

Article

Wnt Signaling Pathway Collapse upon β -Catenin Destruction by a Novel Antimicrobial Peptide SKACP003: Unveiling the Molecular Mechanism and Genetic Activities Using Breast Cancer Cell Lines

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Abstract: Despite progress in breast cancer treatment, the survival rate for patients with metastatic breast cancer remains low due to chemotherapeutic agent resistance and the lack of specificity of the current generation of cancer drugs. Our previous findings indicated that the antimicrobial peptide SKACP003 exhibited anticancer properties, particularly against the MCF-7, MDA-MB-231, and MDA-MB-453 breast cancer cell lines. However, the mechanism of SKACP003-induced cancer cell death is unknown. Here, we investigated the molecular mechanism by which SKACP003 inhibits the cell cycle, cell proliferation, and angiogenesis in breast cancer cell lines. The results revealed that all the breast cancer cell lines treated at their IC_{50} values significantly inhibited the replicative phase of the cell cycle. The SKACP003-induced growth inhibition induced apoptosis, as evidenced by a decrease in BCL-2 and an increase in BAX and caspase gene (Cav-3, Cav-8, and Cav-9) expression. Reduced expression of the β -Catenin signaling pathway was associated with the SKACP003-induced apoptosis. SKACP003-treated breast cancer cells showed decreased expression of Wnt/ β -Catenin targeting genes such as C-Myc, 1^{60} , and COX-2 and significant downregulation of CDK-4 and CDK-6 genes. Furthermore, cytoplasmic β -catenin protein levels in SKACP003-treated cell lines were significantly lower than in control cell lines. The results of the current study suggest that the newly identified antimicrobial peptide SKACP003 has great potential as a candidate for specifically targeting the β -catenin and thus significantly reducing the progression and prognosis of breast cancer cell lines.

Keywords: antimicrobial peptides; anticancer agents; breast cancer; Wnt pathway; β -catenin; down-regulation; oncology; alternative therapy

1. Introduction

The prevalence of breast cancer among women results in a significant reduction in their average lifespan. Similarly, the mortality ratio is skewed in favor of urban women compared to their rural counterparts. Most concerning is that, as per estimates, the number of women impacted by this problem is expected to rise exponentially in the near future [1]. Regarding treatment, a systematic approach is employed to treat the ailment effectively. Chemotherapy is currently one of the most widely used treatment methods. However,



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