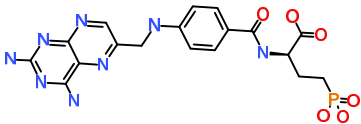
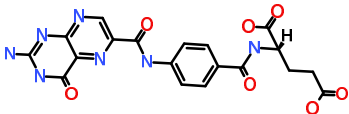
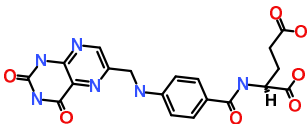
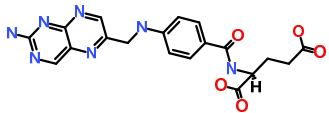
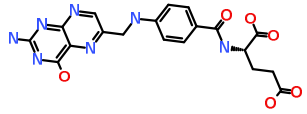
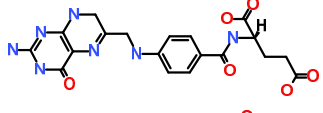
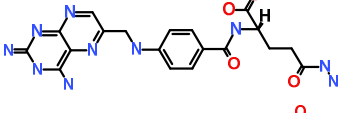
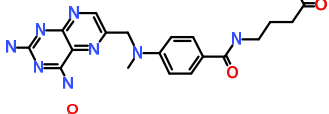
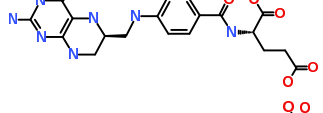
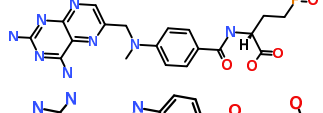
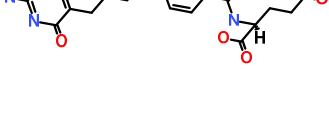
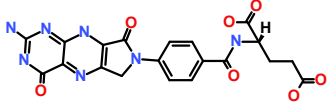
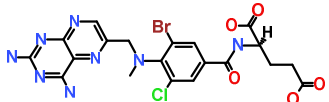
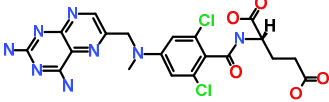
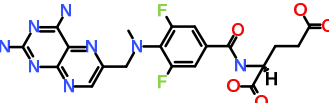
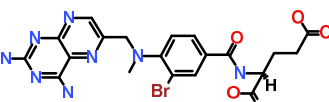
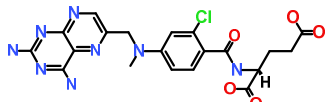
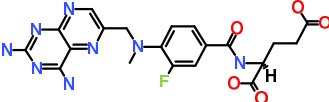
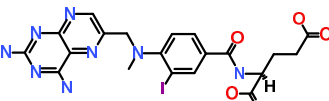
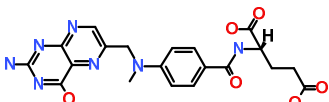
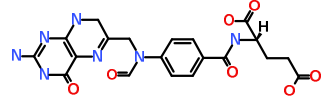
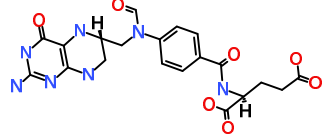
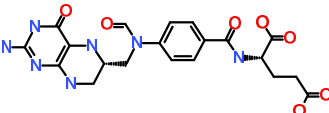
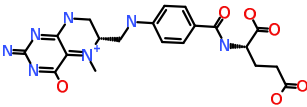
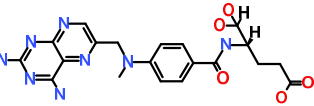
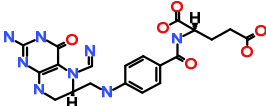
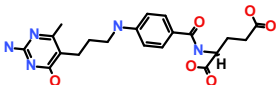
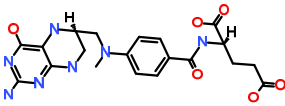
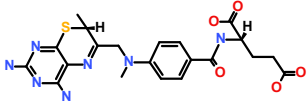
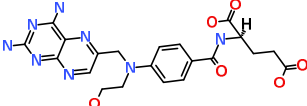
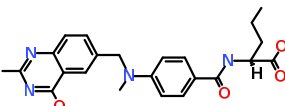
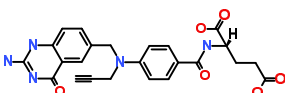


Table S1. List of analog compounds of methotrexate downloaded from ZINC¹⁵ with the description their ZINC ids, molecular formulas and 2D structures representations.

