

# Background of antimetabolite action and development in cancer

(introduction presented at the  
PP11 meeting in Tokyo, Japan)

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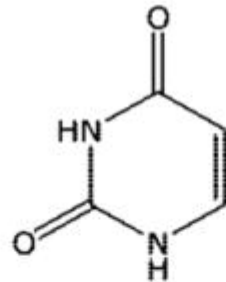


# What are antimetabolites?

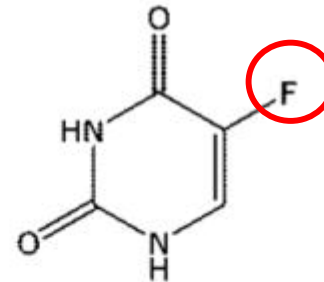
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- **Analogs of purine and pyrimidine bases and (deoxy)nucleosides**
- **Metabolised by purine and pyrimidine enzymes**
- **Target DNA and RNA synthesis**
- **May also affect cellular receptors and signaling pathways**

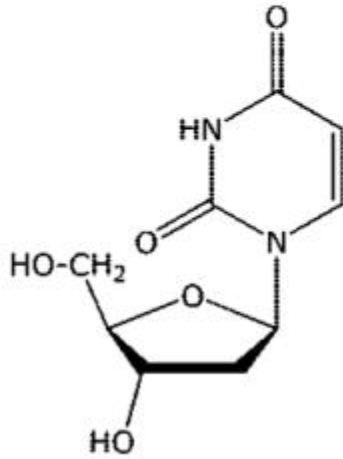
# Analogues can be modified in the base or the sugar: fluoropyrimidines



