**Commentary**
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# From Bench to Bedside: Precision Therapeutics Using Spherical Nucleic Acids for Cancer Treatment

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## Introduction

Cancer is a leading cause of death worldwide, and the development of effective therapeutic strategies remains a major challenge. One promising approach is the use of precision therapeutics, which involves the targeted delivery of drugs to cancer cells, thereby minimizing side effects on healthy cells. Spherical Nucleic Acids (SNAs) have emerged as a new class of nanotherapeutics that have shown great potential in this area. SNAs consist of a nanoparticle core densely functionalized with a shell of radially oriented synthetic oligonucleotides, forming a three-dimensional architecture that protects the oligonucleotides from nuclease-mediated degradation, increases oligonucleotide bioavailability, and enables robust uptake into tumor and immune cells [1].

## Description

SNAs have been shown to silence gene expression and induce immune responses superior to those raised by the oligonucleotides in their "free" form. Early phase clinical trials of gene-regulatory siRNA-based SNAs in glioblastoma (NCT03020017) and immunostimulatory Toll-like receptor 9 (TLR9)-agonistic SNAs carrying unmethylated CpG-rich oligonucleotides in solid tumors (NCT03086278) have shown that SNAs represent a safe, brain-penetrant therapy for inhibiting oncogene expression and stimulating immune responses against tumors [2]. SNAs have been designed to carry TLR-activating oligonucleotides and have been shown to activate the immune system, leading to the destruction of cancer cells. In addition, SNAs have been used to deliver chemotherapeutic agents directly to cancer cells, resulting in increased efficacy and reduced side effects. SNAs have also been used in combination with other therapeutic strategies, such as radiation therapy and immunotherapy, to enhance their anti-cancer effects. For example, SNAs have been shown to enhance the efficacy of immune checkpoint inhibitors, which are a type of immunotherapy that blocks the ability of cancer cells to evade the immune system [3].

The mechanism of action of SNAs is complex and multifaceted. Upon administration, SNAs are taken up by cells through a process called endocytosis, where the cell engulfs the SNA in a membrane-bound vesicle called an endosome. Once inside the cell, the SNA is released from the endosome and the oligonucleotides are released from the nanoparticle core. The oligonucleotides then interact with their target mRNA or DNA, silencing gene expression or inducing an immune response. The unique three-dimensional architecture of SNAs plays a critical role in their mechanism of action. The densely packed oligonucleotides on the surface of the nanoparticle core create a "shell" that protects the oligonucleotides from degradation by nucleases, increasing their bioavailability and half-life. The radial orientation of the oligonucleotides also enhances their ability to interact with target cells, increasing uptake and efficacy [4].

SNAs have also been used in combination with other therapeutic strategies, such as radiation therapy and immunotherapy, to enhance their anti-cancer effects. For example, SNAs have been shown to enhance the efficacy of radiation therapy by silencing genes involved in DNA repair, making cancer cells more sensitive to radiation. In addition, SNAs have been used in combination with immunotherapy to enhance the immune response against cancer cells. For example, SNAs have been shown to stimulate the production of cytokines, such as interleukin-12, which play a critical role in the immune response against cancer. Overall, SNAs represent a promising new class of nanotherapeutics for cancer treatment, with the ability to silence gene expression, induce immune responses, and deliver drugs directly to cancer cells. While further research is needed to fully understand their potential, early phase clinical trials have shown promising results, and it is likely that SNAs will play an increasingly important role in cancer treatment in the future [5].

## Conclusion

In conclusion, SNAs represent a promising new class of nanotherapeutics for cancer treatment. Their unique three-dimensional architecture, combined with their ability to silence gene expression, induce immune responses, and deliver drugs directly to cancer cells, make them an attractive option for precision therapeutics. While further research is needed to fully understand the potential of SNAs, early phase clinical trials have shown promising results, and it is likely that SNAs will play an increasingly important role in cancer treatment in the future. It's important to note that the development of SNAs as a cancer treatment is still in its early stages, and there are many challenges that need to be addressed, such as the development of scalable manufacturing methods and the optimization of SNA design for specific cancer types. However, the potential of SNAs as a cancer treatment is undeniable, and significant progress has been made in recent years.

## Acknowledgement

None.

## Conflict of Interest

None.

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