



Article

A Unique G-Quadruplex Aptamer: A Novel Approach for Cancer Cell Recognition, Cell Membrane Visualization, and RSV Infection Detection

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Abstract: Surface staining has emerged as a rapid technique for applying external stains to trace cellular identities in diverse populations. In this study, we developed a distinctive aptamer with selective binding to cell surface nucleolin (NCL), bypassing cytoplasmic internalization. Conjugation of the aptamer with a FAM group facilitated NCL visualization on live cell surfaces with laser confocal microscopy. To validate the aptamer-NCL interaction, we employed various methods, including the surface plasmon resonance, IHC-based flow cytometry, and electrophoretic mobility shift assay. The G-quadruplex formations created by aptamers were confirmed with a nuclear magnetic resonance and an electrophoretic mobility shift assay utilizing BG4, a G-quadruplex-specific antibody. Furthermore, the aptamer exhibited discriminatory potential in distinguishing between cancerous and normal cells using flow cytometry. Notably, it functioned as a dynamic probe, allowing real-time monitoring of heightened NCL expression triggered by a respiratory syncytial virus (RSV) on normal cell surfaces. This effect was subsequently counteracted with dsRNA transfection and suppressed the NCL expression; thus, emphasizing the dynamic attributes of the probe. These collective findings highlight the robust versatility of our aptamer as a powerful tool for imaging cell surfaces, holding promising implications for cancer cell identification and the detection of RSV infections.

Keywords: G-quadruplex; nucleolin; cancer cell identification; detection of RSV infection; cell surface staining



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1. Introduction

Nucleolin (NCL) has been shown to be involved in several important biological processes, such as ribosome biogenesis [1,2], regulation of DNA replication and repair [3–5], gene expression regulation [6,7], and apoptosis [8,9]. Typically, more than 90% of NCL is localized within the nucleolus in normal cells [10]. Nevertheless, various physiological and pathological processes can cause changes in the subcellular distribution of NCL. For example, in cancerous cells, NCL can be significantly overexpressed on the cellular membrane [10–13]. Recent research has also indicated that cell surface NCL is even tumor-specific, both in vitro and in vivo [14]. Several studies have demonstrated that overexpressed NCL on the membrane surface of cancer cells is a key target that interacts with multiple proteins and is associated with cancer cell proliferation and migration [15].

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Table of Contents Novel Approach To A Unique Man

1. Understanding the eBook Novel Approach To A Unique Man
 - The Rise of Digital Reading Novel Approach To A Unique Man
 - Advantages of eBooks Over Traditional Books
2. Identifying Novel Approach To A Unique Man
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Novel Approach To A Unique Man
 - User-Friendly Interface
4. Exploring eBook Recommendations from Novel Approach To A Unique Man
 - Personalized Recommendations
 - Novel Approach To A Unique Man User Reviews and Ratings
 - Novel Approach To A Unique Man and Bestseller Lists
5. Accessing Novel Approach To A Unique Man Free and Paid eBooks
 - Novel Approach To A Unique Man Public Domain eBooks
 - Novel Approach To A Unique Man eBook Subscription Services
 - Novel Approach To A Unique Man Budget-Friendly Options
6. Navigating Novel Approach To A Unique Man eBook Formats

- ePub, PDF, MOBI, and More
- Novel Approach To A Unique Man Compatibility with Devices
- Novel Approach To A Unique Man Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Novel Approach To A Unique Man
 - Highlighting and Note-Taking Novel Approach To A Unique Man
 - Interactive Elements Novel Approach To A Unique Man
- 8. Staying Engaged with Novel Approach To A Unique Man
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Novel Approach To A Unique Man
- 9. Balancing eBooks and Physical Books Novel Approach To A Unique Man
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Novel Approach To A Unique Man
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Novel Approach To A Unique Man
 - Setting Reading Goals Novel Approach To A Unique Man
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Novel Approach To A Unique Man
 - Fact-Checking eBook Content of Novel Approach To A Unique Man
 - Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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