Chapter 4
Computer Simulation Studies of Non-Thermal Plasma in Cancer Treatment: Understanding Protein Modifications for Enhanced Therapeutic Efficacy

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ABSTRACT

Non-thermal plasma (NTP), the fourth state of matter, holds promise in altering biological matter, particularly in cancer treatment. NTP influences cell signaling by modifying key components, such as membranes, proteins, and DNA. It selectively targets cancer cells through the generation of reactive oxygen and nitrogen species (RONS), which modify amino acids within proteins. Understanding these molecular mechanisms is vital for optimizing NTP's potential in oncology. This book chapter reviews recent computer simulations and experimental findings exploring NTP's impact on proteins in cancer therapy, providing insights into how protein modifications affect cancer cell behavior and therapy responses. This knowledge advances NTP-based cancer treatments, offering the potential for personalized and targeted therapies in the future.

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1. INTRODUCTION

Non-thermal plasma (NTP) as the 4th state of matter has emerged as a promising tool with significant impact on biological matter, particularly in cancer treatment. Exposure to NTP has been shown to influence the signaling pathways of cells by modifying cellular components, including membranes, proteins, and DNA. In particular, NTP has demonstrated potential in selectively targeting and killing cancer cells, making it an intriguing area of research in oncology.

The major impact of NTP on biological matter lies in the generation of reactive oxygen and nitrogen species (RONS). These RONS are crucial in causing damage and alterations to amino acids within proteins. Proteins, as versatile biomolecules, carry out a wide variety of functions in the cell, including catalytic, transporting, and signaling roles. Therefore, understanding the molecular-level mechanisms of protein modifications, such as oxidation and nitration induced by NTP, is crucial to obtain the full potential of this technology in cancer treatment.

Here, we aim to summarize the latest findings from computer simulation studies investigating the effects of NTP on proteins in cancer treatment. By exploring these simulations, we seek to gain deeper insights into the intricate interactions between NTP-derived RONS and protein structures. These insights will enhance our understanding of how specific protein modifications may contribute to altering cancer cell behavior and sensitivity to therapy.

By presenting an overview of computer simulation studies conducted to date in plasma cancer treatment, this chapter provides a comprehensive perspective on the role of NTP-induced protein modifications in cancer cell viability and therapeutic response. Such knowledge is essential for advancing NTP-based cancer treatment strategies and may pave the way for personalized and targeted therapies in the future.

2. POST-TRANSLATIONAL MODIFICATIONS AND THEIR IMPACT ON CATALYTIC PROTEINS

Proteins, particularly catalytic ones, play vital roles in various biochemical reactions and cellular pathways (Alberts, 2017). Their functionality can be affected by various internal and external factors, with RONS being one of the most significant external influencers (Dröge, 2002). This section sheds light on the effects of RONS on several catalytic proteins (Halliwell, 2006), particularly focusing on cytoglobin, catalase, peroxidase, and SOD, detailing their structure, function, and interactions under various conditions. Cytoglobin (CYGB) is a relatively newly discovered globin proposed to play a role in cellular protection against oxidative stress (Burmester et al., 2002; De Backer et al., 2018). One of the emerging tools in cancer therapy is NTP, which primarily generates RONS (Fridman et al., 2008). The interaction of these RONS with cellular proteins, especially redox-regulatory ones like CYGB, can determine the cell's fate (Smith et al., 2010). NTP treatment on CYGB has shown that while the protein undergoes chemical modifications, its secondary structure remains largely unaffected (De Backer et al., 2018). Spectroscopic analysis revealed the oxidations to mainly occur in sulfur-containing and aromatic amino acids (Stadtman & Levine, 2003). With prolonged NTP exposure, nitration of the heme group in CYGB was also observed. Furthermore, the two surface-exposed cysteine residues in CYGB were oxidized, leading to the formation of both intermolecular and potential intramolecular disulfide bridges.