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Targeted Multifunctional Hybrid Agents for Oncotheranostics

Sergey Deyev
Shemyakin - Ovchinnikov Institute of Bioorganic Chemistry, Russia

An important task of successful cancer diagnostics and therapy is the introduction into the arsenal of modern oncology of a wide range of compounds with different mechanisms of action on cancer cells.

Focusing on these goals, a multifunctional agent was created for targeted delivery of two toxic agents — radionuclides and biological toxin — to cancer cells. Specifically, we synthesized hybrid complex, including upconversion nanoparticles (UCNP) doped with beta-emitting radionuclide yttrium-90, and a pseudomonas exotoxin A fragment equipped with the targeted scaffold polypeptide DARPin9.29 specific to tumor receptor HER2. It was shown that the synergistic effect of the simultaneous use of a radionuclide and a toxin is 2200 times stronger than when used separately.

We also developed dual targeting-based HER2-directed cancer cell therapy with biocompatible and biodegradable poly lactic-co-glycolic acid (PLGA) nanoparticles and targeted immunotoxin. The PLGA nanoparticles were equipped with: i) HER2 recognizing scaffold protein ZHER2:342, ii) fluorescent dye for cell imaging and iii) chemotherapeutic drug doxorubicin for cell killing. The capabilities of these multifunctional PLGA nanoparticles for cancer cell theranostics was demonstrated in vitro and in vivo. In order to enhance the targeted cytotoxic effect, we used targeted nanoparticles and a targeted bifunctional immunotoxin DARPin9.29-LoPE. LoPE is low-immunogenic modification of Pseudomonas exotoxin A, which is promising for in vivo applications. We showed that such combined therapy with DARPin9.29-LoPE & PLGA*ZHER2:342 nanoparticles allows reducing the effective concentration of immunotoxin up to about 1000 times.

The results of our other studies on oncotheranostics will also be presented.

Biography:

Prof. Sergey Deyev has completed his PhD from Engelhardt Institute of Molecular Biology, Russia. He is Head of Immunology Department in Shemyakin & Ovchinnikov Institute of Bioorganic Chemistry, Moscow. He holds concurrent appointments as Professor in Lomonosov Moscow State University, the Faculty of Immunology. He is member of Russian Academy of Sciences and Academia Europaea, the recipient of numerous honors, including the Mechnikov Prize of Russian Academy of Sciences in the field of immunology and biotechnology. He has published more than more than 150 papers in reputed journals, including Nature Biotechnology, Nature Nanotechnology, ACS NANO, Proc. Natl. Acad. Sci. USA, Theranostics.