

Delivery Methods for Melittin-Based Cancer Therapy

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Abstract

Melittin (MLT) is a natural cytolytic peptide generated from bee venom that has been explored in preclinical animal models to treat inflammatory illnesses such as arthritis, rheumatism, chronic pain, and others. In recent years, MLT has been widely used as an anticancer medication. MLT attaches to phospholipids and creates pores in plasma and organelle membranes, causing cancer cells and drug-resistant cells to perish. MLT has also emerged as a promising immunotherapeutic medication that promotes the release of tumor-associated antigens and endogenous danger indicators, as well as cytotoxic T and natural killer (NK) cell activation. MLT also promotes the release of anticancer cytokines such IL-2, INF-, and TNF-, which improves antitumor immune responses.

Introduction

By triggering TAM reprogramming and differentiation into immunostimulatory M1-polarized TAMs, MLT has the ability to reverse the immunosuppressive Tumour Microenvironment (TME). Despite mounting evidence of MLT's potent anticancer effects, its therapeutic application is impeded by insufficient tissue distribution, hemolysis, rapid metabolism, limited selectivity, and toxicity [1]. As a result, creating new MLT delivery technologies could be important for improving MLT's anticancer therapy while avoiding ionising radiation. Furthermore, given the highly variable physiology of tumours, such as the TME's aberrant vascular system, MLT delivery methods that enable trigger-based (physiology- or external stimuli-dependent) targeting and release may aid in delivering maximum payload to the targeted region. Many publications have discussed recent advancements in MLT and its delivery strategies, either as an overview of material-based delivery systems or as a focus on general elements of MLT membrane interactions and anti-proliferative molecular pathways from a biological standpoint. However, in terms of applied biotechnology and mechanistic properties, immunomodulatory effects, and translational factors, material-assisted MLT delivery vehicles demand special attention. In recent years, a variety of carriers have been employed in MLT delivery schemes [2]. By modulating the TME, a complex system that encompasses tumour cells, fibroblasts, endothelial cells, and immune cells, these carriers are well-suited to transport MLT to tumour areas and improve antitumor efficiency. Multiple carrier-based MLT delivery techniques for cancer therapy are outlined here. MLT is a poisonous component of *Apis mellifera* bee venom that can be employed as an antibacterial and cytolytic peptide. It is made up of 26 amino acids (NH₂-GIGAVLKVLTGLPALISWIKRKRQQ), with a hydrophobic amino-terminal region (residues 1-20) and a hydrophilic carboxy-terminal region (residues 21-26). 18 MLT is a cationic peptide with a net charge of +6, with four charges in the C-terminal area and the remaining two in the N-terminal region, in addition to its amphiphilic nature. As a result, MLT

is a suitable model peptide for lipid interaction [3]. MLT is normally monomeric and has a random coil structure; however, when it is injected into a lipid membrane, it converges into a tetramer and assumes a α -helical conformation. Temperature, pH, salt concentration, and peptide concentration can all affect MLT's conformation. MLT establishes electrostatic connections with negatively charged cell membrane surfaces in milliseconds, resulting in pore creation, cellular content leakage, and eventually cell death.

REFERENCES

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