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Inhibition of Leukemia Cell Proliferation using c-myb Antisense Oligonucleotides

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Abstract: Antisense oligodeoxynucleotides (AS-ODNs) are short DNA sequences synthesized complementary to the mRNA and they inhibit the expression of the target gene by forming a mRNA-DNA duplex. This strategy can be considered to be an alternative therapy for cancers characterized by amplified oncogene activity. The purpose of this study was to evaluate the inhibitory effect of AS-ODNs on two human leukemia cell lines (HL-60 and K562). Cells were treated with c-myb AS-ODNs at two different concentrations and cell proliferation was monitored on the 5^{th} and 7^{th} days of culture. Sense and scrambled ODNs were used as the control. In both cell lines, AS-ODNs inhibited cell proliferation up to 90%, with inhibition being more important at high ODN concentration. A slight inhibition was also observed with sense ODNs after 5 days of culture; but in contrast with the AS-ODNs, this inhibition was diminished in 7 days. Scrambled ODNs caused a higher inhibition than sense ODNs. This study shows that AS-ODNs, targeted to an oncogene involved in cell proliferation, inhibit malignant cell proliferation. The inhibition observed with sense or scrambled ODNs is due to non-sequence-specific ODN binding. However, these non-specific effects decrease at longer incubation times whereas the antisense effect persists.

Key Words: Gene therapy, antisense oligonucleotides, c-myb, leukemia

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