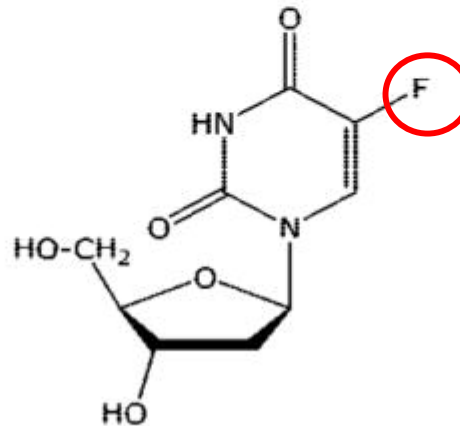
Uracil



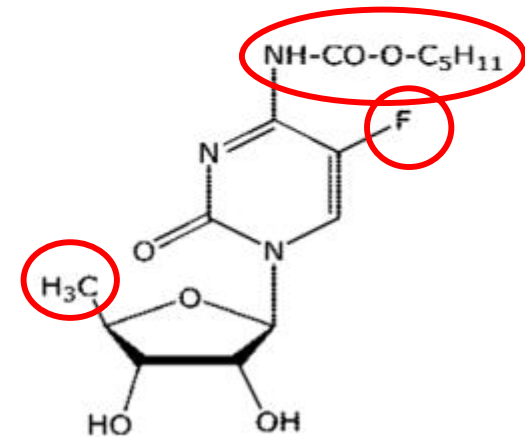
Fluorouracil



Deoxyuridine

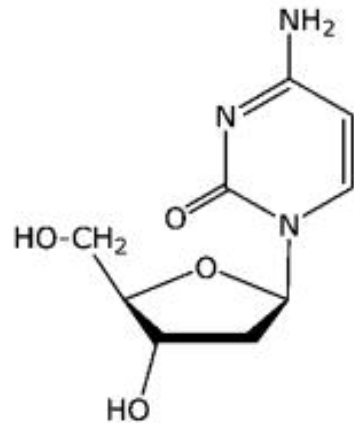


Fluorodeoxyuridine

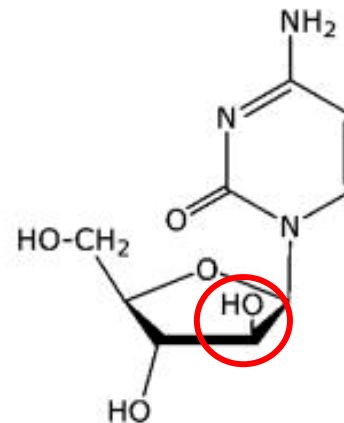


Capecitabine

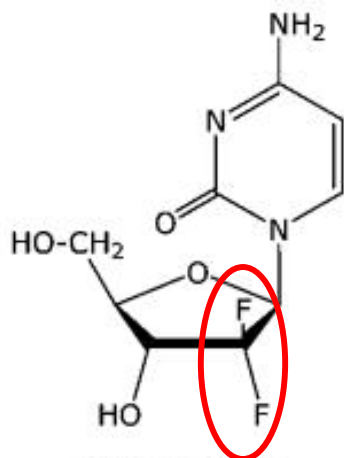
# Deoxycytidine analogs



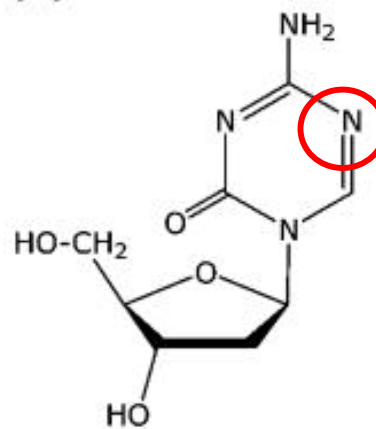
