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In vitro Characterization of the Rapid Cytotoxicity of Anticancer Peptide HPRP-A2 through Membrane Destruction and Intracellular Mechanism against Gastric Cancer Cell Lines

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Abstract

In this study, HPRP-A2, a synthetic 15-mer cationic peptides with all D-amino acids, effectively inhibited the survival of gastric cell lines in a dose-dependent manner. Gastric tumor cells killing by HPRP-A2 involves a rapid collapse of the membrane integrity and intracellular pathways. Propidium iodide (PI) and lactate dehydrogenase (LDH) assays demonstrated that one-hour treatment with HPRP-A2 led to membrane permeability changes of BGC-823 cells in a dose-dependent manner. Moreover, HPRP-A2 induced apoptosis in BGC-823 cells involves a marked increase in generation of reactive oxygen species (ROS), caspase-3, -8 and -9 activation, a reduction of mitochondrial membrane potential (MMP), and cell cycle arrest in G1 phase. In addition to its inherent cytotoxicity, HPRP-A2 synergized strongly with doxorubicin (DOX) to enhance the efficacy of killing gastric tumor cells *in vitro*. We believe that HPRP-A2 with all D-amino acids could be a potent candidate of anticancer therapeutics, especially in combination therapy.

Introduction

Over past decades, although breakthroughs have been achieved in the development of cancer therapies, resistance and nonspecific toxicity of conventional drugs are still bottle-neck issues for potential clinical practices [1–3]. Hence, it is urgently required to develop novel drugs with different modes of action which can overcome the shortcomings of many available drugs.

Currently, the potential applications of anticancer peptides (ACPs) as therapeutic agents for the treatment of cancer progression attract more attention than conventional chemotherapy mainly because of the following properties: (1) high specificity. The positively charged peptides selectively target cancer cells that carry negative charges and have different membrane components from normal cells [4, 5];(2) novel mode of action. It could avoid established multidrug-resistance