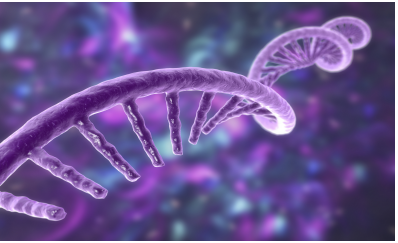
Cytosolic RNA depletion by polymeric nanoparticles

MicroRNAs (miRNAs) are small, double-stranded RNAs that exert fine-tuned, sequence-specific regulation of the cellular transcriptome. While a single miRNA regulates hundreds of mRNAs, each mRNA molecule is commonly regulated by only a few miRNAs that bind to complementary sequences at 3'-untranslated regions to trigger the mechanism of RNA interference. Unfortunately, dysregulated miRNAs play a critical role in many diseases.



Polymer nanoparticle sponges for depleting cytosolic RNA to fight systemic diseases such as cancer

IP RIGHTS

Patent application, PCT filed in 2025

The over-expression of certain miRNAs plays a role in a number of pathogenic processes, such as in the development of cancer. But also in other diseases, such as atherosclerosis, type II diabetes, obesity, viral infections and cardiovascular diseases, miRNA might play an important role. Overexpression of e.g., miR21 in cancer is responsible for increases in colony formation and survival rate of tumor cells.

01 Mucin nanoparticles cross-linked with anti-miRNA oligonucleotides show high selectivity and efficient uptake by target cells

02 Treating systemic diseases associated with increased cellular RNA levels

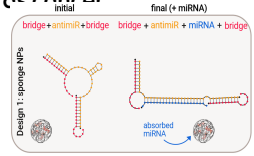
03 Depletion of miRNA-21 reduced tumor growth in vivo by 50%

04 Currently demonstrated with mucins, but any other polymer can be used

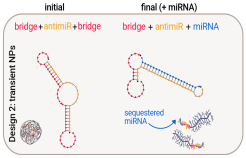
REFERENCES:

Kimna et al. (2020), ASC Nano

Another manuscript in preparation



Mode of action of sponge nanoparticles. These nanoparticles are stabilized by the strands designed to absorb miRNA .



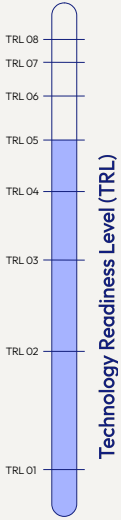
Mode of action of transient nanoparticles. These nanoparticles silence the miRNA through the displacement of the antimiR strand.

CHALLENGE

A challenge for miRNA therapeutics is to maintain the stability and consistency of miRNAs in circulation. Naked miRNAs are degraded by nucleases within seconds or are rapidly removed by renal excretion. Thus, suitable delivery systems are needed that stabilise the antisense DNA, allow efficient uptake by the cells, while avoiding off-targets. They should also be adjustable so they can deplete any target RNA.

INNOVATION

The invention describes nanoparticles (NP) composed of biopolymer-DNA conjugates that have the ability to bind and inactivate cytosolic miRNA in cells. Two types of NPs are described: (1) 'sponge' NPs, which bind miRNA in a condensed state, as the binding sites are exposed and (2) transient NPs, which open in the cell after initial contact with the miRNA and can bind further miRNAs. The transient NP can act as a targeted drug delivery system, releasing a drug only upon contact with a specific trigger DNA sequence. The design of the DNA sequences that stabilise the NPs can be freely adapted to any cytosolic RNA target. It was shown that these NPs were successfully taken up, were able to escape from endosomes and were effective in silencing miRNA.



01 Basic principles observed · **02** Technology concept formulated · **03** Experimental proof of concept · **04** Technology validated in lab · **05** Technology validated in relevant environment · **06** Technology demonstrated in relevant environment · **07** System prototype demonstrated in operational environment · **08** System complete and qualified

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Bayerische Patentallianz GmbH
Dr. Linda Keil
lkeil@baypat.de
+49 (0)89 5480177-30
Prinzregentenstr. 52
80538 München