Samaneh Kabirian Dehkordi et al., Nano Res Appl 2018, Volume 4
DOI: 10.21767/2471-9838-C3-015

Anticancer activity of G rich aptamer AS1411 grafted to gold nanospheres: From synthesis to mechanism study

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AS1411 is a G-rich oligodeoxynucleotide aptamer that has been used in phase II clinical trials for the potential treatment of cancers. Forming a G-quartet structure, AS1411 binds to cell surface nucleolin specifically, and is subsequently internalized into the tumor cell. It remains unclear how AS1411 binding to nucleolin leads to cell proliferation inhibition and cell death. Despite remarkable AS1411 results in a few patients, the overall rate of response has been low, possibly because it has less than optimal pharmacology and relatively low potency. Attaching AS1411 to gold nanospheres (AS1411-GNSs) increases its accumulation in cancer cells and enhances its antitumor efficacy by binding to cellular nucleolin. Nucleolin is associated with ribosomal DNA (rDNA) and is absolutely required for rRNA synthesis. It binds with nanomolar affinities the G-quadruplex rDNA sequences to increase the rate of RNA polymerase I (POL1) transcription. We developed a new complex of AS1411 conjugated to Gold nanospheres (GACGs). This complex was more stable and effective than AS1411 in treated tumor cell lines. GACGs decrease nucleolin expression affecting tumor cell proliferation and POLI targeting genes transcription such as 5'ETS and 18s. Thus, GACGs targeting Nucleolin/rDNA complexes inhibit POLI and represents a novel, nucleolar targeting approach to selectively disrupt proliferation in cancer cells and induce cell death.

Recent Publications

1. Motaghi H, Mehrgardi M A and Bouvet P (2017) Carbon dots-AS1411 aptamer nanoconjugate for ultrasensitive spectrofluorometric detection of cancer cells. Sci Rep. 7:10513.
2. Kumar S et al. (2017) Integrated analysis of mRNA and miRNA expression in HeLa cells expressing low levels of nucleolin. Sci Rep. 7(1):9017.
3. Ugrinova I et al. (2018) Multifaceted nucleolin protein and its molecular partners in oncogenesis. Adv. Protein Chem. Struct. Biol. 111:133-164.
4. Bouvet P (2015) Identification of Nucleic Acid High Affinity Binding Sequences of Proteins by SELEX. In Methods in Molecular Biology. 1334:333-43.
5. Khoshfetrat S M and Mehrgardi M A (2017) Amplified detection of leukemia cancer cells using an aptamer-conjugated gold-coated magnetic nanoparticles on a nitrogen-doped graphene modified electrode. Bioelectrochemistry. 114:24-32.

Biography

Samaneh Kabirian, a Chemist completed her Bachelor's Degree in Pure Chemistry; Master's Degree in Analytical Chemistry (detection of biomolecule in blood). She has her expertise in synthesis, characterization of nanoparticles conjugated to aptamers and passion in improving its application in biology of cancer. She is always curious and enthusiastic to work on multidisciplinary project and bridging gap between different domains of science. She is currently pursuing a double degree PhD in Molecular and Cellular Biology at the University of Lyon (France) and in Analytical Chemistry at Isfahan University (Iran). She has been studying and working in biochemistry and biology laboratory of cancer research center of Lyon (France) for the past 3 years. She gave her a good point of view to biological aspects of applications of nanoparticles in biology of cancer. With strong background in chemistry and specially analytical chemistry, she is also trained in all common molecular and cellular biology manipulations like cell culture, protein and DNA analysis and so on. Her double skilled ability helps build a good connection in multidisciplinary project especially cancer biology and pharmaceutical chemistry.

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