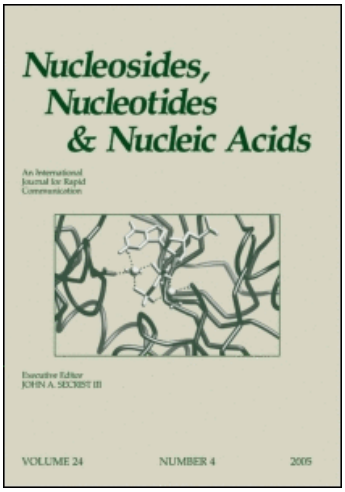

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The Synthesis and Base-Pairing Properties of 2-Deoxy-7-deazanebularine

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THE SYNTHESIS AND BASE-PAIRING PROPERTIES OF 2'-DEOXY-7-DEAZANEBULARINE.

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Summary: 2'-Deoxy-7-deazanebularine-5'-triphosphate (dDNTP) was used as a substrate for DNA polymerase. It was found to be an effective substitute for dATP, but not for dGTP, under standard conditions of in vitro primer extension reactions.

7-Deazanebularine, a highly cytotoxic analogue of purine riboside, was synthesized from tubercidin[1], and converted to the 2'-deoxynucleoside[2]. Its 5'-triphosphate[3] was used as a substrate for DNA polymerase I in a primer extension reaction on a single-stranded DNA template. The progress of the reaction was monitored by the incorporation of [^{32}P] dCMP into acid-insoluble material (fig.1). The substitution of dATP with dDNTP in the mixture of the four deoxynucleoside triphosphates resulted in an appreciable primer extension, albeit at a reduced rate. No extension was observed when dDNTP was substituted for dGTP, or both, dATP and dGTP. These findings contradict those of Ward and Reich[4], who reported that ribo-DNTP possessed ambiguous base-pairing properties when used as a substrate for RNA polymerase.

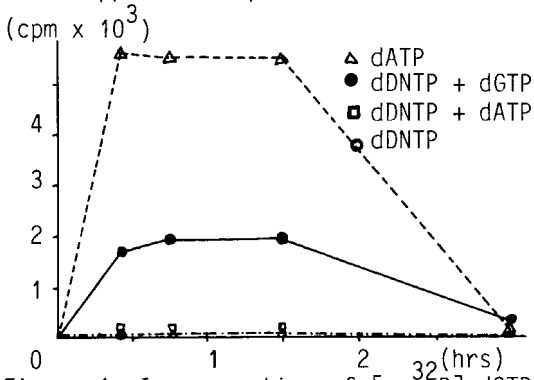

Figure 1: Incorporation of [α-^{32}P] dCTP into TCA-insoluble material. DNA polymerase I on M13mp9 template at 15°C.

In the light of the evidence presented above, it is thought to be extremely unlikely that the toxicity of this nucleoside arises from its incorporation into DNA, and subsequent mutagenesis, arising from its ambiguous base-pairing properties.

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