Keywords: Aptamer; Anticancer delivery systems; Nanoparticles; Tumor treatment; Tumor diagnosis

Changes in the expression of key proteins of the cellular signaling pathways are at the forefront of molecular abnormalities found in cancer. An increasing number of proteins involved in cell growth, including growth factors, receptors, intracellular mediators and transcription factors have been found to be altered through multiple mechanisms of oncogene activation [1]. ese abnormal membrane proteins serve as ideal biomarkers for disease diagnoses, therapeutics and prognosis. Hence, nding speci c ligands capable to detect and measure their expression is a strategic objective for the diagnosis and therapy of cancer. ese ligands should be able to bind and recognize with high a nity and speci city to surface receptors of tumor cells. Di erent types of molecules have shown great potential in achieving this goal, such as antibodies [2], folic acid [3], peptides [4,5], and aptamers [6].

Aptamers are short single-stranded nucleic acid oligomers (ssDNA or RNA) that can form speci c and complex three-dimensional structures which can bind with high a nity to speci c targets, including cancer cells. e term 'aptamer' is derived from the Latin word aptus meaning "to t" [7]. A procedure to derive sequences recognizing speci c targets was rst described under the name of Systematic Evolution of Ligands by Exponential Enrichment (SELEX). e method enables isolating an aptamer of interest from a pool of randomized molecules by repeated steps of incubation with the target, partitioning and ampli cation, until the pool of molecules becomes enriched in a particular clone [8]. Aptamers have been selected against a wide variety of targets, from small molecules to proteins and even whole organisms [9,10] and present the same high speci city and a nity for their targets as antibodies. In addition to e cient binding, aptamers have seem to lack immunogenicity, can be chemically modi ed in order to improve

***Corresponding author:** Andre Luis Branco de Barros, Faculty of Pharmacy, Federal University of Minas Gerais, Av. Antônio Carlos, 6627, 31270-091 Belo Horizonte, MG – Brazil, Tel: +55 31 3409 6840; E-mail: brancodebarros@yahoo.com.br

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drug delivery system (Ap-PTX-NP) decorated with AS1411, a DNA aptamer speci cally binding to nucleolin, which was highly expressed in the plasma membrane of cancer cells, as the targeting ligand to improve the anti-glioma e cacy of paclitaxel (PTX), a widely used chemotherapeutic agent. Biodistribution study in xenogra nude mice models showed that at all time points, PTX concentrations determined in the tumor were higher for those animals that received Ap-PTX-Np than those who received PTX-nanoparticle or only PTX, and the accurate in vivo tumor targeting improved anti-glioma e cacy for PTX on rats-bearing intracranial C6 gliomas. In another study, Jalalian et al. [25] evaluated the use of 5TR1 aptamer – super paramagnetic iron oxide nanoparticles (SPIO) loaded with Epirubicin (therapeutic agent) for the imaging and treatment of murine colon carcinoma cells, showing that the complex was less cytotoxic to nontarget cells when compared to Epirubicin alone. Furthermore, Kim et al. [26] developed a cancer targeting theranostics probe in a single system using an AS1411 aptamer - and miRNA 221 molecular beacon conjugated magnetic uorescence (MF) nanoparticle (MFAS miR-221 MB) to simultaneously target to cancer tissue, image intracellularly expressed miRNA-221 and treat miRNA-221- involved carcinogenesis. AS1411 aptamer-conjugated MF nanoparticles displayed a great selectivity and delivery into various cancer cell lines. e miR-221 MB detached from the MFAS miR-221 MB in the cytoplasm of C6 cells clearly imaged miRNA-221 biogenesis and simultaneously resulted in antitumor therapeutic e ects by inhibiting miRNA function, indicating a successful astrocytoma targeting theranostics. Cao et al. [27] also recently reported cell speci c drug delivery based on aptamer functionalized liposomes.

In conclusion, aptamers possess several advantages as speci c targeted molecules when compared with other traditional substances used to this aim, such as antibodies, and peptides. Aptamers might overcome the drawbacks presented by antibodies (immunogenicity) and peptides (degradation) leading to high-speci city molecules for delivering nanoparticles into targeted area. ese new nanoplatforms may be used as diagnostic probes, therapeutic agents, or even for both applications in multimodal nanostructures, as already published by some groups. Although much remain to be done to e ectively translate those aptamers-functionalized nanoparticles to clinic, such as nanotoxicity studies, it is clear that conjugation of a high-speci city molecule, i.e. aptamer, poses many advantages over conventional approaches. We believe that due to their unusual characteristics, including extraordinary speci city conferred by aptamers is likely that such formulations will have major impact in the nanomedicine eld in the near future.

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