For CK, Sp-ADPαB isomer was a competitive inhibitor of the ADP phosphorylation. For PK, the Rp- and Sp-ADPαB isomers were poor competitive and non-competitive inhibitors, respectively. Preliminary results suggest that the Rp isomer of ADPαB is phosphorylated with comparable efficiency to natural NDPK substrates (GDP, CDP), whereas the Sp isomer is not recognized as a substrate. These enzymes are also being investigated for purification of the two isomers of ddNTPαB. An enzymatic separation where only the Rp isomer is phosphorylated would result in Rp-ddNTPαB and Sp-ddNDPαB, which can readily be separated by HPLC, and provide a straight forward means to investigate the purified isomers in antiviral studies.

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Withdrawn.

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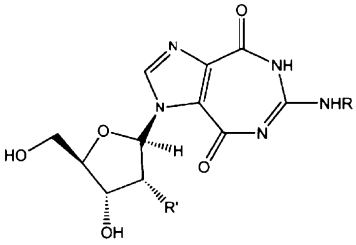
Ring-expanded Nucleosides (RENs) Exhibit Potent ATP-dependent Helicase Activity of RNA Helicase DDX3 with Little or no Toxicity in *Ex Vivo* Cell Culture or *In Vivo* in Mice

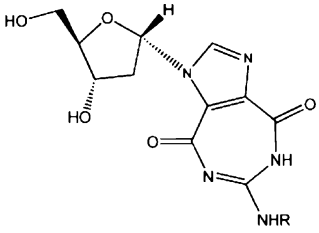
Venkat Yedavalli[2,*], Ning Zhang[1], Hongyi Cai[1], Kuan-Teh Jeang[2], Ramachandra Hosmane[1]

[1] Laboratory for Drug Design & Synthesis, Department of Chemistry & Biochemistry, University of Maryland (UMBC), Baltimore, USA; [2] Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health, Bethesda, USA

A series of ring expanded ("Fat)" nucleoside (REN) analogues shown below were screened for inhibition of HIV-1 replication. We demonstrate that two compounds **NZ-46** and **NZ-51** inhibit the ATP dependent helicase activity of RNA helicaseDDX3. These two compounds also suppressed HIV-1 replication in T cells and monocyte-derived macrophages. These compounds do not exhibit toxicity in *ex vivo* cell culture or *in vivo* in mice. We suggest that cellular RNA helicases can be attractive anti-viral targets for HIV-1 replication, which can circumvent the current problem of drug resistance associated with many anti-HIV drugs.



β–Anomer



α–Anomer

NZ-08; R = CH_2CH_2Ph, R' = OH
NZ-10; R = $(CH_2)_{11}CH_3$, R' = OH
NZ-11; R = Ph, R'=OH
NZ-14; R = $CH_2CH_2CH_3$, R' = OH
NZ-28; R = $(CH_2)_{11}CH_3$, R' = H
NZ-43; R = $(CH_2)_9CH_3$, R' = OH
NZ-45; R = $(CH_2)_{15}CH_3$, R' = OH
NZ-46; R = $(CH_2)_{17}CH_3$, R' = OH

NZ-49; R = $(CH_2)_{13}CH_3$
NZ-50; R = $(CH_2)_{15}CH_3$
NZ-51; R = $(CH_2)_{17}CH_3$

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