The aim of this study is to characterize a newly identified transcript named air (AX538681) whose genomic sequence is missing in human genome draft. air was identified as a differentially expressed cDNA in TNFα-stimulated Jurkat cells, transfected with a IκBa-hyperexpressing vector, versus control cells. Indeed air expression appeared to be induced by a pro-apoptotic stimulus and repressed by NF-κB activity. air mRNA was isolated by differential screening analysis of an expression library from Jurkat cells; its sequence (3.4kb long, 79% A/T rich) didn't show any similarity with annotated sequences. This evidence suggested that air could belong to an unsequenced region, whose secondary structure results in cloning instability. Four main putative ORFs were identified by ORF-Finder tool, but the aminoacidic sequence of three of them did not show any homology with conserved structural motifs, anyway, we don’t exclude that air could be a long non coding RNA, in fact, it is rich in stop codons and it’s strongly predisposed to form stem loop secondary structures. air role in modulating cell apoptosis was investigated: air silencing in lymphoma, neuroblastoma and AML cells, treated with stressful stimuli, showed a significant (p<0.01) reduction of caspase 3 activation, mitochondrial membrane depolarization, cytochrome c release and appearance of apoptotic cells. At the same time, transfection of human PBMC with an air-hyperexpressing construct resulted in more than 25% appearance of apoptotic cells in respect to controls. These findings identify air as a novel potential tool for enhancing cancer response to therapeutics.