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Abstract

Tunable multiple-targeting dendritic nanoscaffolds for diagnostics and therapeutic application

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Abstract:

Antibodies (Ab) conjugation with various scaffolds has found application in therapeutics and diagnostics design. Cysteine and lysine are utilized as the basic moieties during the Ab conjugation with natural and synthetic molecules. But, this strategy leads to formation of undesirable heterogeneous products, aggregates, etc. Researchers have developed various alternative approaches to perform controlled modifications. Recently, the peptides, containing reactive artificial amino acids, were site-specifically conjugated to native IgG Fc regions for delivery into tumor cells. We designed the peptide-decorated 4th generation polyamideamine dendrimer that bind site-specifically Fc domain of IgGs of different species. Carboxyl-terminated dendrimers were coupled PEG and peptide. The 15 amino acids FcIII peptide (N-CDCAWHLGELVWCTC-C) analogue, with substituted Glu9 residue with aminoreactive lysine fluorophenylcarbamate, was conjugated with carboxyl-terminated dendrimers. Z-domain competitive binding analysis displayed site-specific Fc-oriented dendrimer surface opsonization with Abs. SPR data analysis revealed nanomolar Kd value for Herceptin, mouse anti human CD326 IgG2b, and rabbit anti mouse IgG2c. MS data analysis confirmed covalent Abs binding with Lys248. The fluoresceinamine was loaded into conjugate as the marker. The resulted conjugated characterized with 12-15nm size, negative surface charge. The cytofluorometry and fluorescent microscopy results revealed that: Her2+ A549 cells specifically internalized labeled with trastuzumab conjugates; mouse anti-human E-selectin labeled conjugates successfully HUVEC cells layer; rabbit Abs modified conjugate effectively and reversible bound

mouse HRP-conjugated IgGs; EpCAM+ MCF-7 cells actively bound antiEpCAM mouse Ab modified conjugate. These results evidenced that the designed dendrimer-based conjugate have broad perspectives as the universal systems for development of drug delivery systems.

Biography:

Mr Yabbarov has completed his PhD at the age of 26 years from Center of Bioingeneering of Russian academy of sciences. He is the head of Preclinical trials lab in Russian research center for molecular diagnostics and therapy and the young scientists group leader in N.M. Emanuel Institute of Biochemical Physics. He has published more than 35 papers in reputed journals.

Publication of speakers:

1. Soni, Manish & Mehta, Priya & Soni, Anjali & Goswami, Girish. (2017). Mini Review Adv Biotech & Micro miRNA: An Overview of its Role in Cancer Research and Diagnosis. Advances in Biotechnology & Microbiology. 6. 10.19080/AIBM.2017.06.555688.
2. Glaser, Vicki. (2011). New Cancer Research Tools Change Paradigm. Genetic Engineering & Biotechnology News. 31. 48-51. 10.1089/gen.31.9.27.

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