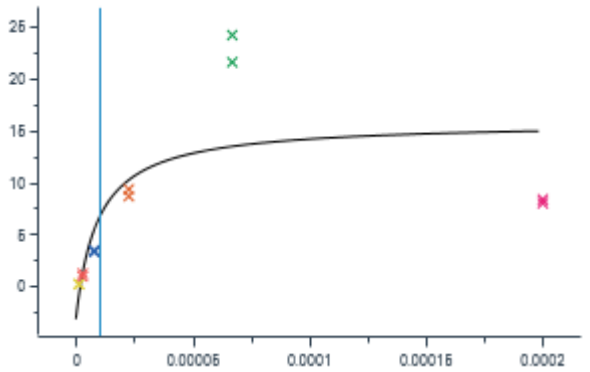
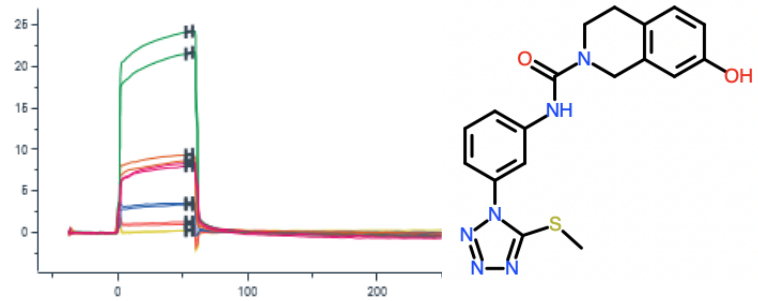
CACHE#2 – NSP13 SARS2
Participant 1413

24 analogs of CACHE_1413_19 were submitted for round 2.
2 compounds, including re-supplied parent molecule showed weak binding profile.

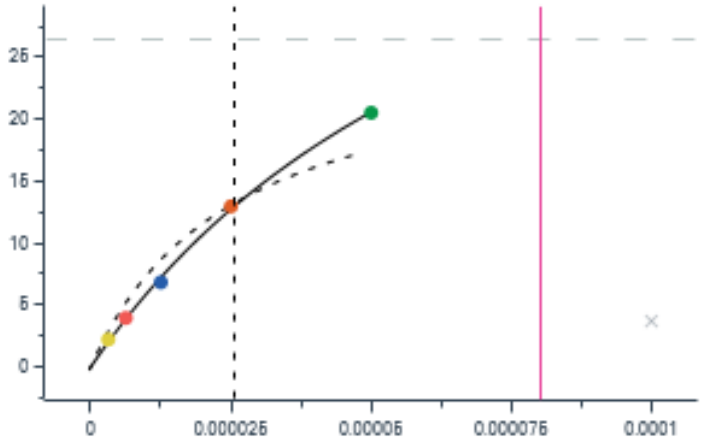
PARENT MOLECULE

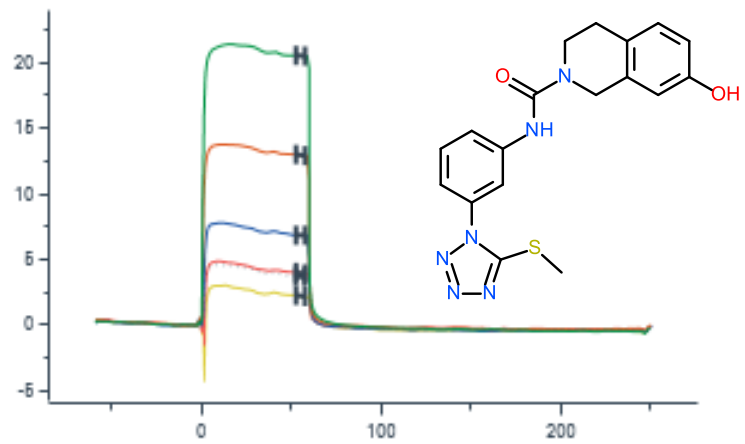




CACHE_1413_19

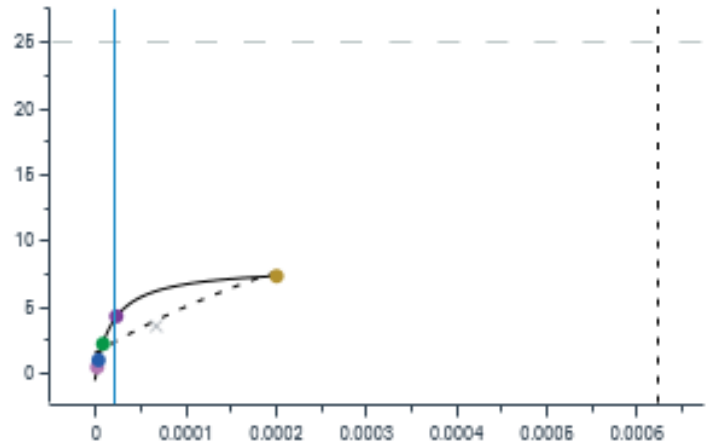
K_D = 10 µM (poor fit) – 62% binding
DLS (solub@200 µM)
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 40

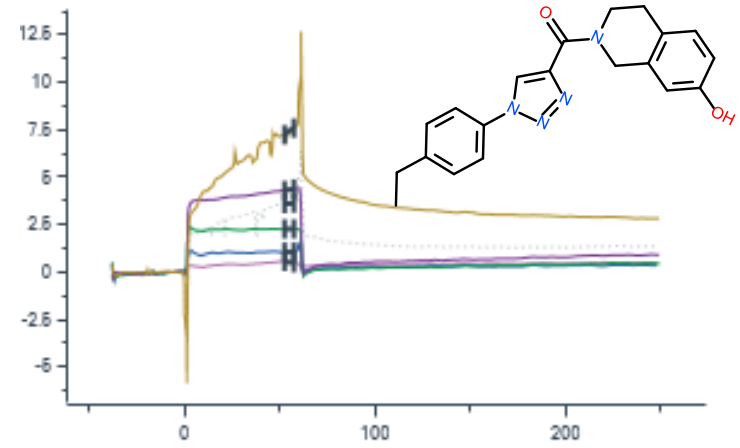




CACHE2-HO_1413_1

K_D (3% DMSO) = 82±4 µM (does not reach saturation) – 207±%7 binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@50 µM)
%inhibition@50 µM_ATPase = 20

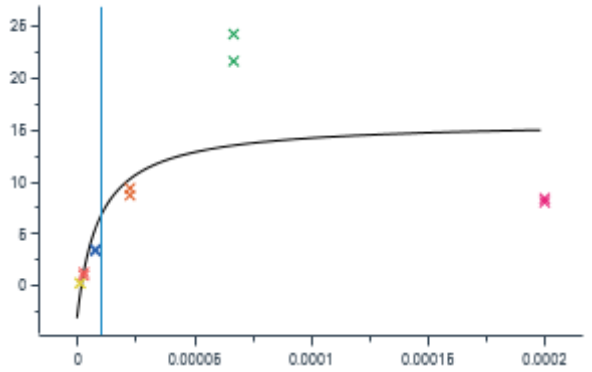


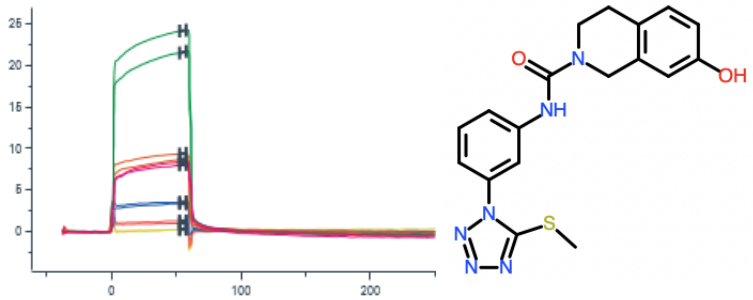


CACHE2-HO_1413_3

K_D = 20 µM – 32% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 11

PARENT MOLECULE

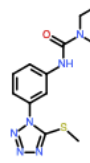
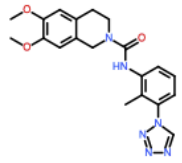
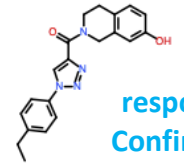
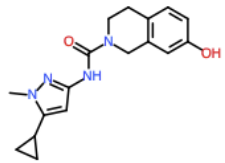
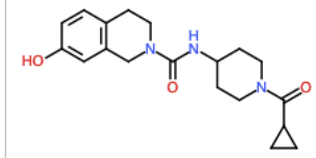
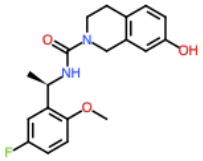
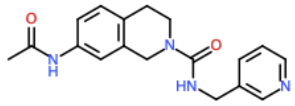
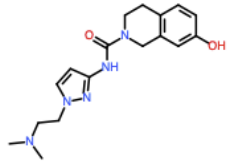
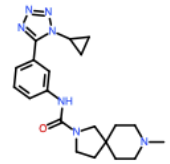
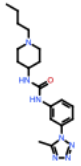
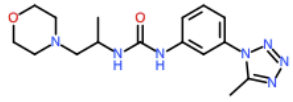
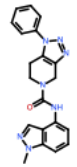
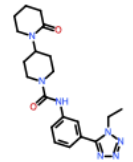
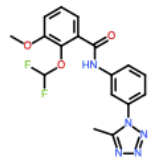
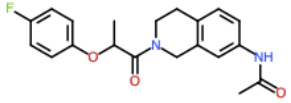




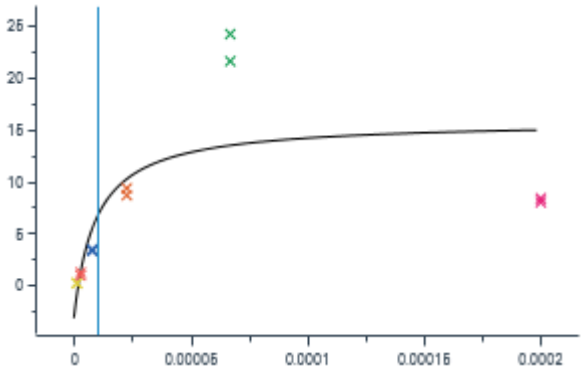
CACHE_1413_19

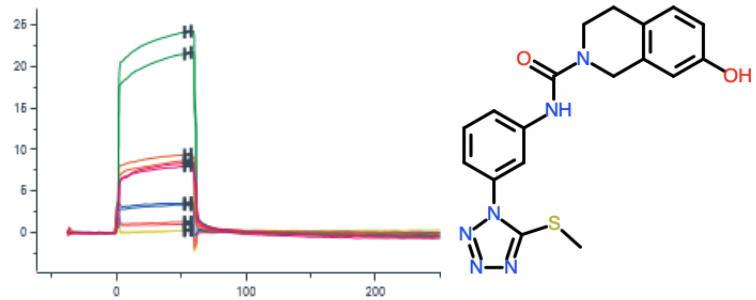
K_D = 10 µM (poor fit) – 62% binding
DLS (solub@200 µM)
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 40

Tested analogs

 Dose response: Confirmed CACHE_ID CACHE2-HO_1413_1 Parent CACHE_1413_19 distance_to_pai 0	 CACHE_ID CACHE2-HO_1413_2 Parent CACHE_1413_19 distance_to_pai 0.1879	 Dose response: Confirmed CACHE_ID CACHE2-HO_1413_3 Parent CACHE_1413_19 distance_to_pai 0.393	 CACHE_ID CACHE2-HO_1413_4 Parent CACHE_1413_19 distance_to_pai 0.3956	 CACHE_ID CACHE2-HO_1413_5 Parent CACHE_1413_19 distance_to_pai 0.407
 CACHE_ID CACHE2-HO_1413_6 Parent CACHE_1413_19 distance_to_pai 0.42	 CACHE_ID CACHE2-HO_1413_7 Parent CACHE_1413_19 distance_to_pai 0.4324	 CACHE_ID CACHE2-HO_1413_8 Parent CACHE_1413_19 distance_to_pai 0.433	 CACHE_ID CACHE2-HO_1413_9 Parent CACHE_1413_19 distance_to_pai 0.4691	 CACHE_ID CACHE2-HO_1413_10 Parent CACHE_1413_19 distance_to_pai 0.4702
 CACHE_ID CACHE2-HO_1413_11 Parent CACHE_1413_19 distance_to_pai 0.495	 CACHE_ID CACHE2-HO_1413_12 Parent CACHE_1413_19 distance_to_pai 0.4961	 CACHE_ID CACHE2-HO_1413_13 Parent CACHE_1413_19 distance_to_pai 0.5098	 CACHE_ID CACHE2-HO_1413_14 Parent CACHE_1413_19 distance_to_pai 0.5159	 CACHE_ID CACHE2-HO_1413_15 Parent CACHE_1413_19 distance_to_pai 0.517

PARENT MOLECULE

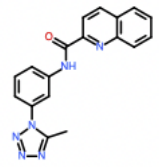
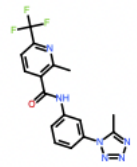
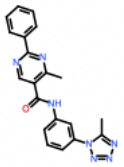
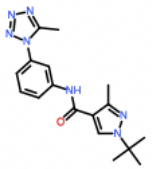
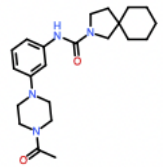
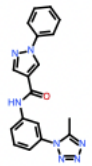
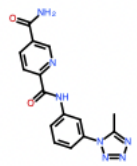
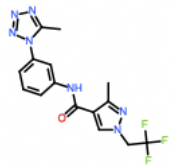
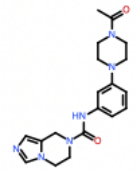




