Supporting Information
For

Monte Carlo method and GA-MLR based QSAR modeling of NS5A inhibitors against the Hepatitis C Virus

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Table S1: SMILES notation for the 36 compounds and their experimental activity data.

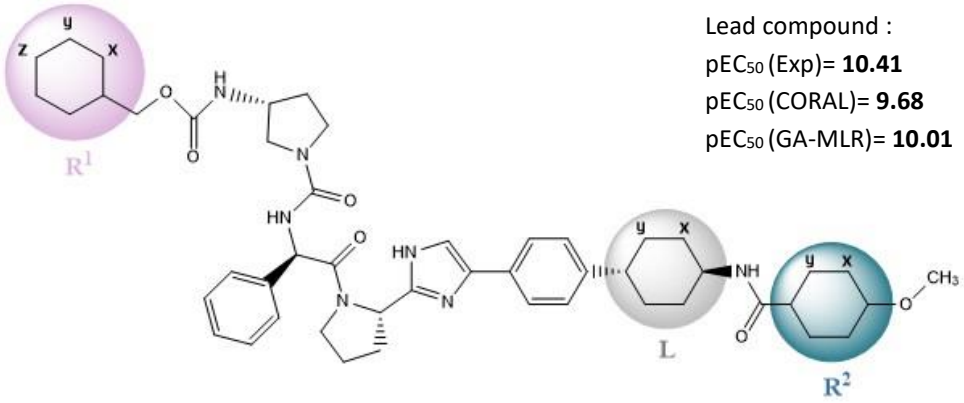
ID	SMILES	EC_{50} (nM)
1	COC(=O)N[C@@H](C(=O)N1CCC[C@H]1C1=NC(=CN1)C1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@H]1CCCN1C(=O)[C@@H](NC(=O)OC)C1=CC=CC=C1)C1=CC=CC=C1	0,098
2	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)OC)C1=CC=CC=C1	2800
3	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)C1=CC=CC=C1)C1=CC=CC=C1	2400
4	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)CCCC1=CC=CC=C1)C1=CC=CC=C1	1300
5	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)CCCCCCC1=CC=CC=C1)C1=CC=CC=C1	642
6	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)CCCNC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	56
7	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@H]1CCCN1C(=O)C(NC(=O)C1=CC=CC=C1NC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	614
8	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)C1=CC(NC(=O)OCC2=CC=CC=C2)=CC=C1)C1=CC=CC=C1	44
9	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)C1=CC=C(NC(=O)OCC2=CC=CC=C2)C=C1)C1=CC=CC=C1	131
10	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@H]1CCCN1C(=O)[C@@H](NC(=O)N1CCC[C@H](C1)NC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	247
11	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@H]1CCCN1C(=O)[C@@H](NC(=O)N1CCC[C@@H](C1)NC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	100
12	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)N1CC[C@@H](C1)NC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	82
13	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)N1CC[C@H](C1)NC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	1.1
14	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@H]1CCCN1C(=O)[C@@H](NC(=O)N1CCCC1)C1=CC=CC=C1	353
15	CCCC(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@H]1CCCN1C(=O)[C@@H](NC(=O)N1CC[C@@H](C1)NC(=O)OC)C1=CC=CC=C1	353
16	O=C(CCCNC(=O)OCC1=CC=CC=C1)N[C@@H](C(=O)N1CCC[C@H]1C1=NC(=CN1)C1=CC=C(C=C1)C1=CC=C(NC(=O)C2=CC=CC=C2)C=C1)C1=CC=CC=C1	34
17	COCC1=CC=C(C=C1)C(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)CCCNC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	3.5
18	COC1CCC(CC1)C(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)CCCNC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	8.1
19	COC1CCN(CC1)C(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)CCCNC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	2.3
20	COC1CCN(CC1)C(=O)NC1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)N1CC[C@H](C1)NC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	0.039
21	COC(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC=CN1)C1=CC=CC=C1	10000