**Deoxycytidine**



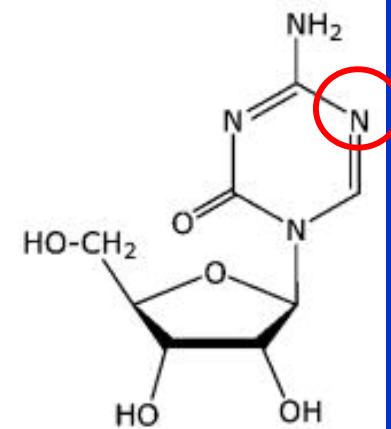
**AraC**



**Gemcitabine**

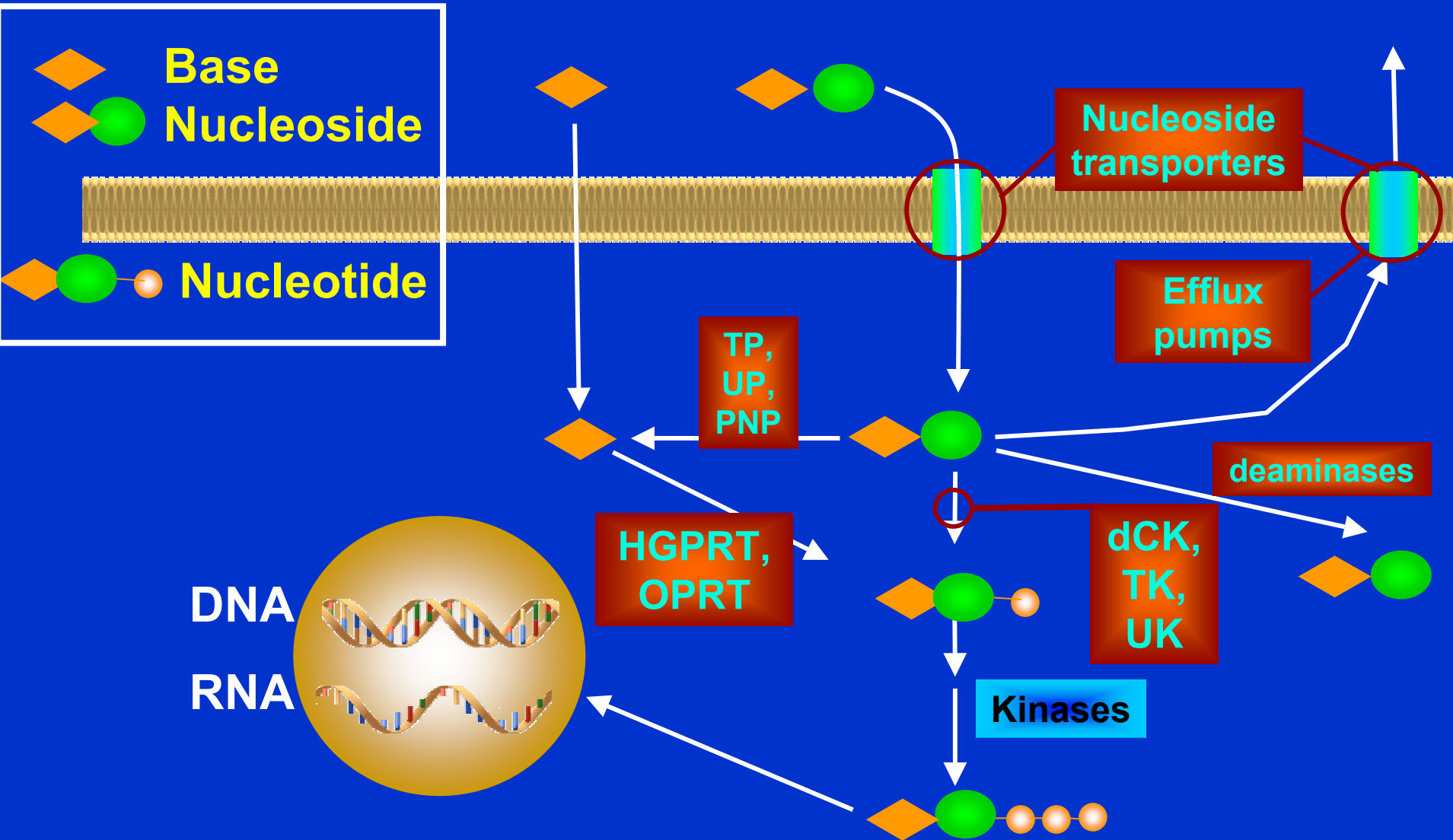


**Decitabine**

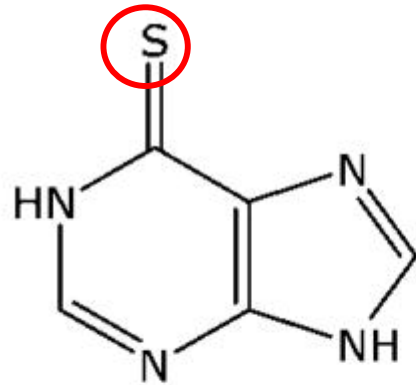


**Vidaza**

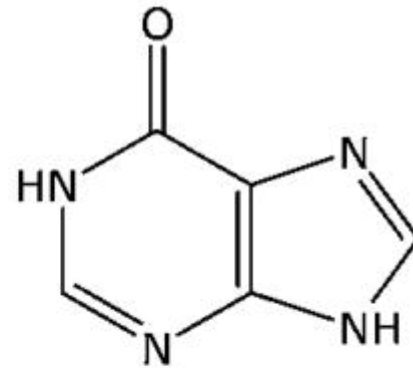
# Simplified purine and pyrimidine metabolism