CACHE_1413_19

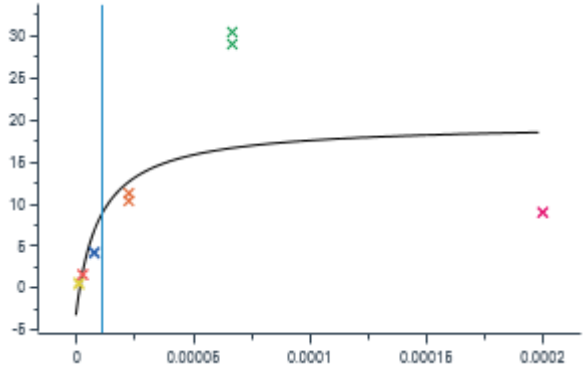
K_D = 10 µM (poor fit) – 62% binding
DLS (solub@200 µM)
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 40

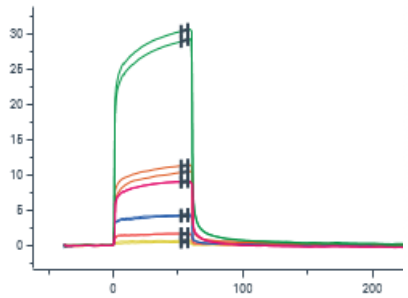
Tested analogs (cont…)

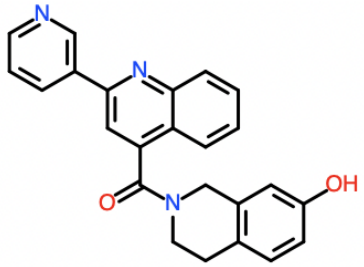
 CACHE_ID CACHE2-HO_1413_21 Parent CACHE_1413_19 distance_to_pai 0.5468	 CACHE_ID CACHE2-HO_1413_22 Parent CACHE_1413_19 distance_to_pai 0.5517	 CACHE_ID CACHE2-HO_1413_23 Parent CACHE_1413_19 distance_to_pai 0.5538	 CACHE_ID CACHE2-HO_1413_24 Parent CACHE_1413_19 distance_to_pai 0.5635	 CACHE_ID CACHE2-HO_1413_25 Parent CACHE_1413_19 distance_to_pai 0.5636
 CACHE_ID CACHE2-HO_1413_26 Parent CACHE_1413_19 distance_to_pai 0.5641	 CACHE_ID CACHE2-HO_1413_27 Parent CACHE_1413_19 distance_to_pai 0.5656	 CACHE_ID CACHE2-HO_1413_28 Parent CACHE_1413_19 distance_to_pai 0.5689	 CACHE_ID CACHE2-HO_1413_29 Parent CACHE_1413_19 distance_to_pai 0.6069	

15 analogs of CACHE_1413_21 were submitted for round 2.
1 compound (re-supplied parent molecule) confirmed binding by SPR, showing the tendency to reach saturation.

PARENT MOLECULE

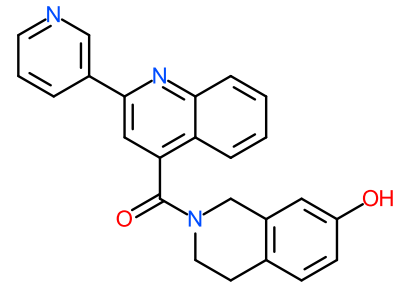


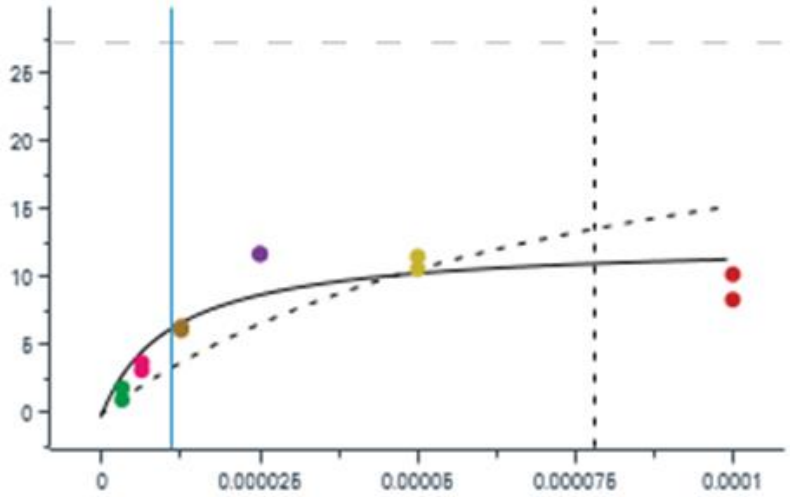


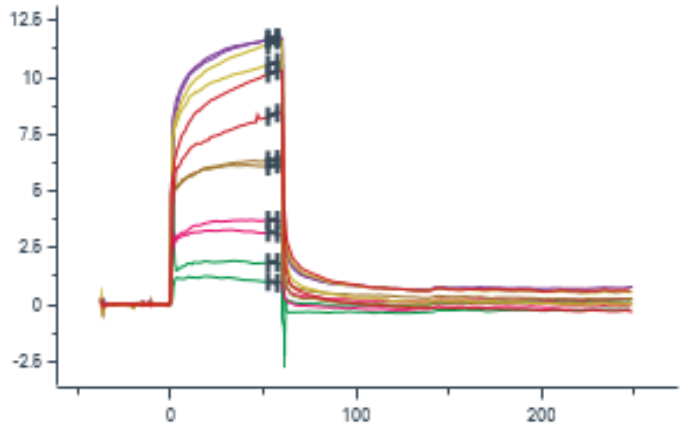


CACHE_1413_21
K_D = 11 µM (poor fit) – 74% binding
DLS (solub@200 µM)
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 3

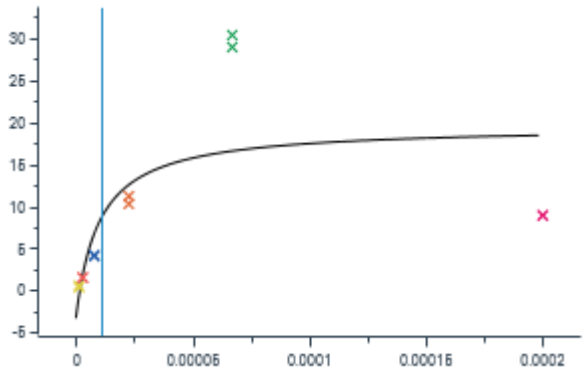
CACHE2-HO_1413_30
K_D = 11 µM (poor fit) – 46% binding
DLS (solub@50 µM)
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 3

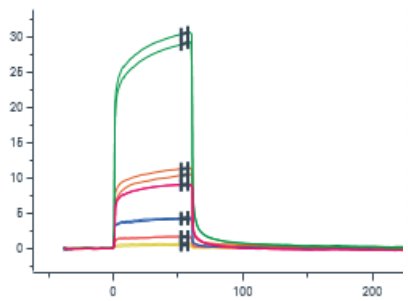


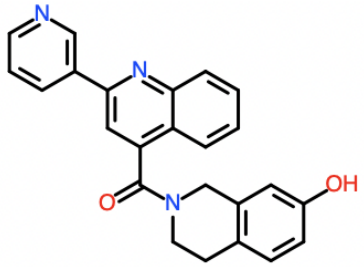




PARENT MOLECULE



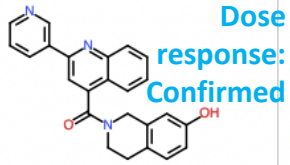
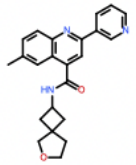
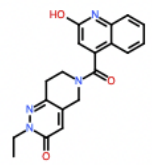
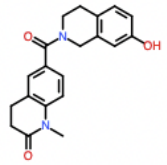
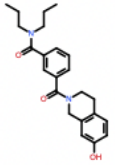
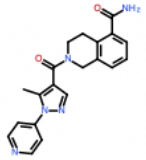
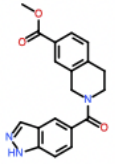
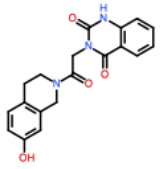
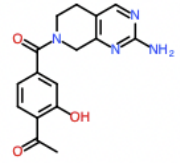
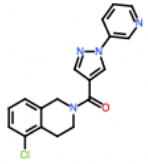
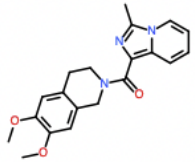
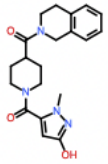
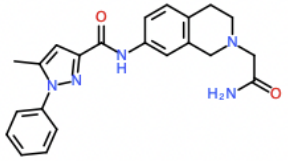
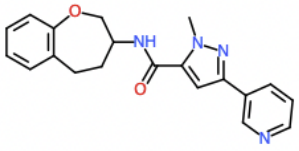
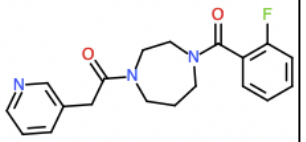




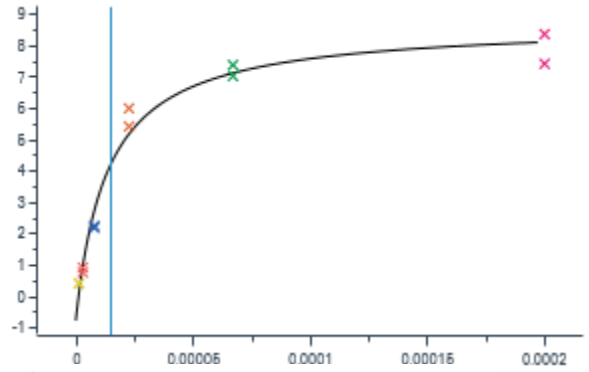
CACHE_1413_21

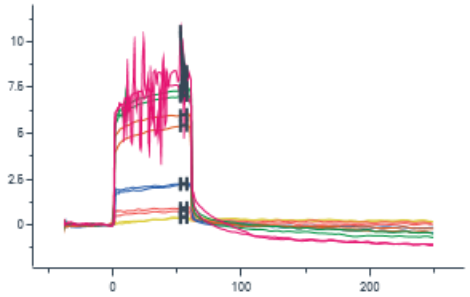
K_D = 11 µM (poor fit) – 74% binding
DLS (solub@200 µM)
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 3

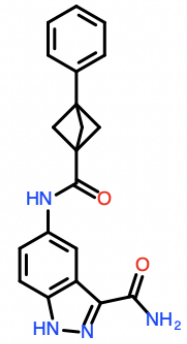
Tested analogs

Dose response: Confirmed  CACHE_ID CACHE2-HO_1413_30 Parent CACHE_1413_21 distance_to_pai 0	 CACHE_ID CACHE2-HO_1413_31 Parent CACHE_1413_21 distance_to_pai 0.3322	 CACHE_ID CACHE2-HO_1413_32 Parent CACHE_1413_21 distance_to_pai 0.3365	 CACHE_ID CACHE2-HO_1413_33 Parent CACHE_1413_21 distance_to_pai 0.3589	 CACHE_ID CACHE2-HO_1413_34 Parent CACHE_1413_21 distance_to_pai 0.3594
 CACHE_ID CACHE2-HO_1413_35 Parent CACHE_1413_21 distance_to_pai 0.4164	 CACHE_ID CACHE2-HO_1413_36 Parent CACHE_1413_21 distance_to_pai 0.4295	 CACHE_ID CACHE2-HO_1413_37 Parent CACHE_1413_21 distance_to_pai 0.4451	 CACHE_ID CACHE2-HO_1413_38 Parent CACHE_1413_21 distance_to_pai 0.4482	 CACHE_ID CACHE2-HO_1413_39 Parent CACHE_1413_21 distance_to_pai 0.4603
 CACHE_ID CACHE2-HO_1413_40 Parent CACHE_1413_21 distance_to_pai 0.479	 CACHE_ID CACHE2-HO_1413_41 Parent CACHE_1413_21 distance_to_pai 0.4845	 CACHE_ID CACHE2-HO_1413_42 Parent CACHE_1413_21 distance_to_pai 0.4985	 CACHE_ID CACHE2-HO_1413_43 Parent CACHE_1413_21 distance_to_pai 0.5634	 CACHE_ID CACHE2-HO_1413_44 Parent CACHE_1413_21 distance_to_pai 0.5647

PARENT MOLECULE



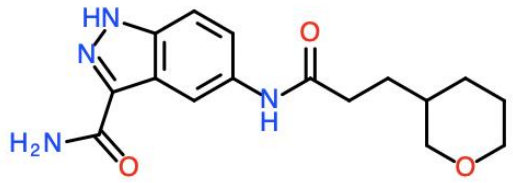




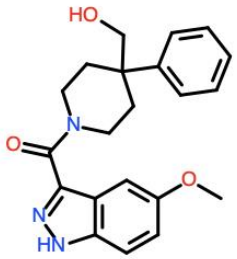
CACHE_1413_5

K_D = 14 µM – 34% binding
DLS (solub@200 µM)
Selectivity (unrelated WDR5 protein) – Yes
IC_{50} _ATPase > 100 µM

