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DISSERTATION ABSTRACT

“Synthesis and characterization of triazolic ligands of regulatory RNA structures of HIV-1”

The aim of my work was to develop an effective method for the synthesis of nucleobases derivatives, 5-aminopent-3-ynoic acid derivatives, design and synthesis of monomers and oligomers of triazolic nucleic acid (TKN). TKN sequences have been designed to bind to the key RNA structures in HIV-1 replication. The obtained analogs could be used for treatment of HIV-1 infection. TKN monomers were synthesized using "click chemistry" - 1,3-dipolar Huisgen cycloaddition reaction which gives 1,2,3-triazole derivatives. I designed two classes of monomers (TKN1 and TKN2) and triazole derivatives of amino acids (TzlAA). Following, I synthesized of 3- and 6-mer of TKN being ligands for HIV TAR stem-loop-bulge structure and anticodon stem-loop domain of human tRNALys3. An interaction between selected RNA targets and synthesized TKN2 and TzlAA fragments were analyzed by capillary electrophoresis, circular dichroism and fluorescence spectroscopy. The results show that designed TKN2 and TzlAA fragments bind to the regulatory RNA structures of HIV-1, which makes them potentially useful as new inhibitors of HIV-1 replication.