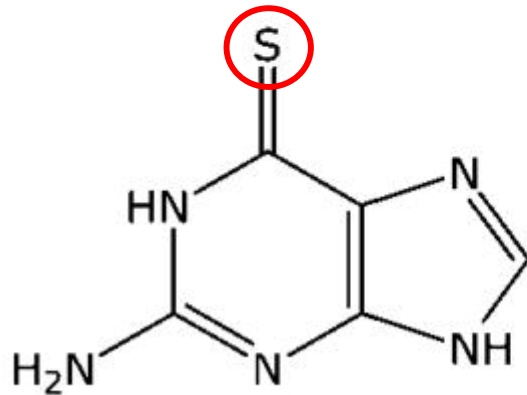
# Classical purine base analogs



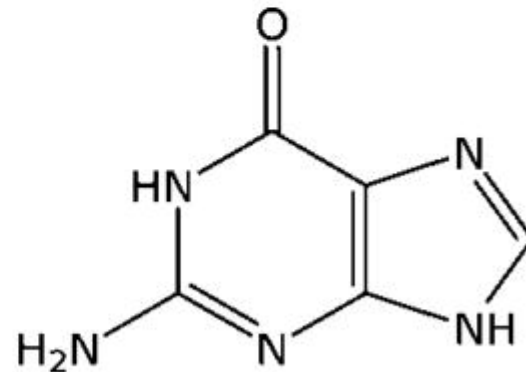
**Mercaptopurine**



**Hypoxanthine**

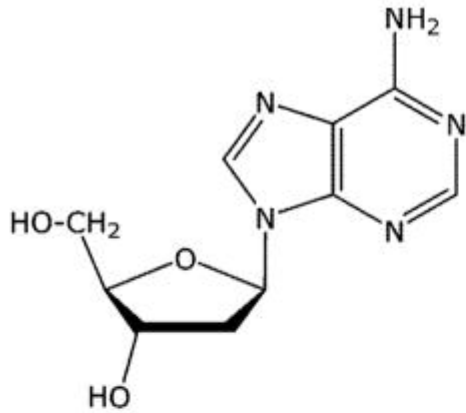


**Thioguanine**

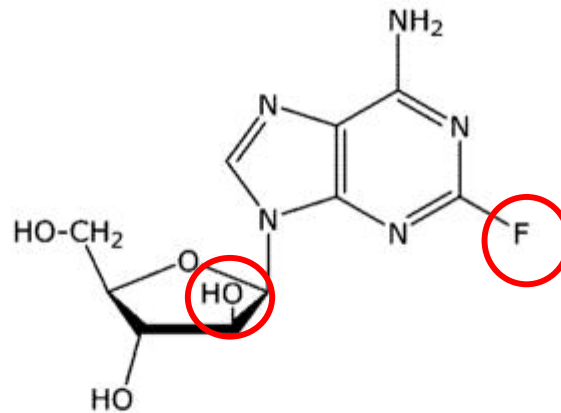


**Guanine**

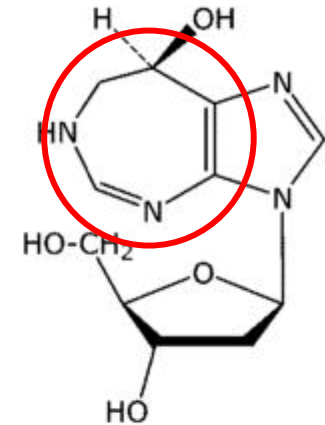
# Deoxyadenosine analogs



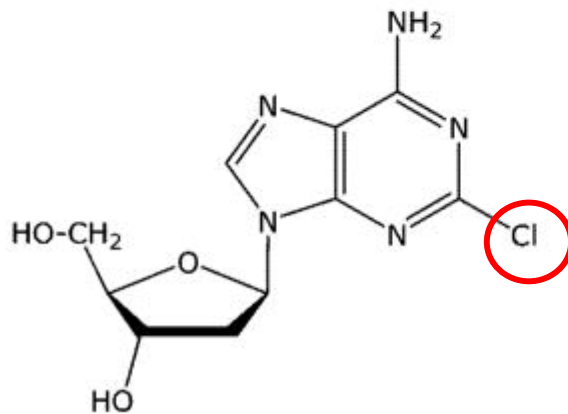
**Deoxyadenosine**



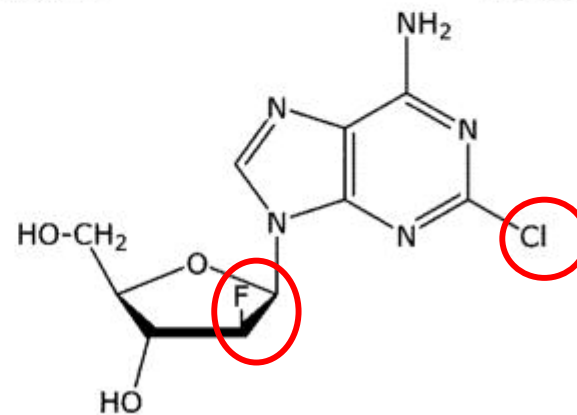
**Fludarabine**



**Pentostatin**

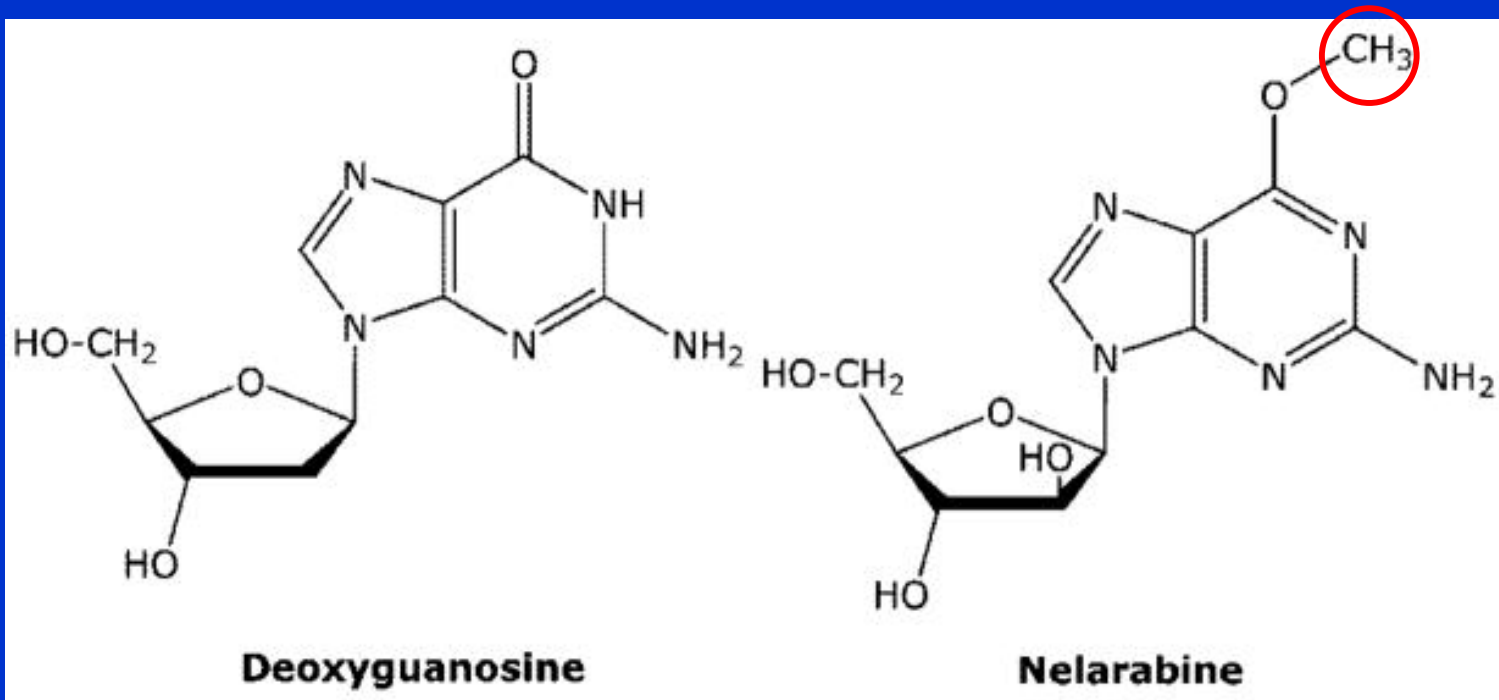