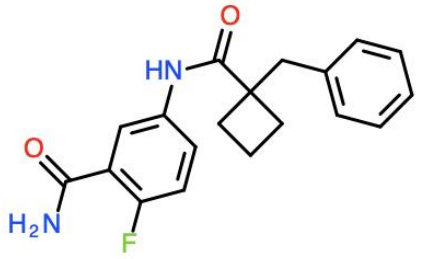
Tested analogs



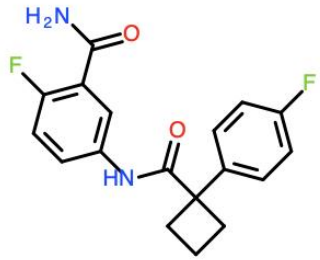
CACHE_ID	CACHE2-HO_1413_45
Parent	CACHE_1413_5
distance_to_pai	0.2762



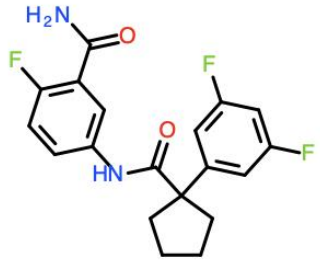
CACHE_ID	CACHE2-HO_1413_46
Parent	CACHE_1413_5
distance_to_pai	0.4013



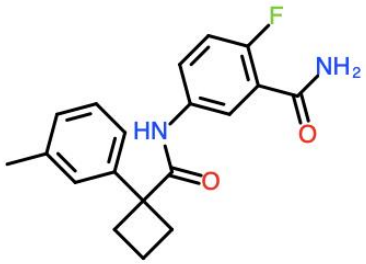
CACHE_ID	CACHE2-HO_1413_47
Parent	CACHE_1413_5
distance_to_pai	0.576



CACHE_ID	CACHE2-HO_1413_48
Parent	CACHE_1413_5
distance_to_pai	0.5825

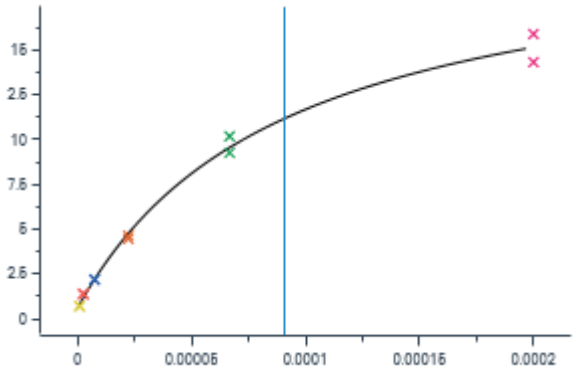


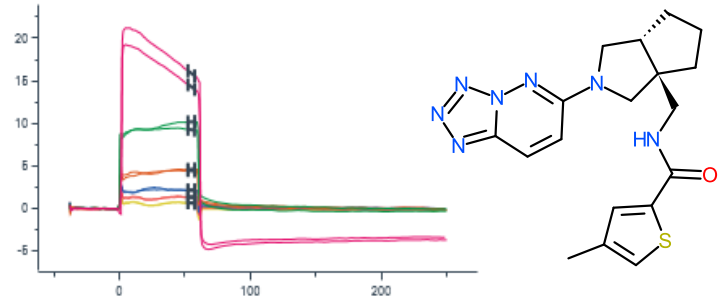
CACHE_ID	CACHE2-HO_1413_49
Parent	CACHE_1413_5
distance_to_pai	0.5848



CACHE_ID	CACHE2-HO_1413_50
Parent	CACHE_1413_5
distance_to_pai	0.5868

Round 1 HIT MOLECULE





CACHE_1413_41

K_D = 91 µM – 82% binding

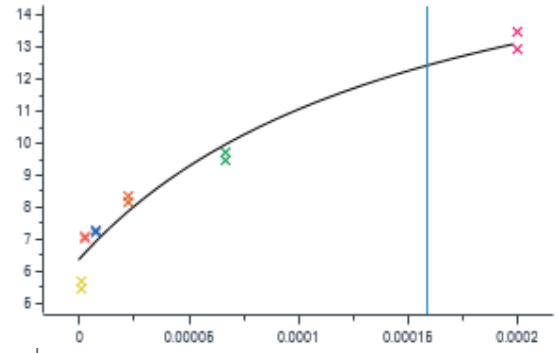
%inhibition@50 µM_ATPase = 8

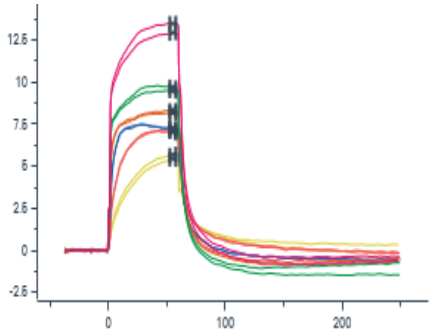
No compound in Round 2

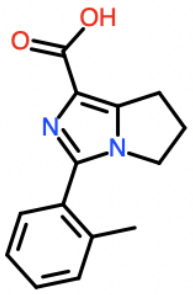
CACHE#2 – NSP13 SARS2

Participant 1414

PARENT MOLECULE







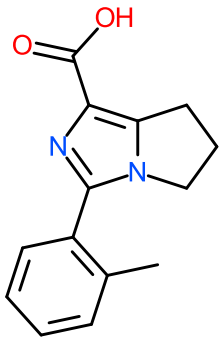
CACHE_1414_34

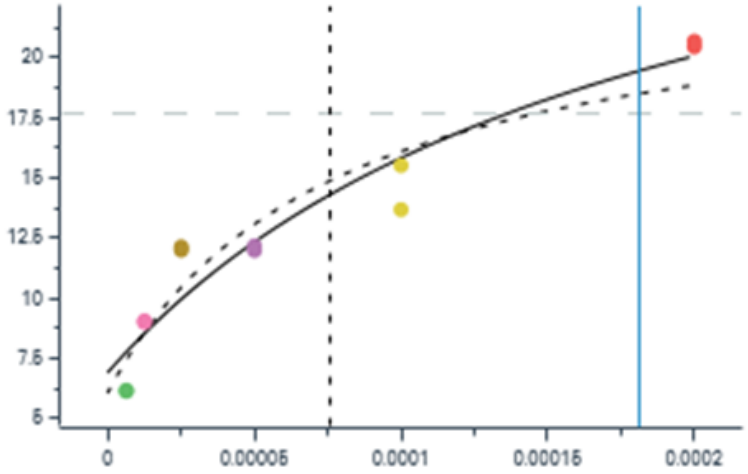
K_D = 159 µM – 75% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 2

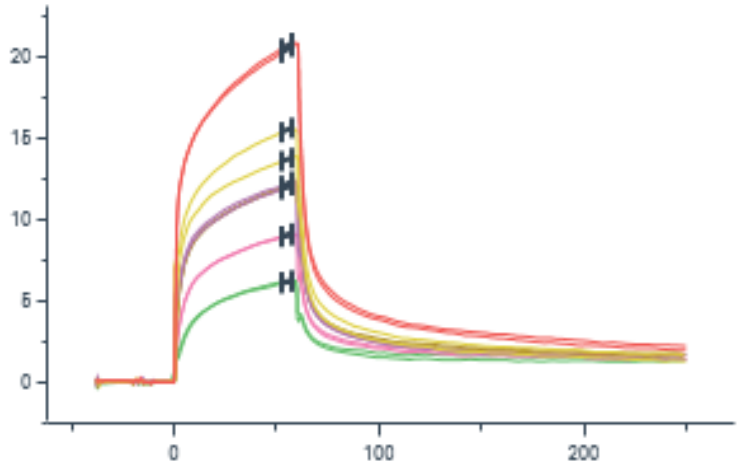
10 analogs of CACHE_1414_34 were submitted for round 2.
1 compound (re-supplied parent molecule) confirmed binding by SPR, showing a tendency to reach saturation.

CACHE2-HO_1414_1

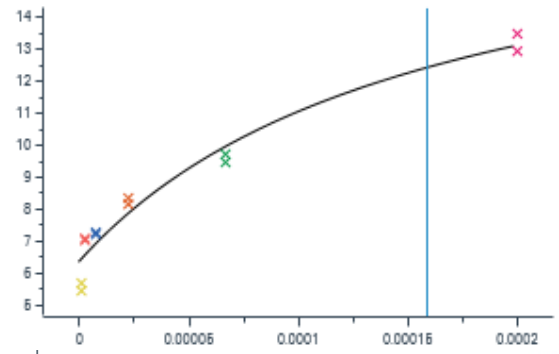
K_D = 182 µM – 142% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@50 µM)
%inhibition@50 µM_ATPase = 11

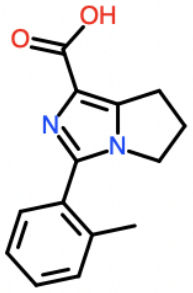






PARENT MOLECULE



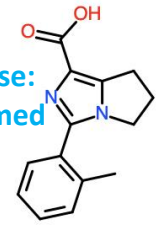
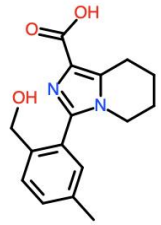
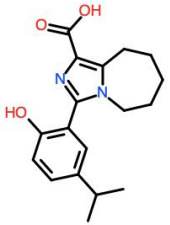
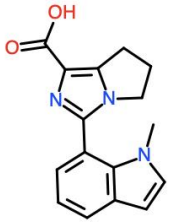
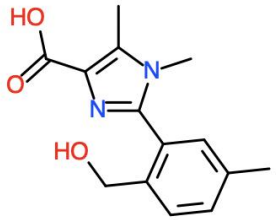
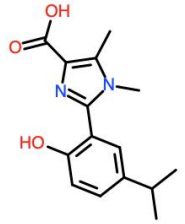
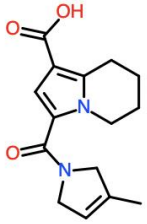
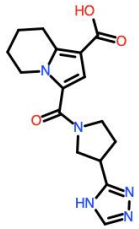
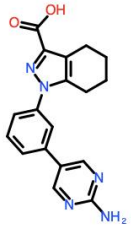


CACHE_1414_34

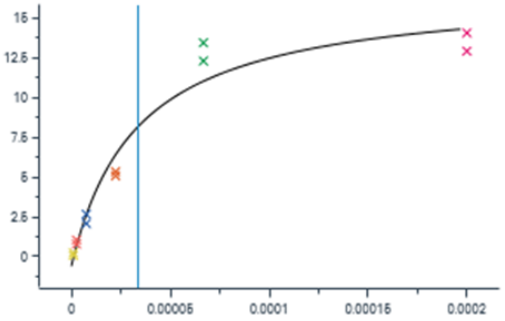
K_D = 159 µM – 75% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 2

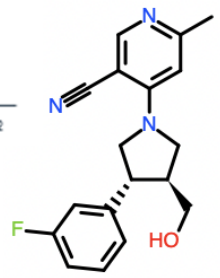
Blank means inactive

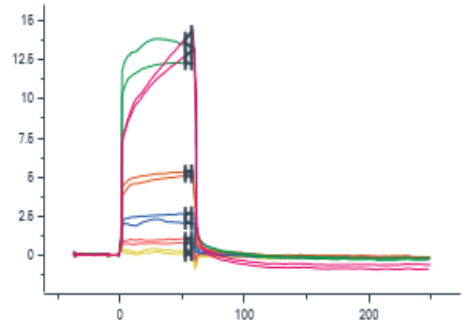
Tested analogs

Dose response: Confirmed  CACHE_ID CACHE2-HO_1414_1 Parent CACHE_1414_34 distance_to_pai 0	 CACHE_ID CACHE2-HO_1414_2 Parent CACHE_1414_34 distance_to_pai 0.112	 CACHE_ID CACHE2-HO_1414_3 Parent CACHE_1414_34 distance_to_pai 0.112	 CACHE_ID CACHE2-HO_1414_4 Parent CACHE_1414_34 distance_to_pai 0.1633
 CACHE_ID CACHE2-HO_1414_5 Parent CACHE_1414_34 distance_to_pai 0.28	 CACHE_ID CACHE2-HO_1414_6 Parent CACHE_1414_34 distance_to_pai 0.428	 CACHE_ID CACHE2-HO_1414_7 Parent CACHE_1414_34 distance_to_pai 0.44	 CACHE_ID CACHE2-HO_1414_8 Parent CACHE_1414_34 distance_to_pai 0.5161
 CACHE_ID CACHE2-HO_1414_9 Parent CACHE_1414_34 distance_to_pai 0.5292	 CACHE_ID CACHE2-HO_1414_10 Parent CACHE_1414_34 distance_to_pai 0.6281		

