co-stimulation with IL-2 was not significant. Furthermore, B-CLL cells of all the patients studied developed an immunogenic phenotype and entered stimulated apoptosis upon in vitro incubation with IMT504 independently of the mutational status of their IgV(H) genes, becoming a good marker for tumor progression.