

Biological activity of nanocomposites consisting of TiO₂ nanoparticles and antisense oligonucleotides

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Nanocomposites consisting of titanium dioxide nanoparticles (TiO₂) and oligonucleotides or their analogs were prepared to deliver nucleic acid-based compounds into cells. The nanocomposites (TiO₂•PL-oligo) were designed by the immobilization of polylysine-containing oligonucleotides on TiO₂ nanoparticles. It was shown that the proposed nanocomposites exhibited a low toxicity and very high activity against influenza A virus (IAV) in vitro and in vivo. The nanocomposites bearing the oligonucleotide targeted to the chosen regions of (-)RNA and (+)RNA of segment 5 of different IAV subtypes inhibited the virus reproduction by >99%. Moreover, it was shown a possibility of using the proposed nanocomposites for the treatment of hypertensive disease by introducing them into the hypertensive ISIAH rats developed as a model of the stress-sensitive arterial hypertension. Oligonucleotides should be targeted to some genes involved in the pathogenesis of essential hypertension. The angiotensin-converting enzyme (ACE) involved in the synthesis of angiotensin-II was chosen as a target. Two ways of administration (intraperitoneal injection and inhalation) were examined. Both methods showed a significant (by 20-30 mm/Hg) decrease in systolic blood pressure, when the nanocomposite contained the ACE gene-targeted oligonucleotide. When using the oligonucleotide with a random sequence, no effect was observed. Thus, it was demonstrated a possibility of using the proposed nanocomposites as efficient drugs to achieve a high biological efficacy.

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Biography:

Asya S. Levina was born in Novosibirsk, Russia. She received the MS degree in chemistry from Novosibirsk State University, Russia, in 1969 and the Ph.D. degree in bioorganic chemistry from Novosibirsk Institute of Organic Chemistry in 1974. From 1969 to 1993, she worked in the Laboratory of Nucleic Acids Chemistry at the Institute of Bioorganic Chemistry. From 1993 to 1997, she was Senior Research Associate with the Laboratory in Worcester Foundation for Biomedical Research, Shrewsbury, MA, USA. Since 1997, she has been a Senior Research Scientist at the Institute of Chemical Biology and Fundamental Medicine, Siberian Branch of Russian Academy of Sciences. She is the author of more than 100 articles and more than 10 patents. Her research interests include the synthesis of oligonucleotides and their derivatives, preparation of DNA arrays, and the synthesis of nucleic acid-based nanocomposites. Currently she works at the Novosibirsk State University.