PARENT MOLECULE

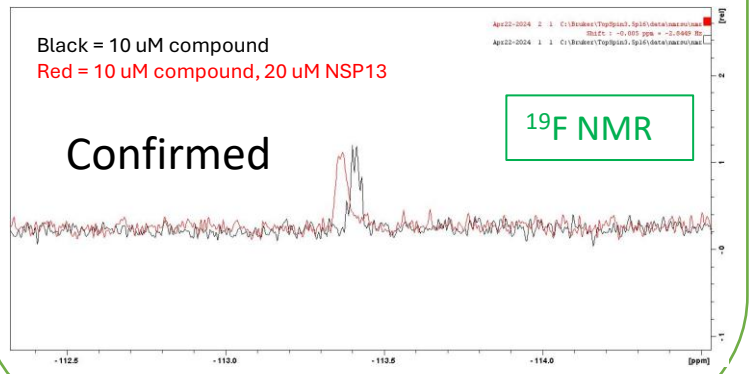




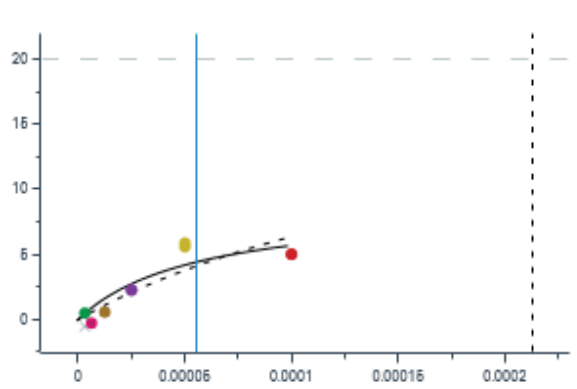


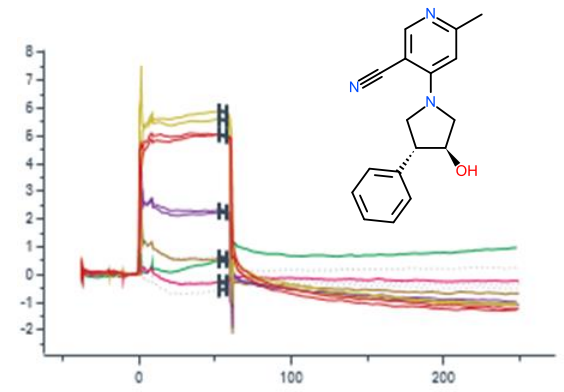
CACHE_1414_40

K_D = 33 µM – 84% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 10



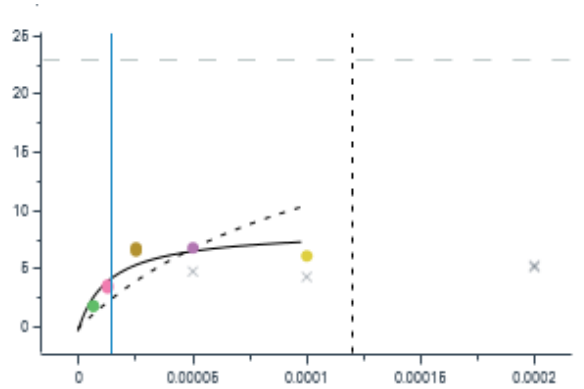
24 analogs of CACHE_1414_40 were submitted for round 2.
3 compounds showed a binding response by SPR.

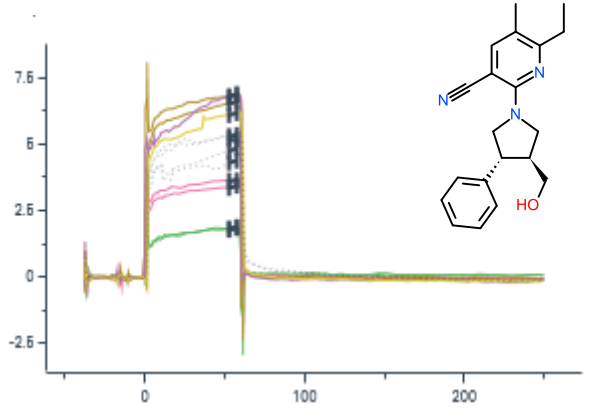




CACHE2-HO_1414_13

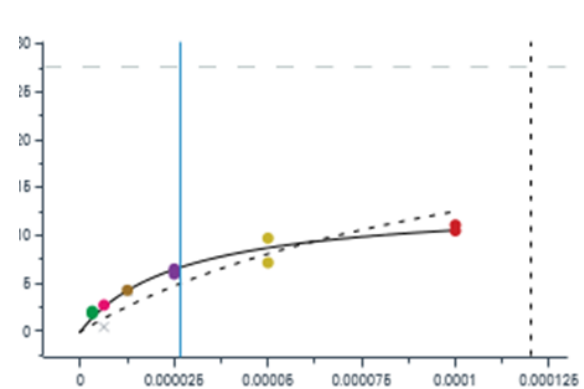
K_D _1 = 41 µM – 66% binding
K_D _2 = 56 µM – 44% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 11

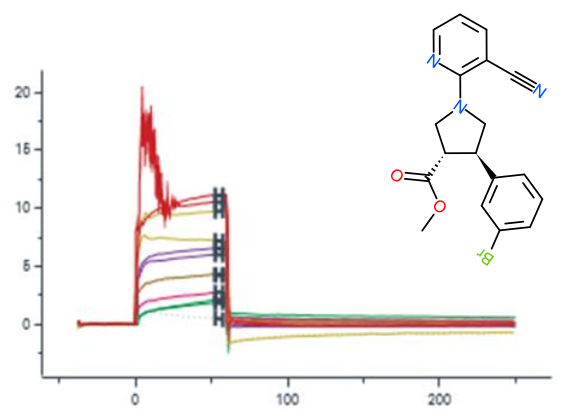




CACHE2-HO_1414_14

K_D (3% DMSO) = 14 µM – 36% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 5

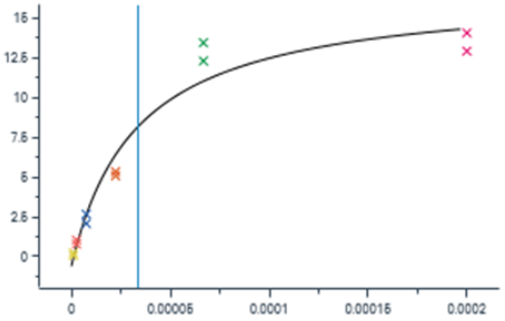


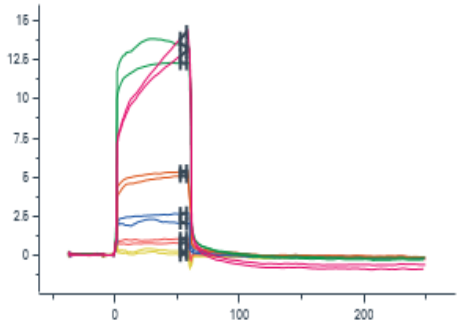


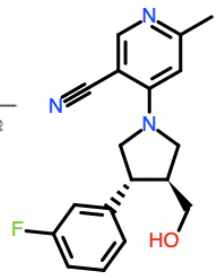
CACHE2-HO_1414_20

K_D _1 = 36 µM – 62% binding
K_D _2 (3% DMSO) = 27 µM – 49% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 8

PARENT MOLECULE

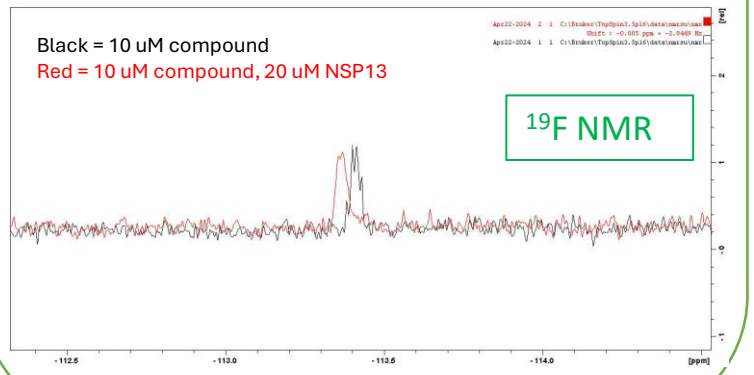




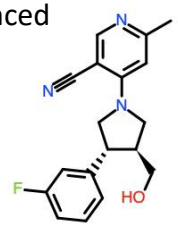
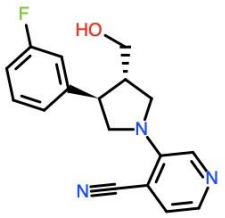
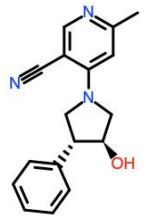
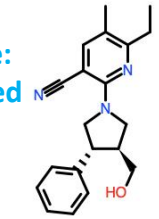
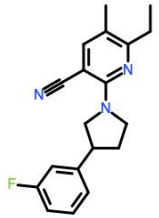
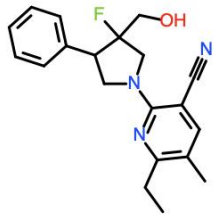
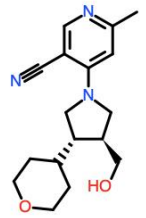
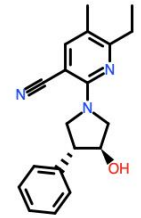
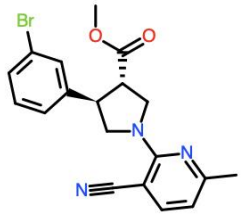
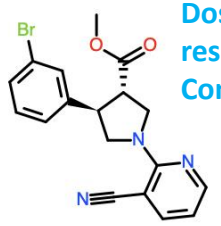
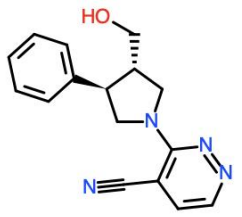
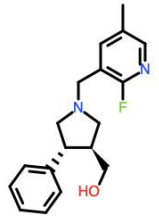


CACHE_1414_40

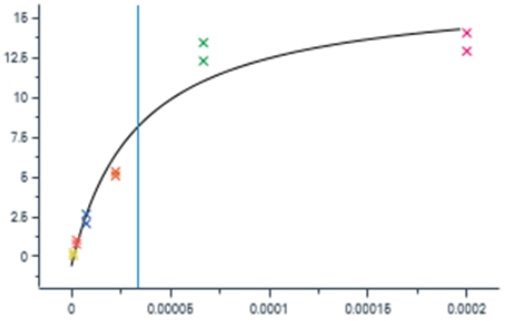
K_D = 33 µM – 84% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 10

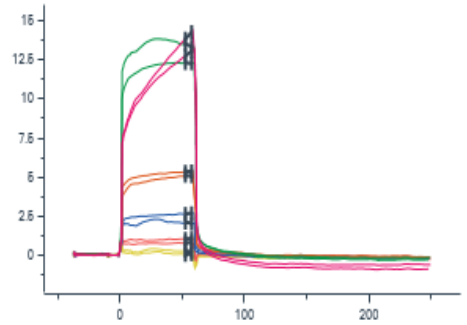


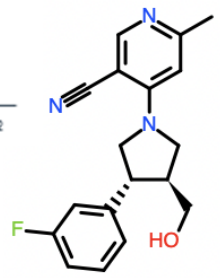
Tested analogs

not advanced to dose-response  CACHE_ID CACHE2-HO_1414_11 Parent CACHE_1414_40 distance_to_pai 0	 CACHE_ID CACHE2-HO_1414_12 Parent CACHE_1414_40 distance_to_pai 0.1475	**Dose response: Confirmed**  CACHE_ID CACHE2-HO_1414_13 Parent CACHE_1414_40 distance_to_pai 0.1657	**Dose response: Confirmed**  CACHE_ID CACHE2-HO_1414_14 Parent CACHE_1414_40 distance_to_pai 0.2121
 CACHE_ID CACHE2-HO_1414_15 Parent CACHE_1414_40 distance_to_pai 0.2374	 CACHE_ID CACHE2-HO_1414_16 Parent CACHE_1414_40 distance_to_pai 0.2582	 CACHE_ID CACHE2-HO_1414_17 Parent CACHE_1414_40 distance_to_pai 0.2656	 CACHE_ID CACHE2-HO_1414_18 Parent CACHE_1414_40 distance_to_pai 0.2754
 CACHE_ID CACHE2-HO_1414_19 Parent CACHE_1414_40 distance_to_pai 0.2877	**Dose response: Confirmed**  CACHE_ID CACHE2-HO_1414_20 Parent CACHE_1414_40 distance_to_pai 0.2963	 CACHE_ID CACHE2-HO_1414_21 Parent CACHE_1414_40 distance_to_pai 0.314	 CACHE_ID CACHE2-HO_1414_22 Parent CACHE_1414_40 distance_to_pai 0.3161

PARENT MOLECULE

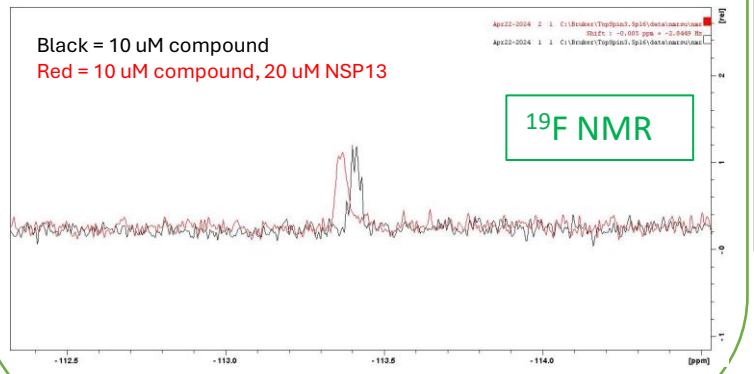




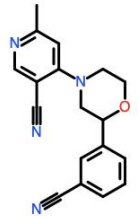


CACHE_1414_40

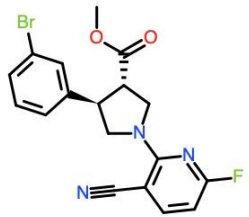
K_D = 33 µM – 84% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 10



