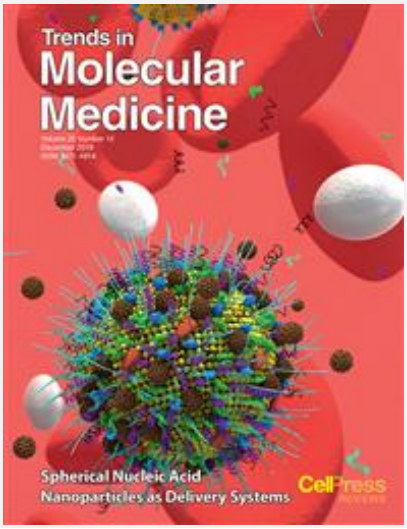

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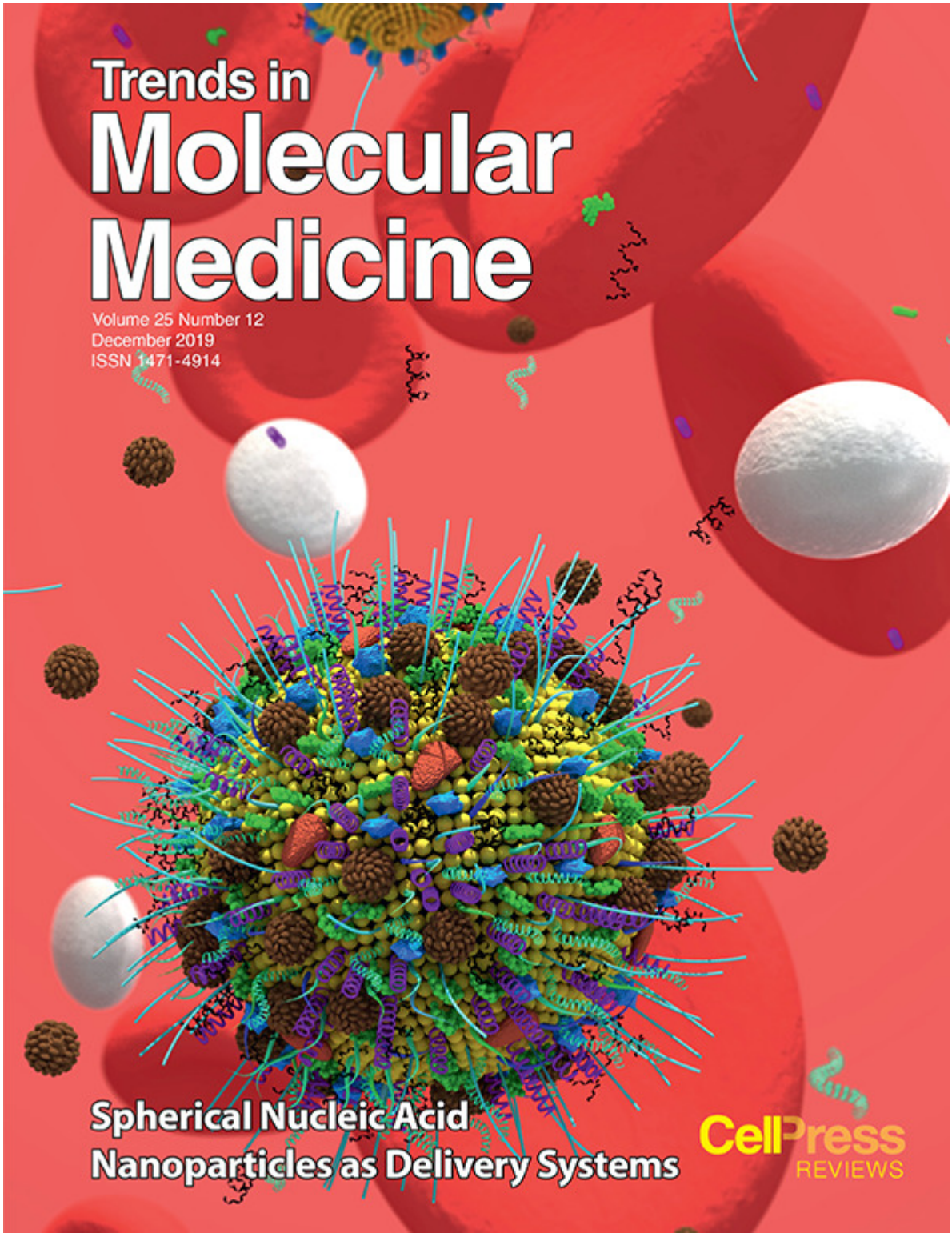
طرح برتر روی جلد ژورنال پژوهشی

تصویر طراحی شده توسط آقای امیر باغبان زاده به عنوان طرح برتر نتخاب گردید.