Compound No.	2D Structure	Molecular Formula	ZINC ID
Compound 1		C18 H21 N8 O6 P	ZINC000028764059
Compound 2		C19 H17 N7 O7	ZINC000068590381
Compound 3		C19 H18 N6 O7	ZINC000001698171
Compound 4		C19 H19 N7 O5	ZINC000002944400
Compound 5		C19 H19 N7 O6	ZINC000008577218
Compound 6		C19 H21 N7 O6	ZINC000004228265
Compound 7		C19 H22 N10 O4	ZINC000504557614
Compound 8		C19 H22 N8 O3	ZINC000001653972
Compound 9		C19 H23 N7 O6	ZINC000004228237
Compound 10		C19 H23 N8 O6 P	ZINC000028763233
Compound 11		C19 H24 N6 O6	ZINC000008642279

Compound 12		C20 H17 N7 O7	ZINC000002035058
Compound 13		C20 H20 Br Cl N8 O5	ZINC000008619351
Compound 14		C20 H20 Cl2 N8 O5	ZINC000001728420
compound15		C20 H20 F2 N8 O5	ZINC000001722686
Compound 16		C20 H21 Br N8 O5	ZINC000001643916
Compound 17		C20 H21 Cl N8 O5	ZINC000008628726
Compound 18		C20 H21 F N8 O5	ZINC000001698176
Compound 19		C20 H21 I N8 O5	ZINC000001722685
Compound 20		C20 H21 N7 O6	ZINC000008214609
Compound 21		C20 H21 N7 O7	ZINC000011536135
Compound 22		C20 H22 N7 O6	ZINC000004228269
Compound 23		C20 H23 N7 O7	ZINC000004228247

Compound 24		C20 H24 N7 O6	ZINC000070451053
Compound 25		C20 H24 N8 O5	ZINC000584577528
Compound 26		C20 H24 N8 O6	ZINC000004228294
Compound 27		C20 H25 N5 O6	ZINC000008626527
Compound 28		C20 H25 N7 O6	ZINC000013508844
Compound 29		C21 H25 N7 O5 S	ZINC000033884989
Compound 30		C21 H24 N8 O6	ZINC000013508844
Compound 31		C23 H26 N4 O4	ZINC000725274512
Compound 32		C24 H23 N5 O6	ZINC000008655373

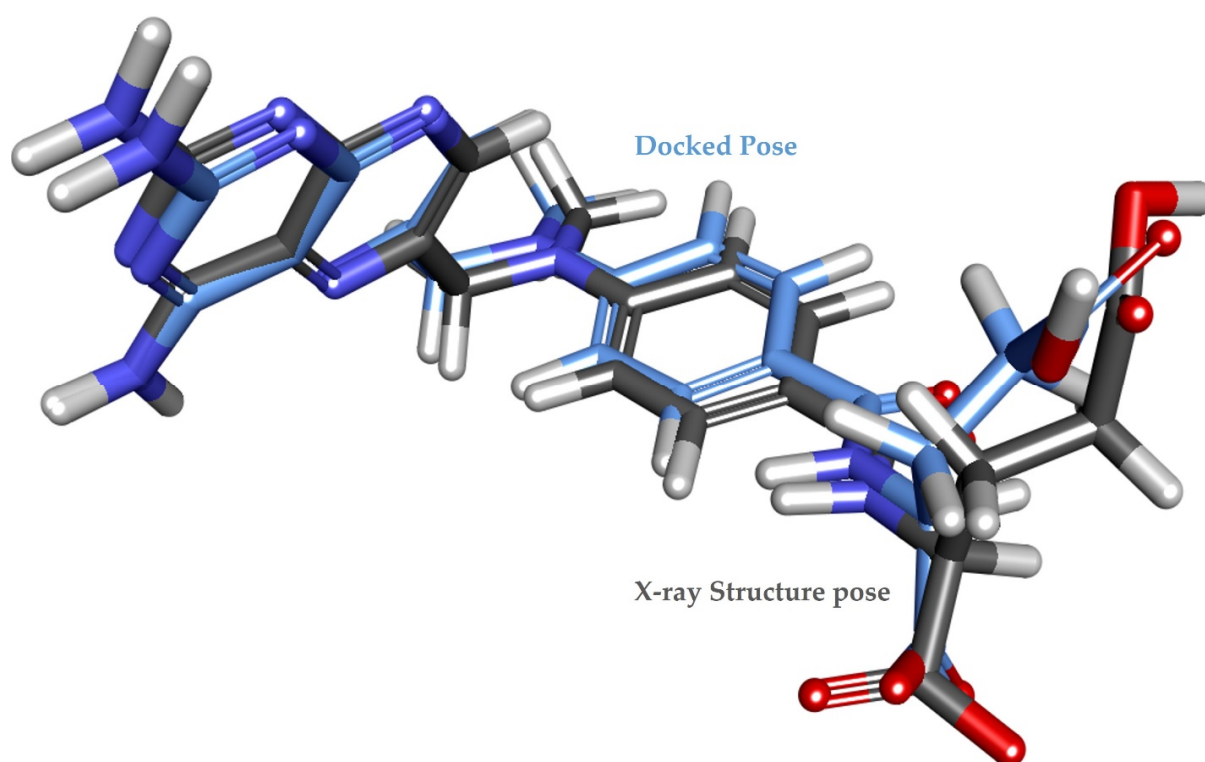


Figure S1. Superimposition of docked pose and crystal structure pose of methotrexate in wild type hDHFR. A low RMSD difference of 0.58Å suggested high suitability of docking protocol.