Phenotypic screening of a focused nucleoside library

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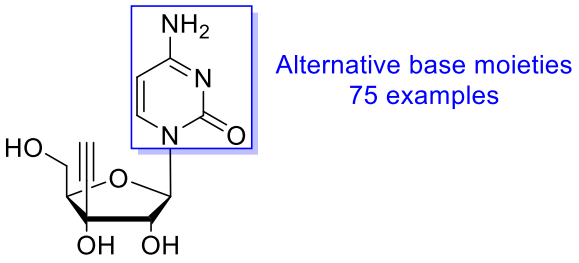
Nucleoside analogues have been used as therapeutics for the treatment of cancer or viral infections for over 50 years. Despite this fact, agents with intriguing and improved efficacy, tolerability etc. have been discovered over the past decade.[1] With this in mind, research was initiated to explore untapped potential of certain nucleoside scaffolds. It was envisioned to screen a focused in-house prepared nucleoside library phenotypically against a vast array of viruses as well as tumor cell lines.

Library construction entailed selection of a central modified ribofuranose moiety and concomitantly a collection of heterocyclic bases. In this work, a branched 3'-*C*-ethynylribofuranose was chosen, as is present in a former Phase-II clinical trial compound, 3'-*C*-ethynylcytidine ECyd, TAS-106.[2]



ECyd, TAS-106

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2. (a) Hattori, H.; Tanaka, M.; Fukushima, M.; Sasaki, T.; Matsuda, A., Nucleosides and Nucleotides. 158. 1-(3-C-Ethynyl-β-d-ribo-pentofuranosyl)-cytosine, 1-(3-C-Ethynyl-β-d-ribo-pentofuranosyl)uracil, and Their Nucleobase Analogues as New Potential Multifunctional Antitumor Nucleosides with a Broad Spectrum of Activity. *J. Med. Chem.* **1996,** *39*, 5005-5011; (b) Abdelrahim, M.; Matsuda, A.; Naing, A., TAS-106: preclinical, clinical and beyond. *Oncology* **2013,** *85*, 356-63.