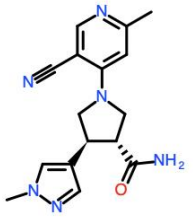
Tested analogs (cont…)



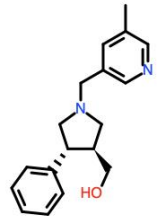
CACHE_ID	CACHE2-HO_1414_23
Parent	CACHE_1414_40
distance_to_pai	0.3168



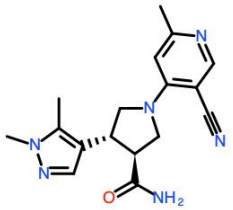
CACHE_ID	CACHE2-HO_1414_24
Parent	CACHE_1414_40
distance_to_pai	0.3172



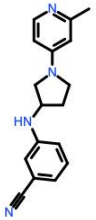
CACHE_ID	CACHE2-HO_1414_25
Parent	CACHE_1414_40
distance_to_pai	0.3333



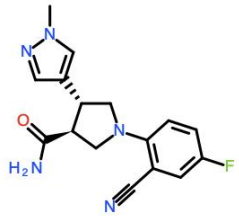
CACHE_ID	CACHE2-HO_1414_26
Parent	CACHE_1414_40
distance_to_pai	0.3478



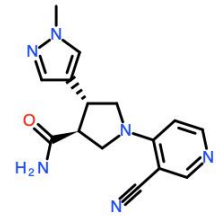
CACHE_ID	CACHE2-HO_1414_27
Parent	CACHE_1414_40
distance_to_pai	0.3568



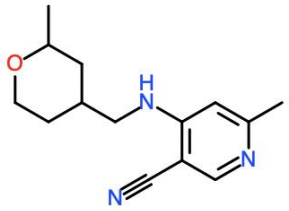
CACHE_ID	CACHE2-HO_1414_28
Parent	CACHE_1414_40
distance_to_pai	0.3646



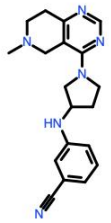
CACHE_ID	CACHE2-HO_1414_29
Parent	CACHE_1414_40
distance_to_pai	0.3694



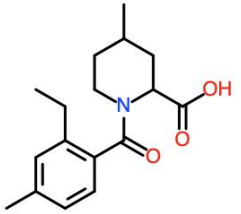
CACHE_ID	CACHE2-HO_1414_30
Parent	CACHE_1414_40
distance_to_pai	0.3744



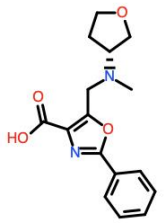
CACHE_ID	CACHE2-HO_1414_31
Parent	CACHE_1414_40
distance_to_pai	0.4363



CACHE_ID	CACHE2-HO_1414_32
Parent	CACHE_1414_40
distance_to_pai	0.5125



CACHE_ID	CACHE2-HO_1414_33
Parent	CACHE_1414_40
distance_to_pai	0.6096

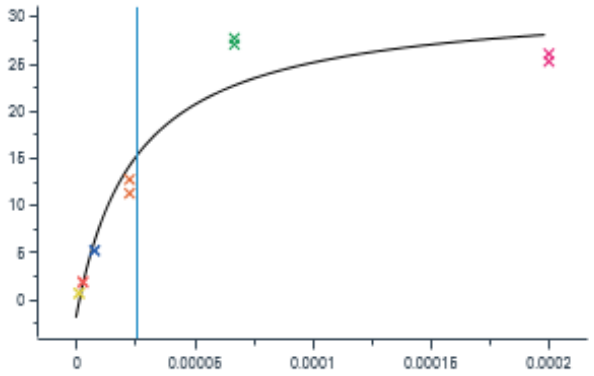


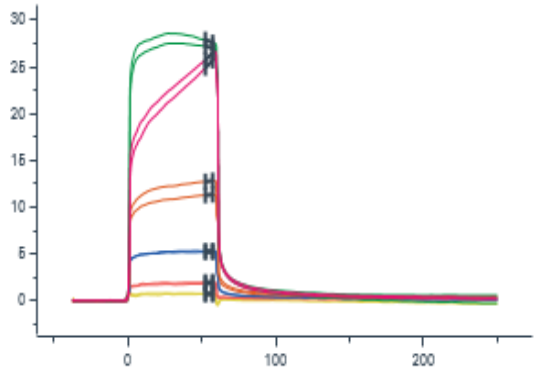
CACHE_ID	CACHE2-HO_1414_34
Parent	CACHE_1414_40
distance_to_pai	0.6426

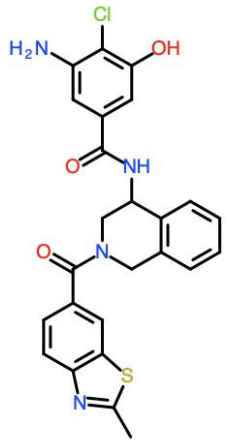
CACHE#2 – NSP13 SARS2

Participant 1418

PARENT MOLECULE







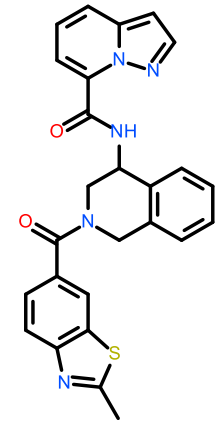
CACHE_1418_68

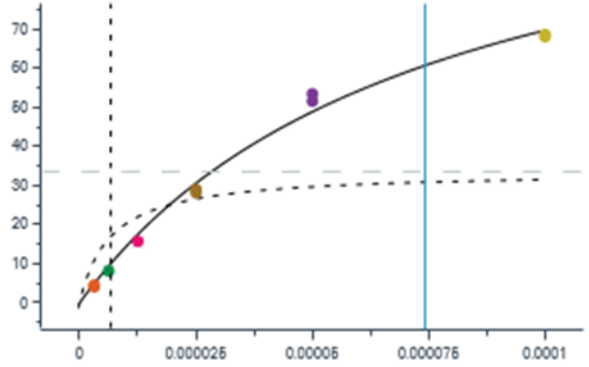
K_D = 25 µM (poor fit/solubility issues) – 100 %binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 3

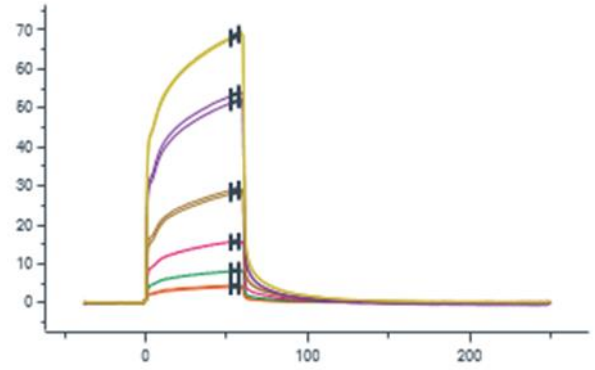
6 analogs of CACHE_1418_68 were submitted for round 2.
1 of them showed a super stoichiometric binding to NSP13 in addition to weak non-selective binding to the unrelated protein WDR5.

CACHE2-HO_1418_34

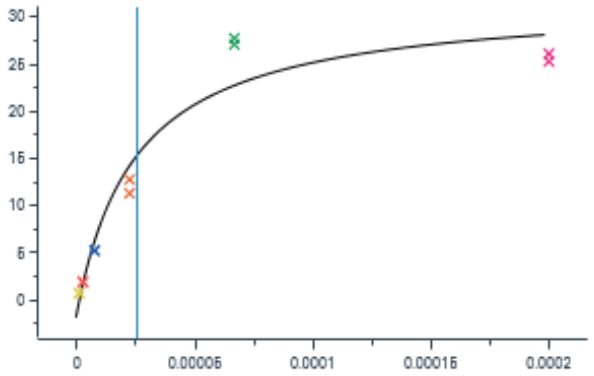
K_D _1 = 61 µM – 298 %binding
K_D _2 = 74 µM – 362 %binding
Selectivity (unrelated WDR5 protein) – weak binding
DLS (solub/no aggreg@200 µM)
%inhibition@50 µM_ATPase = 6

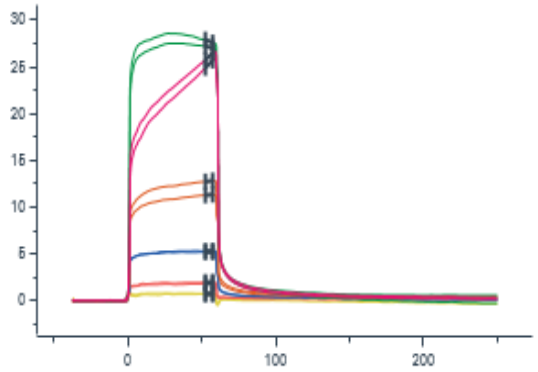


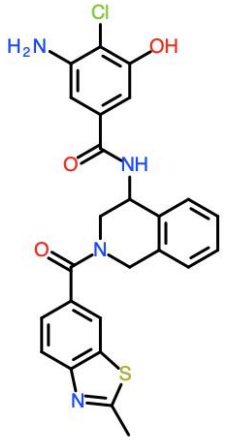




PARENT MOLECULE



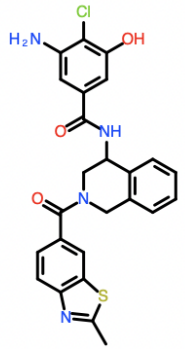




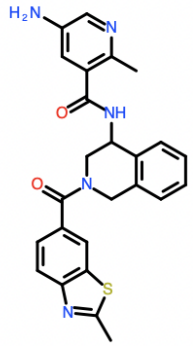
CACHE_1418_68

K_D = 25 µM (poor fit/solubility issues) – 100 %binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 3

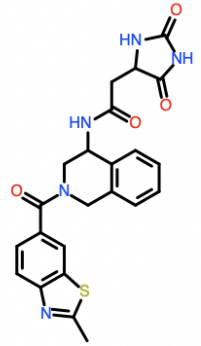
Tested analogs



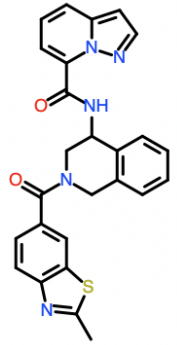
CACHE_ID	CACHE2-HO_1418_31
Parent	CACHE_1418_68
distance_to_pare	0



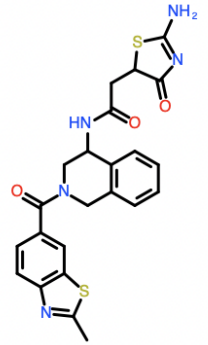
CACHE_ID	CACHE2-HO_1418_32
Parent	CACHE_1418_68
distance_to_pare	0.1185



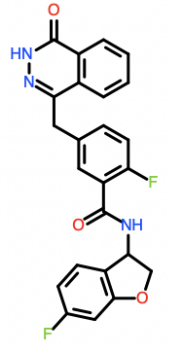
CACHE_ID	CACHE2-HO_1418_33
Parent	CACHE_1418_68
distance_to_pare	0.2056



CACHE_ID	CACHE2-HO_1418_34
Parent	CACHE_1418_68
distance_to_pare	0.2426

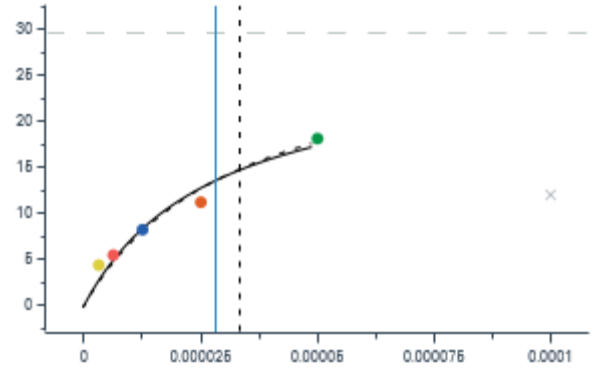


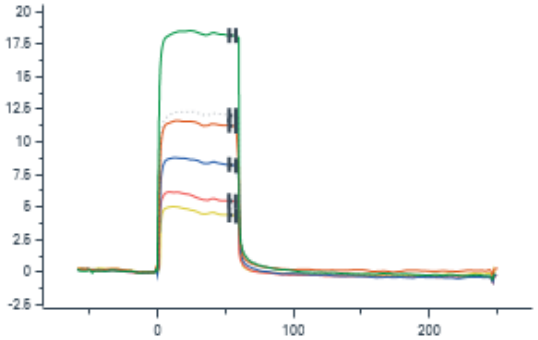
CACHE_ID	CACHE2-HO_1418_35
Parent	CACHE_1418_68
distance_to_pare	0.2559

