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Low-dose anisomycin is sufficient to alter the bio-behaviors of Jurkat T cells

Research Article

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Abstract: Anisomycin is a pyrrolidine antibiotic isolated from Streptomyces griseolus. It has been found that a quite low dose of anisomycin is sufficient to block proliferation of primary T lymphocytes. The focus of this study is to explore the possibility of anisomycin to treat human acute leukemia Jurkat T cells *in vitro*. The results indicated that the low dose of anisomycin could significantly inhibit the colony formation of Jurkat T cells and elevate the inhibition rate of Jurkat T cell growth along with its increasing concentrations. Jurkat T cell cycle was blocked into S-phase by anisomycin. Consistent with the increased proportion of sub-G1 phase, anisomycin promoted Jurkat T cell apoptosis. The CD69 and CD25 expression on the surface of Jurkat T cells was also down-regulated prominently along with the enhancing concentrations of anisomycin, followed by the decreased production of IL-4, IL-10, IL-17, TGF-β and IFN-γ, and the down-regulated expression of phosphorylated-ERK1/2. The results suggest that the suppressive effect of anisomycin on Jurkat T cell growth may be related to inhibiting TGF-β production and ERK1/2 activation, arresting the cell cycle at S-phase and promoting the apoptosis of Jurkat T cells.

Keywords: *Anisomycin • Proliferation • Activation • Cell cycle • Apoptosis • Jurkat T cell*

1. Introduction

Anisomycin, as an antiprotozoal agent with antibacterial or antifungal activity, is a pyrrolidine antibiotic originally and the chemical formula is C_{14}-H_{19}-N-O_4, designated as 2-*p*-methoxyphenylmethyl-3-acetoxy-4-hydroxypyrrolidine (Figure 1A). Its pyrrolidine ring is important for the translational inhibitory activity of anisomycin. Acetylation of the nitrogen or deacetylation at the 3′ position inhibits this activity [1]. It can bind with the 60S ribosomal subunit and prevent peptide bond formation to result in block of peptide elongation and degradation of polyribosome, functionally inhibiting synthesis of numerous proteins and DNA [2]. Recent studies show that anisomycin activates c-jun N-terminal kinase/stress-activated protein kinase (JNK) and p38 mitogen activated protein kinase (p38) to protect the neurons of cerebral cortex [3]. Therefore, it is frequently used as an activation agent in mitogen-activated protein kinase signaling pathways. It is also discovered that anisomycin induces macrophage apoptosis in rabbit atherosclerotic plaques through p38 signaling [4]. Our group accidentally found that a quite low-dose anisomycin could dramatically inhibit biological behaviors of primary T lymphocytes [5]. Jurkat T cell line, isolated from the peripheral blood of a patient with acute T cell leukemia, is a tumor cell line derived from human T lymphocytes. Thus, the phenotype and certain biological features of Jurkat T cells are similar to normal T cells. Dissimilarly, the former possesses malignant proliferation properties. We suppose that anisomycin may exert the same influence on human leukemia Jurkat T cells. In this study effect of anisomycin on biological behaviors of Jurkat T cells was observed to explore possibility of anisomycin applied to treating Jurkat T cells *in vitro*. The results indicate that the suppressive action

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