

Biomolecular Study of Human Thymidylate Synthase
Inactive Conformer Inhibitors as a New Chemotherapeutic
Approach

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

"يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ
دَرَجَاتٍ وَاللَّهُ بِمَا تَعْمَلُونَ خَبِيرٌ"

صدق الله العظيم

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List of Abbreviations

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ΔF	Change in intrinsic fluorescence
5-FU	5-fluorouracil
AIF	Apoptosis inducing factor
Apaf-1	Apoptotic protease activating factor 1
Bak	B-cell lymphoma-2 antagonist killer protein
Bax	B-cell lymphoma-2 associated X protein
Bcl-2	B-cell lymphoma-2
BSA	Bovine serum albumin
CHL	Chinese hamster lung fibroblast
CIP	Chromosomal instability pathway
CNT	Concentrative nucleoside transporter
CRC	Colorectal cancer
DBD	DNA-binding domain
DHF	Dihydrofolate
DHFR	Dihydrofolate reductase
DPM	Disintegrations per minute
dTMP	2'-Deoxythymidine-5'-monophosphate (thymidylate)
dTTP	Deoxythymidine triphosphate
dUMP	2'-Deoxyuridine-5'-monophosphate
ENT	Equilibrative nucleoside transporter
ETMPR	N ₂ , N ₃ -etheno-6-thiomethylpurine riboside
FasL	Fas ligand
FdUMP	5-Fluoro-2'-deoxyuridine-5'- monophosphate
FdUTP	5-Fluoro-2'-deoxyuridine-5'-triphosphate
FLT	3'-Fluoro-3'-deoxythymidine
FP	Fluoro-pyrimidine
FPLC	Fast protein liquid chromatography
FUTP	5-Fluorouridine-5'-triphosphate
GSH	Reduced glutathione
hTS	Human thymidylate synthase
IF	Intrinsic fluorescence
<i>k_{cat}</i>	The amount of product formed per second per 1 mole of the enzyme
Mcl-1	Myeloid cell leukemia-1 protein
MMR	Mismatch repair
MTHF	N ⁵ ,N ¹⁰ methylene tetrahydrofolate
NAD ⁺	Nicotinamide adenine dinucleotide
NADP ⁺	Nicotinamide adenine dinucleotide phosphate

NADPH	Reduced nicotinamide adenine dinucleotide phosphate
NBTI	Nitrobenzylthioinosine
NLS	Nuclear localization signal
NT	Nucleoside transporter
PAR	Poly(ADP-ribose)
PARP	Poly(ADP-ribose) polymerase
PCD	Programmed cell death (apoptosis)
PDPA	1,3-Propanediphosphonic acid
R163K-hTS	Active-stabilized mutant of human thymidylate synthase
RFU	Relative fluorescence units
ROS	Reactive oxygen species
RTX	Raltitrexed
SEER	Surveillance Epidemiology and End Results Program
TBHP	Tertiary butyl hydroperoxide
THF	Tetrahydrofolate
TK	Thymidine kinase
TNF- α	Tumor necrosis factor- α
TRAIL	Tumor necrosis factor-related apoptosis-inducing ligand
TS	Thymidylate synthase
<i>TYMS</i>	Thymidylate synthase gene
WHO	World Health Organization

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