22	COC(=O)N[C@@H](C(=O)N1CCC[C@H]1C1=NC(=CN1)C1=CC=C(C=C1)C1=CC=CC=C1)C1=CC=CC=C1	2800
23	COC1CCN(CC1)C(=O)N[C@H]1CC[C@@H](CC1)C1=CC=C(C=C1)C1=CNC(=N1)[C@H]1CCCN1C(=O)[C@@H](NC(=O)N1CC[C@@H](C1)NC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	0.15
24	COC1CCC(CC1)C(=O)N[C@H]1CC[C@@H](CC1)C1=CC=C(C=C1)C1=CNC(=N1)[C@H]1CCCN1C(=O)[C@@H](NC(=O)N1CC[C@@H](C1)NC(=O)OCC1=CC=CC=C1)C1=CC=CC=C1	0.17
25	COC1CCC(CC1)C(=O)N[C@H]1CC[C@@H](CC1)C1=CC=C(C=C1)C1=CNC(=N1)[C@H]1CCCN1C(=O)[C@@H](NC(=O)N1CC[C@@H](C1)NC(=O)OCC1CCCCC1)C1=CC=CC=C1	0.039
26	O=C(N[C@H]1CCN(C1)C(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)[C@H]1CC[C@@H](CC1)NC(=O)C1=CN=CC=N1)C1=CC=CC=C1)OCC1CCCCC1	0.35
27	CCCCCOC(=O)N[C@H]1CCN(C1)C(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)[C@H]1CC[C@@H](CC1)NC(=O)C1=CN=CC=N1)C1=CC=CC=C1	0.97
28	CC#CCCOC(=O)N[C@H]1CCN(C1)C(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)[C@H]1CC[C@@H](CC1)NC(=O)C1=CN=CC=N1)C1=CC=CC=C1	3.4
29	CCC#CCOC(=O)N[C@H]1CCN(C1)C(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)[C@H]1CC[C@@H](CC1)NC(=O)C1=CN=CC=N1)C1=CC=CC=C1	0.39
30	CC#CCOC(=O)N[C@H]1CCN(C1)C(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)[C@H]1CC[C@@H](CC1)NC(=O)C1=CN=CC=N1)C1=CC=CC=C1	2.1
31	CCCC#CCOC(=O)N[C@H]1CCN(C1)C(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)[C@H]1CC[C@@H](CC1)NC(=O)C1=CN=CC=N1)C1=CC=CC=C1	0.27
32	CC(C)C#CCOC(=O)N[C@H]1CCN(C1)C(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)[C@H]1CC[C@@H](CC1)NC(=O)C1=CN=CC=N1)C1=CC=CC=C1	0.18
33	CC(C)(C)C#CCOC(=O)N[C@H]1CCN(C1)C(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)[C@H]1CC[C@@H](CC1)NC(=O)C1=CN=CC=N1)C1=CC=CC=C1	0.13
34	CC(C)C#CCOC(=O)N[C@H]1CCN(C1)C(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)[C@H]1CC[C@@H](CC1)NC(=O)C1=CN=C(CO)C=N1)C1=CC=CC=C1	0.12
35	CC(C)(C)C#CCOC(=O)N[C@H]1CCN(C1)C(=O)N[C@H](C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)[C@H]1CC[C@@H](CC1)NC(=O)C1=CN=C(CO)C=N1)C1=CC=CC=C1	0.059
36	COC(=O)N[C@@H](C(C)C)C(=O)N1CCC[C@@H]1C1=NC(=CN1)C1=CC=C(C=C1)C1=CC=C(C=C1)C1=CNC(=N1)[C@@H]1CCCN1C(=O)[C@H](NC(=O)OC)C(C)C	0.05

Table S2: Mathematical equations of statistical parameters used.

No	Equation
1	$R^2_{tr} = 1 - \frac{\Sigma\,(Y_{obs} - Y_{pred})^2}{\Sigma\,(Y_{obs} - \bar{Y})^2}$
2	$Q^2_{loo} = 1 - \frac{\Sigma\,(Y_{obs} - Y_{pred})^2}{\Sigma\,(Y_{obs} - \bar{Y})^2}$
3	$R^2_{ext} = \left[\frac{\sum_{i=1}^{n_{ext}}(Y_{obs} - \overline{Y}_{obs})\,(Y_{pred} - \overline{Y}_{pred})}{\sqrt{\sum_{i=1}^{n_{ext}}(Y_{obs} - \overline{Y}_{obs})^2\,(Y_{pred} - \overline{Y}_{pred})^2}}\right]^2$
4	$Q^2_{F1} = 1 - \frac{\sum_{i=1}^{n_{ext}}(Y_{obs} - Y_{pred})^2}{\sum_{i=1}^{n_{ext}}(Y_{obs} - Y_{train})^2}$
5	$Q^2_{F2} = 1 - \frac{\sum_{i=1}^{n_{ext}}(Y_{obs} - Y_{pred})^2}{\sum_{i=1}^{n_{ext}}(Y_{obs} - Y_{ext})^2}$
6	$Q^2_{F3} = 1 - \frac{\sum_{i=1}^{n_{ext}}\frac{(y_i - \hat{y}_i)^2}{n_{test}}}{\sum_{j=1}^{n_{ext}}\frac{\left(y_j - \hat{y}_{TR}\right)^2}{n_{TR}}} = 1 - \frac{RMSEP^2}{S^2_{TR}}$
7	$IIC = \mathrm{R}_{set} \times \frac{\min(\bar{}MAEset,\ {}^{+}MAEset)}{\max(\bar{}MAEset,\ {}^{+}MAEset)}$
8	$R^2_m = r^2(1 - \sqrt{\lvert r^2 - r_0^2\rvert})$
9	$CCI_{cal} = \Sigma\Delta R_{j\,calc};\ \Delta R_{j\,calc} < 0$
10	$CCC = \frac{2\sum_{i=1}^{n_{ext}}(Y_{obs} - \overline{Y}_{obs})\,(Y_{pred} - \overline{Y}_{pred})}{\sum_{i=1}^{n_{ext}}(Y_{obs} - \overline{Y}_{obs})^2 + \sum_{i=1}^{n_{ext}}(Y_{pred} - \overline{Y}_{pred})^2 + n_{ext}(Y_{obs} - \overline{Y}_{pred})^2}$
11	$C_{R^2_p} = R\sqrt{(R^2 - R^2_r)}$
12	$MAE = \frac{1}{n} \times \Sigma\lvert Y_{obs} - Y_{pred}\rvert$
13	$RMSE = \sqrt{\frac{1}{n} \times\ \Sigma\,(Y_{obs} - Y_{pred})^2}$