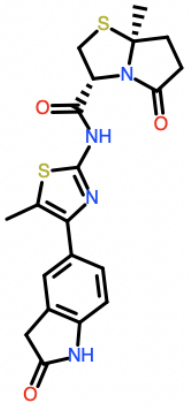


CACHE_ID	CACHE2-HO_1418_36
Parent	CACHE_1418_68
distance_to_pare	0.5714

PARENT MOLECULE







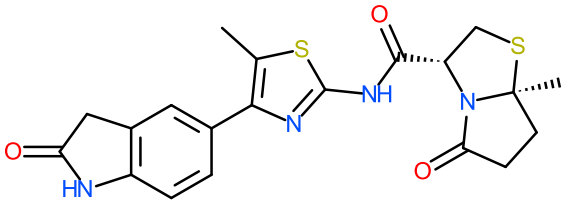
CACHE_1418_3

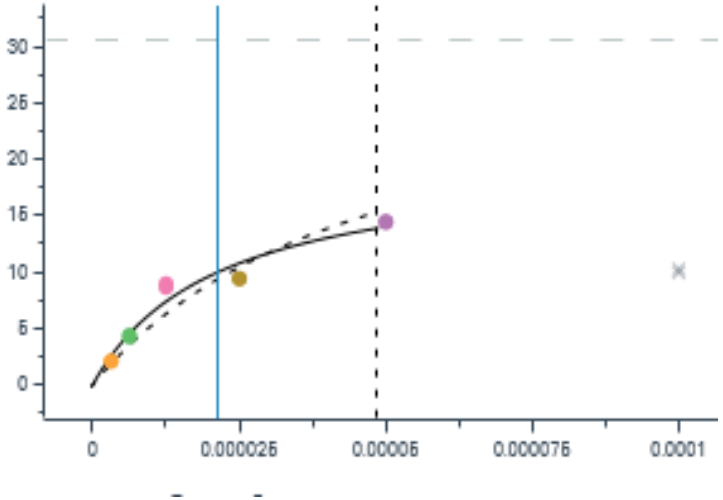
K_D = 28 µM (solubility issues) – 93% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 14

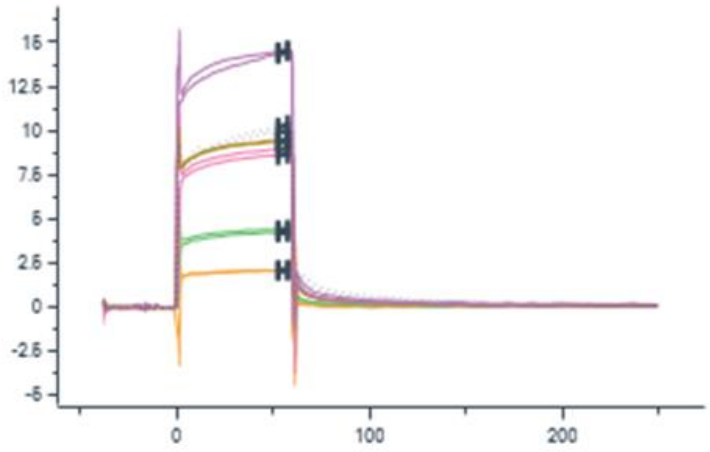
11 analogs of CACHE_1418_3 were submitted for round 2 including the re-supplied parent molecule. The Re-supplied hit confirmed dose dependent binding to NSP13.

CACHE2-HO_1418_1

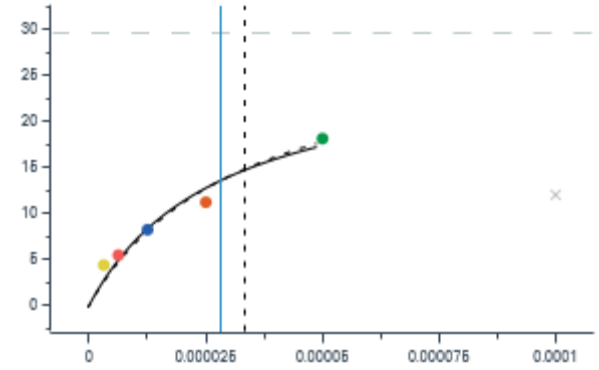
K_D (3% DMSO) = 21 µM (solubility issues) – 65% binding
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 13

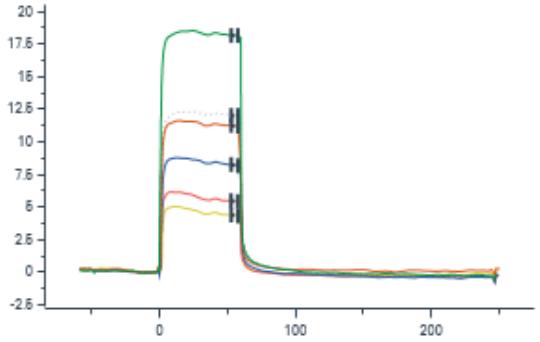


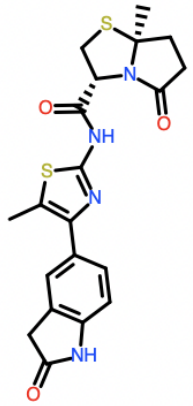




PARENT MOLECULE



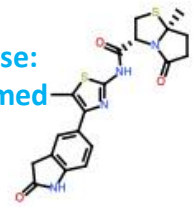
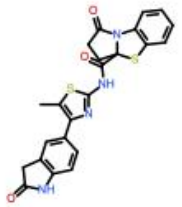
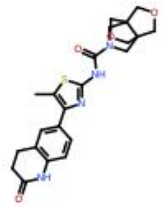
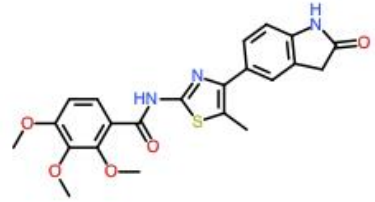
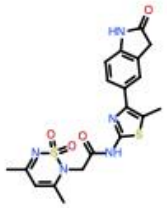
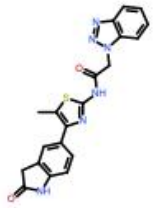
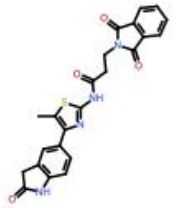
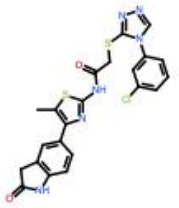
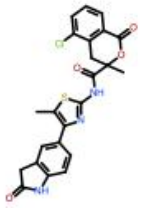
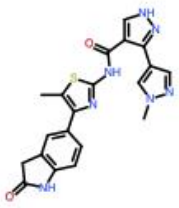
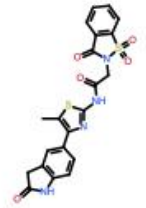




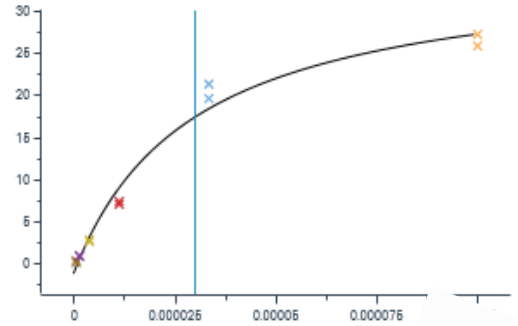
CACHE_1418_3

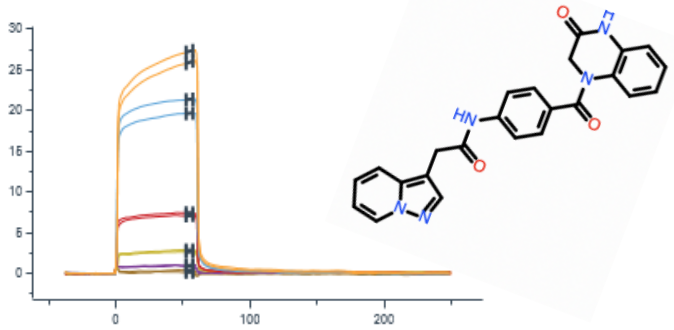
K_D = 28 µM (solubility issues) – 93% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 14

Tested analogs

Dose response: Confirmed  CACHE_ID CACHE2-HO_1418_1 Parent CACJE_1418_3 distance_to_pai 0	 CACHE_ID CACHE2-HO_1418_2 Parent CACJE_1418_3 distance_to_pai 0.2863	 CACHE_ID CACHE2-HO_1418_3 Parent CACJE_1418_3 distance_to_pai 0.343	 CACHE_ID CACHE2-HO_1418_4 Parent CACJE_1418_3 distance_to_pai 0.3552
 CACHE_ID CACHE2-HO_1418_5 Parent CACJE_1418_3 distance_to_pai 0.3584	 CACHE_ID CACHE2-HO_1418_6 Parent CACJE_1418_3 distance_to_pai 0.3615	 CACHE_ID CACHE2-HO_1418_7 Parent CACJE_1418_3 distance_to_pai 0.3617	 CACHE_ID CACHE2-HO_1418_8 Parent CACJE_1418_3 distance_to_pai 0.3636
 CACHE_ID CACHE2-HO_1418_9 Parent CACJE_1418_3 distance_to_pai 0.3727	 CACHE_ID CACHE2-HO_1418_10 Parent CACJE_1418_3 distance_to_pai 0.3922	 CACHE_ID CACHE2-HO_1418_11 Parent CACJE_1418_3 distance_to_pai 0.3929	

PARENT MOLECULE

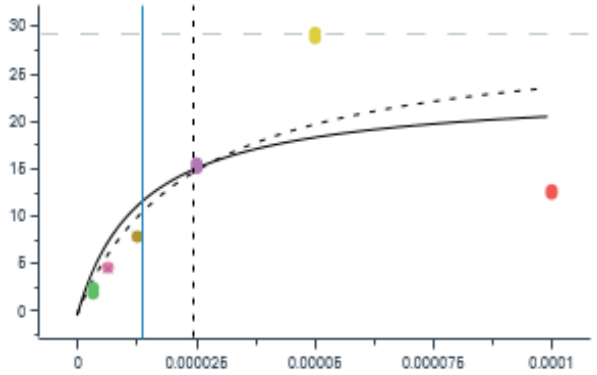


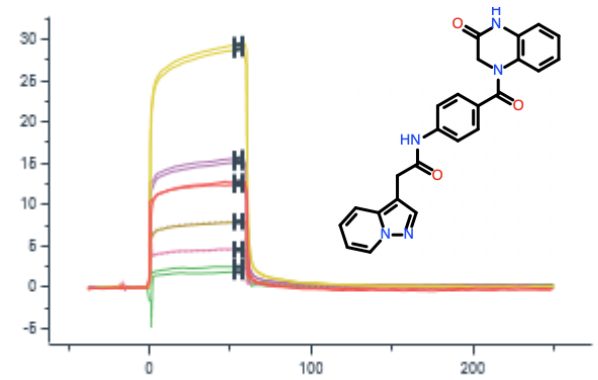


CACHE_1418_52

K_D = 30 µM – 118% binding
WDR5 selectivity – 15% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = no inhibition

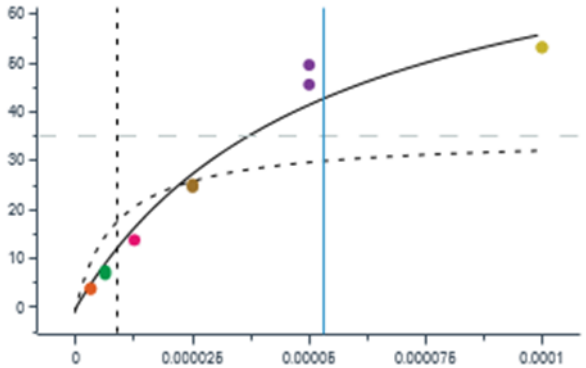
9 analogs of CACHE_1418_52 were submitted for round 2.
1 of them showed clear dose dependent binding response by SPR.

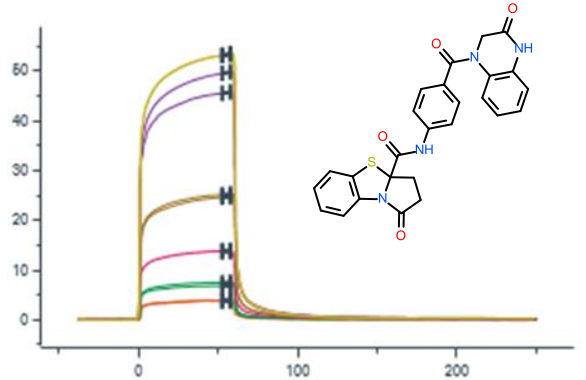




CACHE2-HO_1418_22

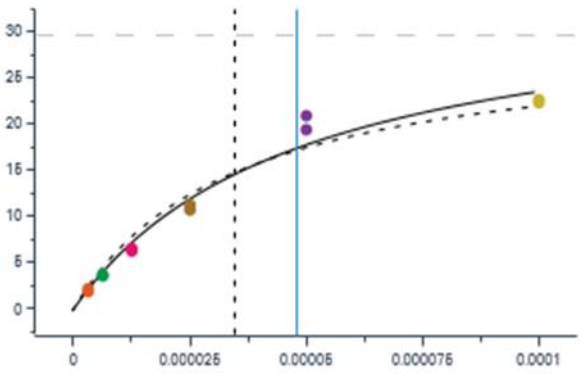
K_D = 14 µM (poor fit) – 80% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 19

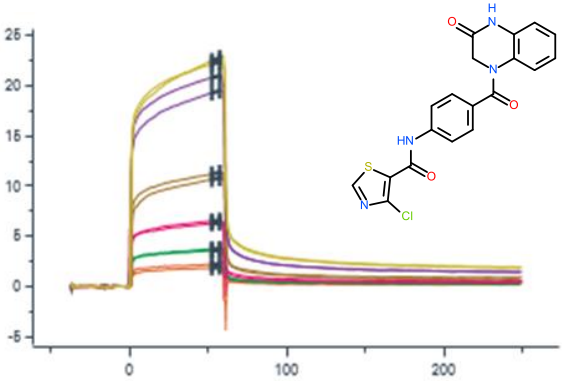




CACHE2-HO_1418_28

K_D _1 = 56 µM – 781% binding
K_D _2 = 53 µM – 246% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 21

