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Mechanism of Anticancer Effects of Antimicrobial Peptides

Xuan Liu [a,*], Yi Li [a,*], Zhi Li [a], Xiqian Lan [b], Polly Hang-Mei Leung [c]
Jiashen Li [a], Mo Yang [d], Frank Ko [e], Ling Qin [f]

[a] *Institute of Textiles and Clothing, The Hong Kong Polytechnic University, Hong Kong, China*

[b] *Institute of Sericulture and Systems Biology, Southwest University, Chongqing 400716, China*

[c] *Department of Health Technology and Informatics, The Hong Kong Polytechnic University Hong Kong, China*

[d] *Interdisciplinary Division of Biomedical Engineering, The Hong Kong Polytechnic University Hong Kong, China*

[e] *Department of Materials Engineering, The University of British Columbia Vancouver, B.C. V6T1Z4, Canada*

[f] *Department of Orthopadics & Traumatology, The Chinese University of Hong Kong Hong Kong, China*

Abstract

Antimicrobial Peptides (AMPs) were first known as a group of innate immune products that mainly targets on the invading pathogens among multiple species. The essential mechanisms of action of AMPs toward microbial cells have been reported as electrostatic attraction and hydrophobic interaction between AMPs (cationic AMPs) and microbial cell membranes. These effects also contribute to the potential mechanism of anticancer activities of AMPs as well. The membrane difference between cancer cells and normal cells are believed to play significant roles in AMPs orienting process. Membrane selective targeting properties make AMPs promising candidates for alternative approach to solve the problems from anticancer drug resistance.

Keywords: Antimicrobial Peptides; Anticancer Activity; Electrostatic Attraction; Hydrophobic Interaction; Anticancer Drug Resistance

1 Introduction

Among the abundant anticancer therapeutic approaches, the main measure, conventional chemotherapy usually accompany with severe side effects. Current anticancer drugs mostly focus on highly proliferated cells, which do not spare healthy cells that grow with similar rate. Meanwhile,

*Corresponding author.
Email addresses: liu.xuan@connect.polyu.hk (Xuan Liu), tcliyi@polyu.edu.hk (Yi Li).

the appearance of Multi Drug Resistant (MDR) cancer cells has greatly hindered the efficiency of drugs. Drug compounds can be transported out of the cells via resistance mechanism from cancerous cells [1, 2]. There are other mechanisms that cancer cells involved to failure anticancer drugs, including repairing damaged DNA, overcoming the stress conditions (ROS) and expression of drug detoxifying enzymes in response.

Antimicrobial Peptides (AMPs), as an innate defense guard, place heavy force on membrane targeting towards invading pathogens. Destruction of membrane structure or indirectly trigger the cascade consequences make the pathogenic microbe less possible to develop resistance. This property of AMPs is believed play significant role in anticancer activity as well. AMPs not only show adverse effect on the expression of receptor of angiogenic endothelial cells, but also associate with immune response. It renders the cancer cells more susceptible to immune system navigation which can be easily escaped under pathological state. This short manuscript tends to review the mode of mechanism of AMPs owing anticancer activity through following points of views.

2 Membrane Differences Contribute to the Selective Targeting of Antimicrobial Peptides

The progression of cancer correlated with alteration and transformation of cell membranes which is vital to neoplasm cells in cellular response to surrounding signals. Biological membranes are composed of phospholipid bilayer which is a fundamental component being amphipathic, having both hydrophobic and hydrophilic domains. It is believed that multiple membrane proteins are represented on the surface of mammalian cells with complex ingredients or modifications, but the portions of proteins which carry net electrons often face to the inner side of the membrane. Healthy plasma membranes usually present a zwitterionic amphiphile distribution. Cancer cell membranes, on the other hand, usually express a vast number of anionic molecules (such as phosphatidylserine (PS) [3-9], sialic acid [10-15], membrane-associated glycoproteins [16, 17], chaperone proteins HSP90 and GRP78 [18-20]) which are contributed to the net negative charge of membrane surface. The membrane structures of normal cells and cancerous cells are shown in Fig. 1.

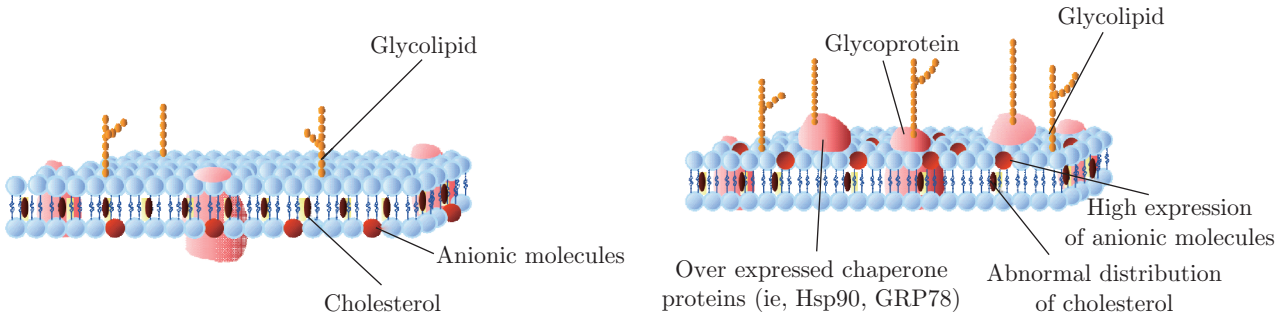

Fig. 1: Schematic diagrams of membrane structure of mammalian cells. Compared to normal cells (left), over expressed anionic molecules or proteins and abnormal distribution of cholesterol may contribute to the negative charged membrane surface in cancerous cells (right)

Among these membrane-associated proteins, the abnormal vitality of post-translational modification of proteins on the cancer cell membrane surface made cancerous cells more susceptible to