Table S3: Chemical structures of designed NS5A inhibitors



Lead compound :
pEC_{50} (Exp)= **10.41**
pEC_{50} (CORAL)= **9.68**
pEC_{50} (GA-MLR)= **10.01**

No.			Promoter of increase	Feature	pEC_{50} (CORAL)	pEC_{50} (GA-MLR)
1	R^1	x	C...(.....	—CH_3	9.77	10.17
2			C...C.....	—C_2H_5	9.75	10.16
3			C...O...C...	—OCH_3	9.92	11.09
4			O...C...C...	—OC_2H_5	10 .24	10.64
5			N...C.....	—$NHCH_3$	9.23	10.63
6			N...C...C...	—NHC_2H_5	10.03	11.11
7		y	C...(.....	—CH_3	9.88	10.50
8			C...C.....	—C_2H_5	11.78	10.13
9			C...O...C...	—OCH_3	9.95	11.20
10			O...C...C...	—OC_2H_5	12.27	11.23
11			N...C.....	—$NHCH_3$	11.95	10.71
12			N...C...C...	—NHC_2H_5	12.05	10.70
13		z	C...(.....	—CH_3	9.84	10.17
14			C...C.....	—C_2H_5	11.73	10.16
15			C...O...C...	—OCH_3	12.18	11.18
16			O...C...C...	—OC_2H_5	12.23	10.68
17			N...C.....	—$NHCH_3$	11.91	10.67
18			N...C...C...	—NHC_2H_5	12.01	11.16

No.			Promoter of increase	Feature	pEC_{50} (CORAL)	pEC_{50} (GA-MLR)
19	L	x	C...(.....	—CH_3	9.95	10.14
20			C...C.....	—C_2H_5	9.82	10.11
21			C...O...C...	—OCH_3	9.29	10.75
22			O...C...C...	—OC_2H_5	9.18	10.82
23			N...C.....	—$NHCH_3$	10.03	10.53
24			N...C...C...	—NHC_2H_5	9.35	10.52
25		y	C...(.....	—CH_3	9.45	10.14
26			C...C.....	—C_2H_5	9.67	10.11
27			C...O...C...	—OCH_3	9.98	10.70
28			O...C...C...	—OC_2H_5	9.47	10.67
29			N...C.....	—$NHCH_3$	9.56	10.49
30			N...C...C...	—NHC_2H_5	9.78	10.47
31	R^2	x	C...(.....	—CH_3	9.95	10.17
32			C...C.....	—C_2H_5	9.47	10.03
33			C...O...C...	—OCH_3	10.03	11.31
34			O...C...C...	—OC_2H_5	9.65	11.30
35			N...C.....	—$NHCH_3$	9.74	10.72
36			N...C...C...	—NHC_2H_5	9.96	10.71
37		y	C...(.....	—CH_3	9.82	10.17
38			C...C.....	—C_2H_5	9.54	10.03
39			C...O...C...	—OCH_3	9.98	11.19
40			O...C...C...	—OC_2H_5	9.72	11.17
41			N...C.....	—$NHCH_3$	9.81	10.66
42			N...C...C...	—NHC_2H_5	10.05	10.65