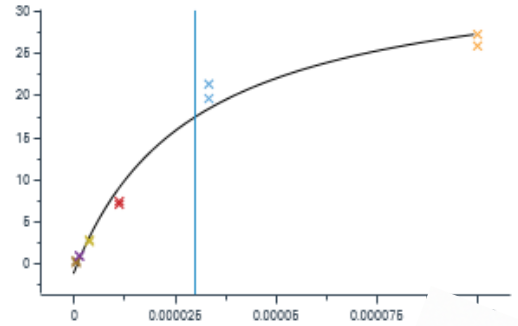


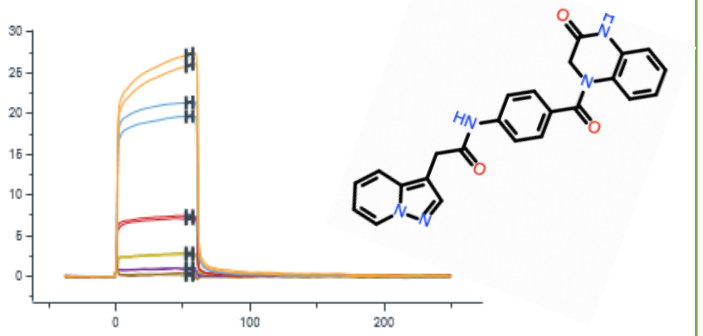


CACHE2-HO_1418_26

K_D = 48 µM – 118% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 15

PARENT MOLECULE

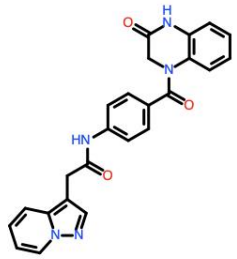




CACHE_1418_52

K_D = 30 µM – 118% binding
WDR5 selectivity – 15% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = no inhibition

Tested analogs



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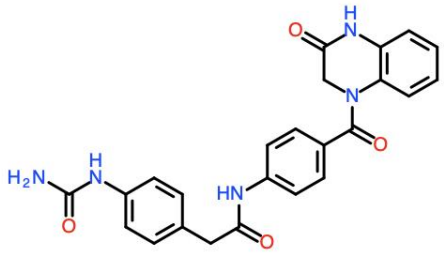
Parent CACHE_1418_52
distance_to_par 0



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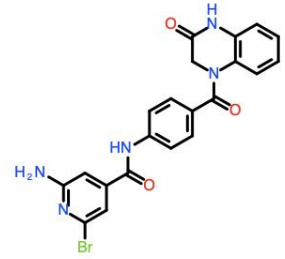
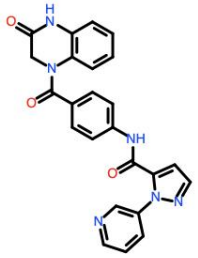
Parent CACHE_1418_52
distance_to_par 0.2867

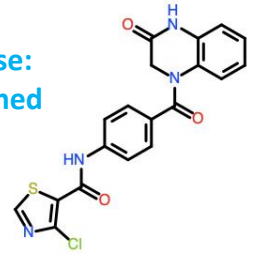


CACHE_ID CACHE2-HO_1418_24
Parent CACHE_1418_52
distance_to_par 0.3365

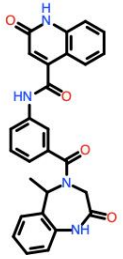


CACHE_ID CACHE2-HO_1418_25
Parent CACHE_1418_52
distance_to_par 0.3473

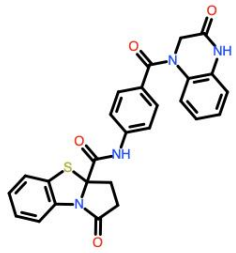
Dose response: Confirmed



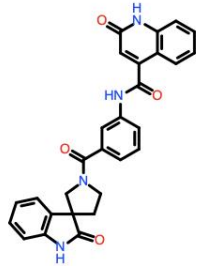
CACHE_ID CACHE2-HO_1418_26
Parent CACHE_1418_52
distance_to_par 0.3947



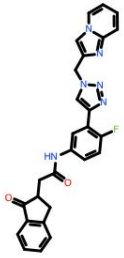
CACHE_ID CACHE2-HO_1418_27
Parent CACHE_1418_52
distance_to_par 0.4236



CACHE_ID CACHE2-HO_1418_28
Parent CACHE_1418_52
distance_to_par 0.4657

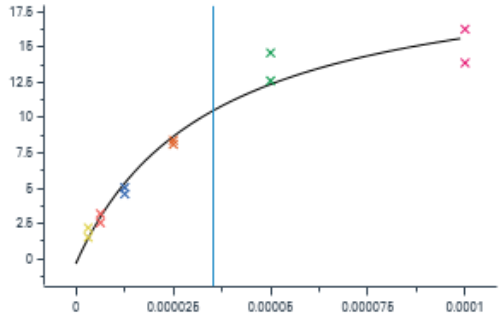


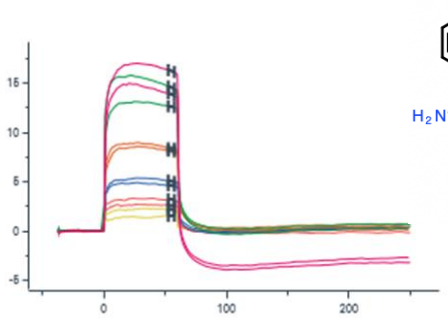
CACHE_ID CACHE2-HO_1418_29
Parent CACHE_1418_52
distance_to_par 0.4884

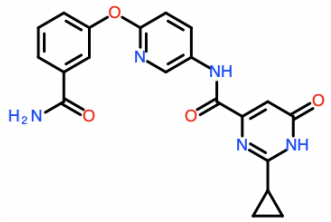


CACHE_ID CACHE2-HO_1418_30
Parent CACHE_1418_52
distance_to_par 0.5293

PARENT MOLECULE







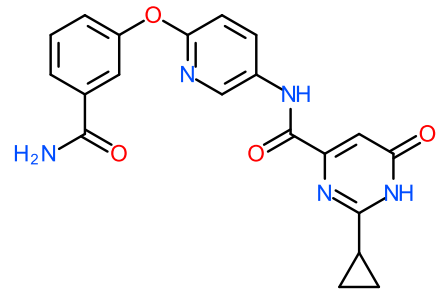
CACHE_1418_37

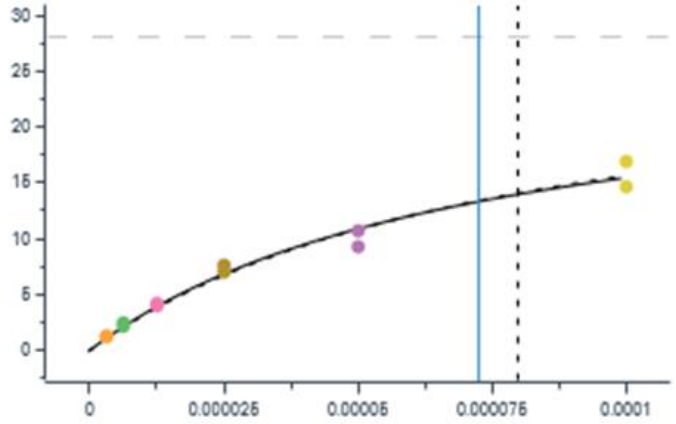
K_D = 33±1 µM – 89±17% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 72%
Not confirmed by dose response IC_{50}>150

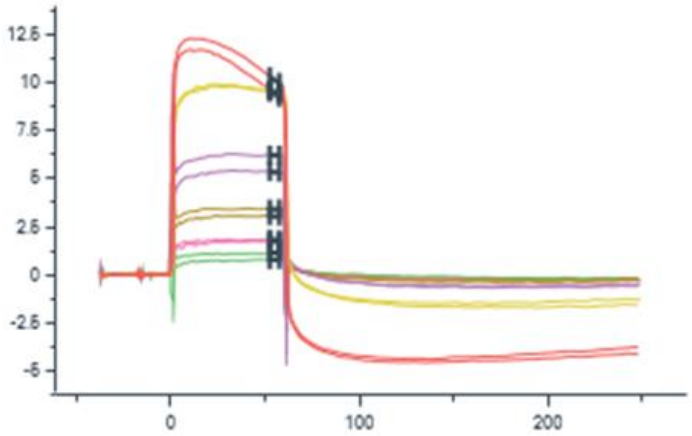
6 analogs of CACHE_1418_37 were submitted for round 2.
1 of them (re-supplied parent molecule) confirmed a selective dose dependent binding response.

CACHE2-HO_1418_15

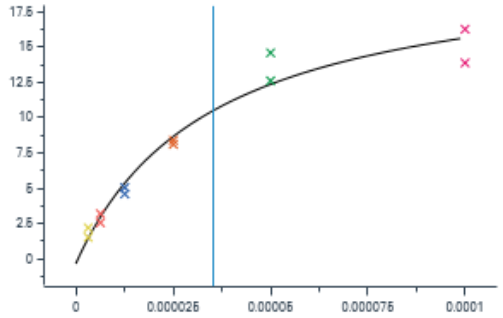
K_D (3% DMSO) = 72 µM – 95% binding
At 100 uM concentration shows binding to the reference cell
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 16

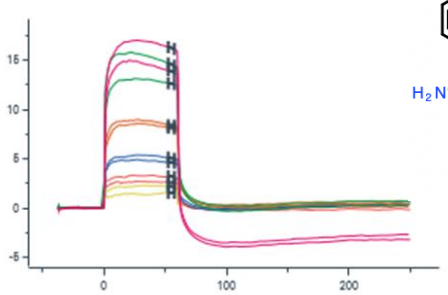


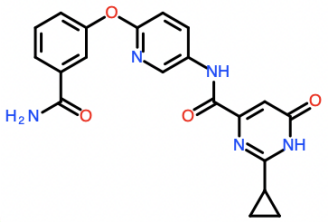




PARENT MOLECULE



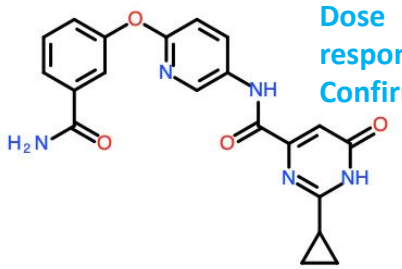
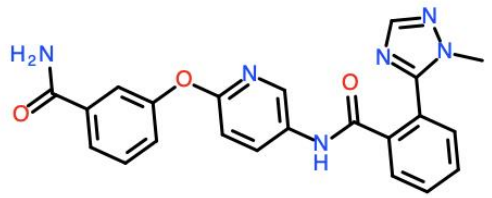
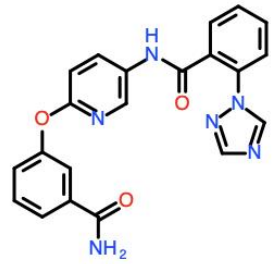
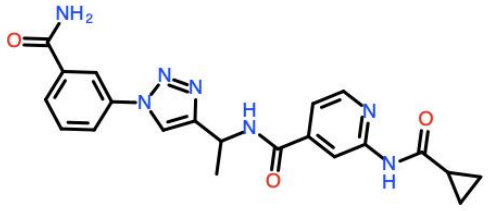
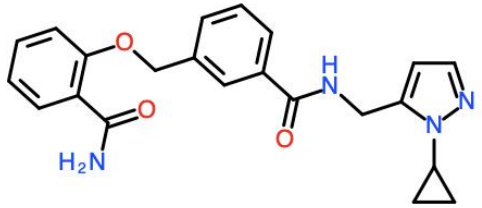
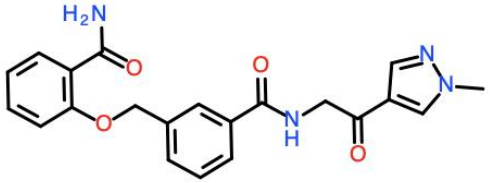




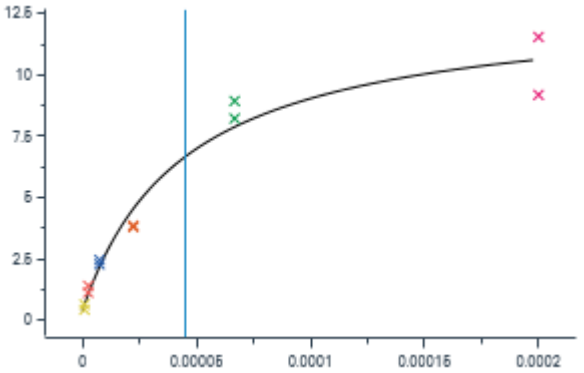
CACHE_1418_37

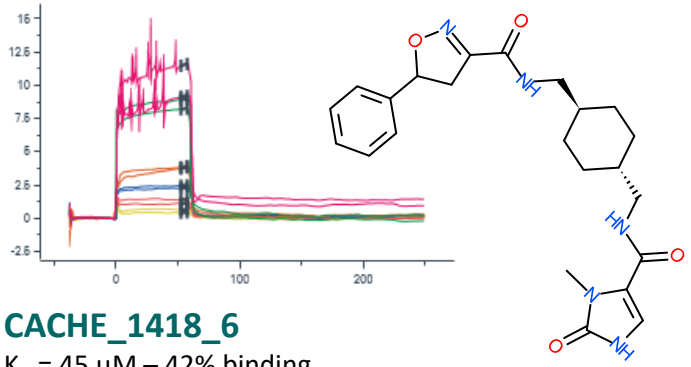
K_D = 33±1 µM – 89±17% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 72%
Not confirmed by dose response IC_{50}>150