طرح برتر روی جلد ژورنال (Trends in molecular medicine (Impact Factor: 11.028 ،

به گزارش روابط عمومی معاونت تحقیقات و فناوری دانشگاه علوم پزشکی تبریز ، تصویر طراحی شده توسط آقای امیر باغبان زاده در ژورنال (Trends in molecular medicine(Impact Factor: 11.028 ، به عنوان طرح برتر روی جلد انتخاب گردید.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Spherical Nucleic Acid
Nanoparticles as Delivery Systems
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Feature Review

Applications of Spherical Nucleic Acid Nanoparticles as Delivery Systems

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Spherical nucleic acids (SNAs) are nanostructures consisting of highly oriented, dense layers of oligonucleotides arranged in a spherical 3D geometry. Owing to their unique properties and function, SNAs occupy a material space distinct from 'DNA nanotechnology' and DNA origami. Over the past two decades SNAs have revolutionized gene regulation, drug delivery, gene therapy, and molecular diagnostics, and show promise for both antisense and RNAi therapy. We focus here on recent advances in the synthesis and application of SNAs in gene and drug delivery, diagnostics, and immunomodulation, as well as on the utility of nanoflares as intracellular mRNA detection systems.

Highlights

Nanotechnology provides new approaches for cancer therapy via the delivery of anticancer drugs using nanoparticles (NPs), by more sensitive diagnosis of cancer biomarkers and cancer cells, and by monitoring therapeutic efficacy and tumor burden over time.

The recent evolution of NP synthesis and functionalization allows targeted delivery of anticancer drugs to tumor sites with minimal cellular damage or side effects on healthy tissues and organs.

SNAs are an emerging class of intracellular delivery systems for the delivery of bioactive molecules, such as drugs and antisense-based therapeutics, and they are efficient for monitoring mRNA levels in living cells.

Spherical Nucleic Acids as Delivery Systems of Bioactive Molecules

Spherical nucleic acids (SNAs) are structures composed of chemically modified inorganic nanoparticles (NPs; e.g., gold nanoparticles, AuNPs) at the core, and a dense layer of highly arranged thiol-modified oligonucleotides as the shell – which are chemically bound to the surface of the core via thiol bonds. Initially introduced by Mirkin and coworkers in 1996 [1], the advantages of SNA NPs include; (i) highly specific molecular recognition via specific Watson–Crick base-pairing, (ii) grafted oligonucleotides provide negative charge and increased colloidal stability as well as steric stabilization in solutions of elevated ionic strength, and (iii) the ability to couple with other biomolecules for molecular imaging or drug delivery [2]. NPs are an emerging class of intracellular delivery systems for bioactive molecules, and are promising carriers for antisense-based therapeutics and **immunomodulators** (see Glossary) in the absence of off-target effects, immunogenicity, or apparent cell toxicity [3]. A variety of single-stranded (ss) and double-stranded (ds) oligonucleotides, such as DNA, RNA, peptide nucleic acid (PNA), miRNA, small interfering RNA (siRNA), and locked nucleic acid (LNA), typically 25–40 nt and 7–12 nm in length, have been conjugated to the core to generate the NP shell [4–7]. Whole-transcriptome profiling of HeLa cells showed no significant up- or downregulation of genes in SNA-treated cells [8].

SNAs elicit a minimal immune response relative to cationic nanocarriers (>25-fold reduced immune response) [9,10]. Because of the high density of oligonucleotides at the surface of SNAs, they are resistant to degradation by nucleases and have better stability compared with linear nucleic acids. Furthermore, the association of cations with SNAs screens the negative charges of neighboring oligonucleotide strands and inhibits the activity of nucleases [11,12].

Unlike linear DNA, SNAs can enter cells without the assistance of transfection reagents. Although SNAs have a negative charge as a result of the high density of oligonucleotides (**zeta potential** of <30 mV), they can be recognized by class A scavenger receptors by their 3D structure, and are rapidly internalized by the caveolin endocytotic process in almost all cell types [13,14]. Interactions between DNA–AuNPs and these receptors seem to depend on the high density of oligonucleotides at the NP surface. When systemically administered, SNAs can cross the blood–brain barrier (BBB) and can traverse the epidermal barrier in C57BL/6 mouse models when applied topically [10,14]. In this review we discuss recent advances in the synthesis and properties of SNA NPs, their utility in the measurement of intracellular genetic material, for gene or drug delivery, and as potent gene regulation agents.

Synthesis and Properties of SNAs

The Core of SNAs

The properties of SNAs depend on the type of NP core used as the framework for assembling and arranging nucleic acids into a packed layer on the surface. A wide range of NPs including AuNPs,

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