

ARYL-CONTAINING ESTERS OF TRIPHOSPHORIC ACID AS SUBSTRATES OF DNA POLYMERASES OF X-FAMILY

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The X polymerase family is a subclass of an ancient nucleotidyltransferase superfamily, which includes such enzymes as terminal deoxynucleotidyltransferase (TDT, EC 2.7.7.31), DNA polymerases λ , β , μ , and some others. Natural 2'-deoxynucleoside 5'-triphosphates are substrates for this family. Unlike other DNA polymerases, TDT *in vitro* can also recognize ribonucleotides and various modified nucleoside triphosphates. We synthesized a novel series of triphosphates lacking a nucleoside moiety but bearing various substituents attached to the triphosphate group through linkers of different structures and lengths and studied them as substrates/inhibitors of TDT and DNA polymerases λ and β . The efficacy of recognition of these compounds by the enzymes depends on substituent and linker structures and length. The affinities of some of the compounds of this series towards TDT were similar to those of natural substrates. Moreover, the synthesized non-nucleoside triphosphates were demonstrated to be substrates/terminators of other polymerases of the X family, particularly, of human β and λ polymerases and showed distinct base-pairing properties with normal bases. Acknowledgments: The work was supported by the Russian Foundation for Basic Research, project 06-04-48248. The authors are grateful to Prof. G. Maga (Istituto di Genetica Molecolare IGM-CNR, Pavia, Italy) for fruitful collaboration.

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