**Cladribine**



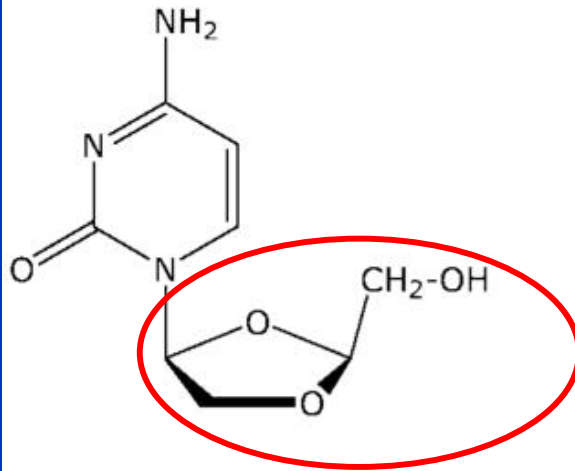
**Clofarabine**

# Deoxyguanosine analog

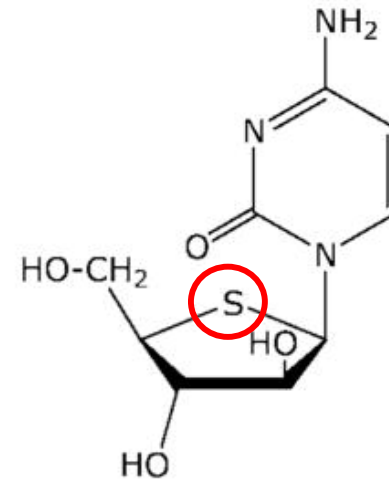




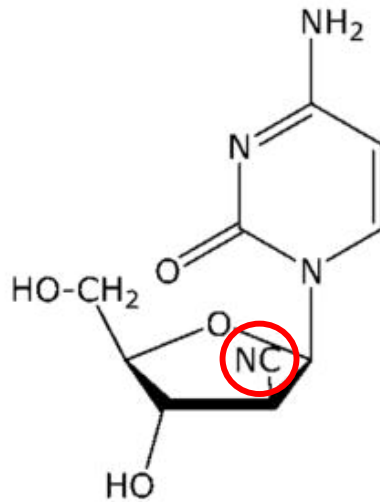
# Pyrimidine and purine analogs in development



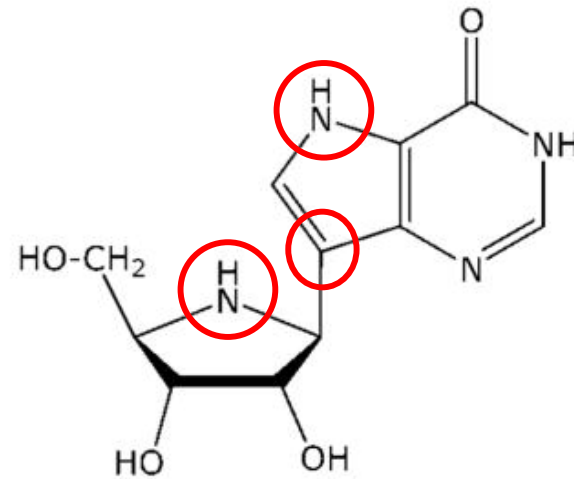
**The L-nucleoside:  
Troxacitabine**



**Thiarabine**



**CNDAC**



**Forodesine**

# FDA Approved Purine and Pyrimidine Antimetabolites

drug	date approved
5-aza-2'-deoxycytidine (decitabine)	2006
O <sup>6</sup> -methylarabinofuranosyl guanine (nelarabine)	2005
clofarabine	2004
5-aza-cytidine (vidaza)	2004
Capecitabine (Xeloda)	1998
2,2-difluoro-2'-deoxycytidine (gemcitabine)	1996
2-chloro-2'-deoxyadenosine (cladribine)	1992
arabinofuranosyl-2-fluoroadenine (fludarabine)	1991
2'-deoxycoformycin (pentostatin)	1991
5-fluoro-2'-deoxyuridine (floxuridine)	1970
arabinofuranosylcytosine (cytarabine)	1969
6-thioguanine	1966
5-fluorouracil	1962
6-mercaptopurine	1953

# Cellular mechanisms of drug resistance to be bypassed