Tested analogs

 Dose response: Confirmed CACHE_ID CACHE2-HO_1418_15 Parent CACHE_1418_37 distance_to_pai 0	 CACHE_ID CACHE2-HO_1418_16 Parent CACHE_1418_37 distance_to_pai 0.413	 CACHE_ID CACHE2-HO_1418_17 Parent CACHE_1418_37 distance_to_pai 0.4329
 CACHE_ID CACHE2-HO_1418_18 Parent CACHE_1418_37 distance_to_pai 0.5167	 CACHE_ID CACHE2-HO_1418_19 Parent CACHE_1418_37 distance_to_pai 0.5587	 CACHE_ID CACHE2-HO_1418_20 Parent CACHE_1418_37 distance_to_pai 0.5752

Round 1 HIT MOLECULE





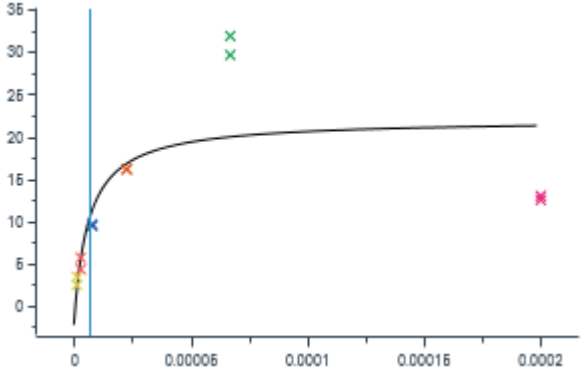
CACHE_1418_6

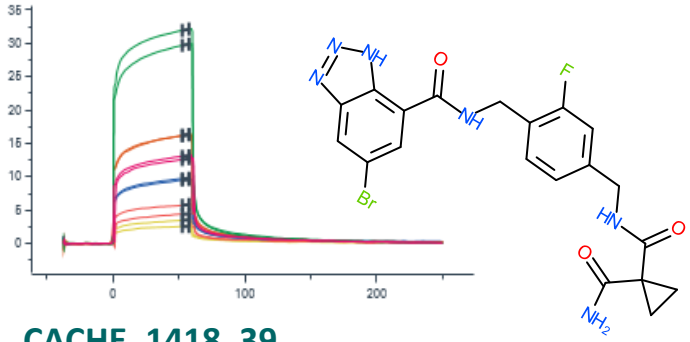
K_D = 45 µM – 42% binding

Selectivity (unrelated WDR5 protein) – Yes

%inhibition@50 µM_ATPase = 5

Round 1 HIT MOLECULE





CACHE_1418_39

K_D = 7 µM (poor fit) – 67% binding

Selectivity (unrelated WDR5 protein) – Yes

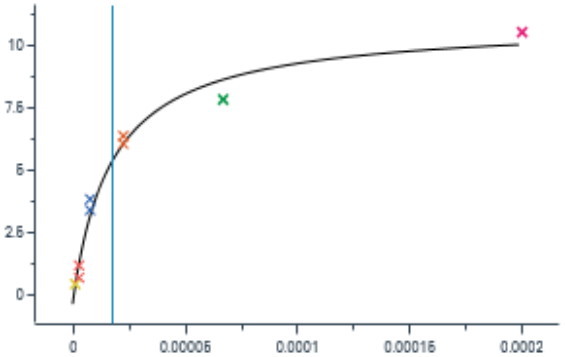
%inhibition@50 µM_ATPase = 6

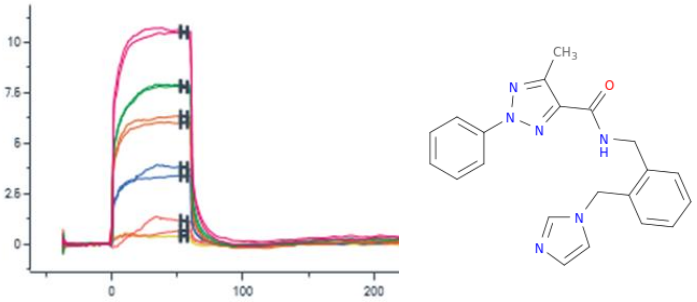
No analogs in Round 2

CACHE#2 – NSP13 SARS2

Participant 1419

PARENT MOLECULE

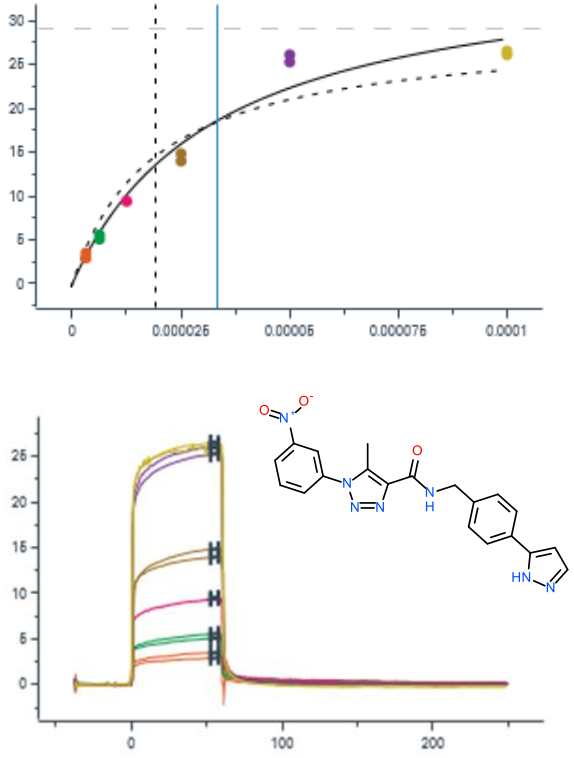




CACHE_1419_42

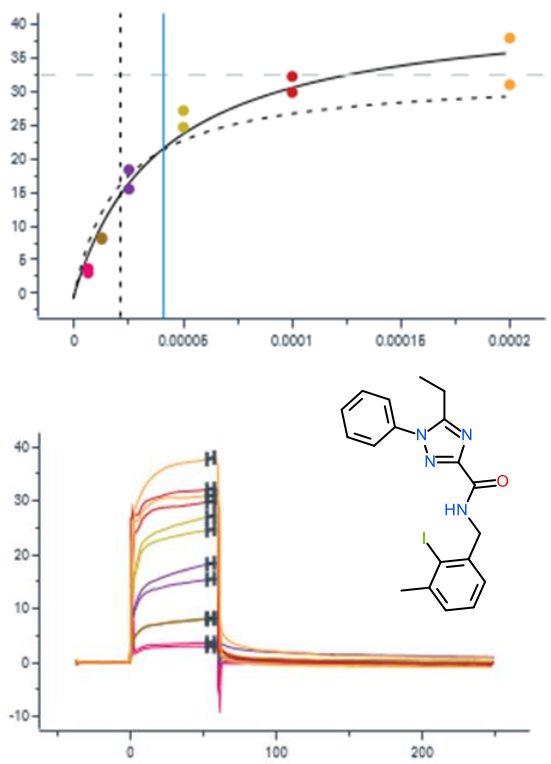
K_D = 18 µM – 39% binding
Selectivity (unrelated WDR5 protein) – 67% binding
%inhibition@50 µM_ATPase = 3

48 analogs of CACHE_1419_42 were submitted for round 2.
3 compounds including re-supplied parent molecule showed a binding response by SPR.



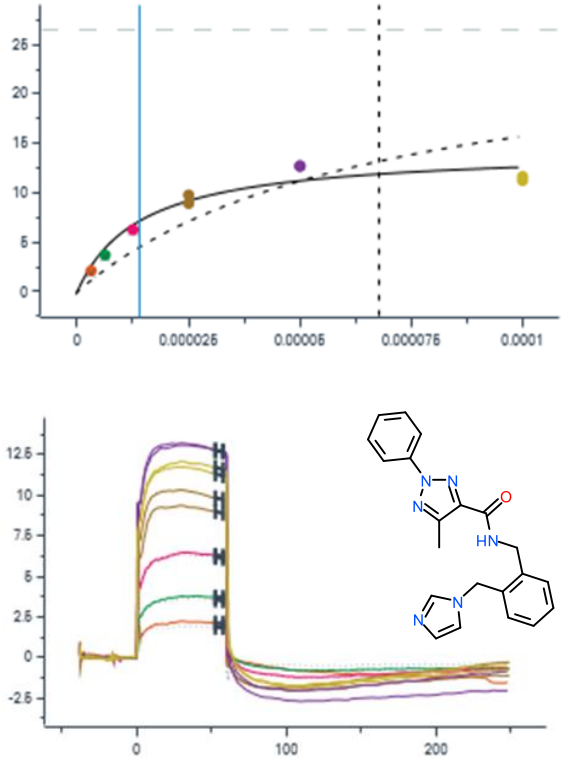
CACHE2-HO_1419_18

K_D = 33 µM – 128% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub/@200 uM)
%inhibition@50 µM_ATPase = 11



CACHE2-HO_1419_30

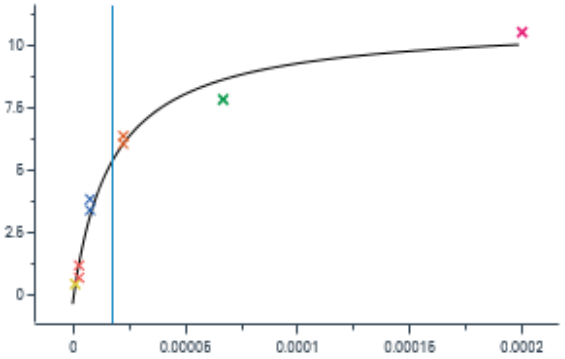
K_D = 41 µM – 133% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 14

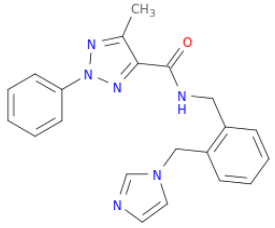


CACHE2-HO_1419_1

K_D = 14 µM – 54% binding
Selectivity (unrelated WDR5 protein) – 16% binding
DLS (solub@100 µM)
%inhibition@50 µM_ATPase = 8

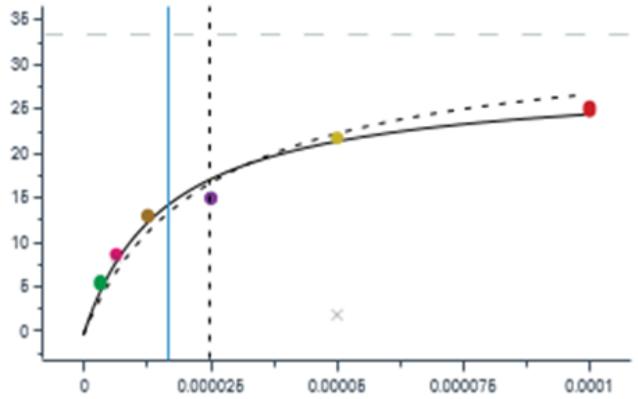
PARENT MOLECULE

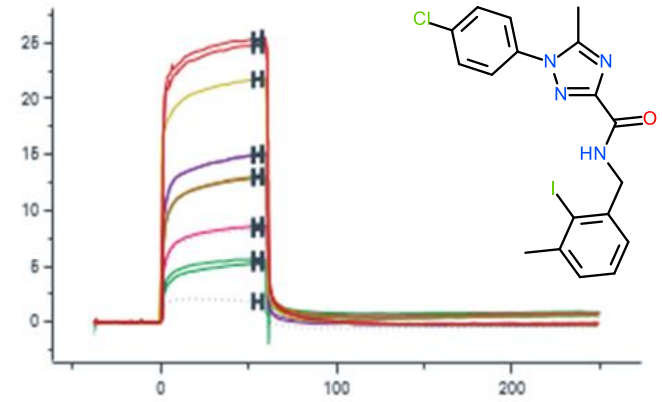




CACHE_1419_42

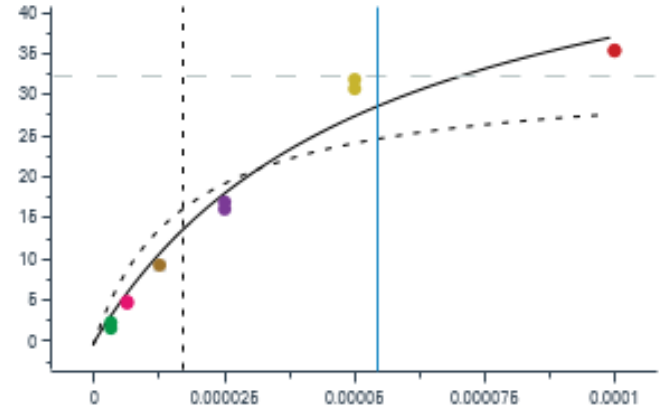
K_D = 18 µM – 39% binding
Selectivity (unrelated WDR5 protein) – 67% binding
%inhibition@50 µM_ATPase = 3

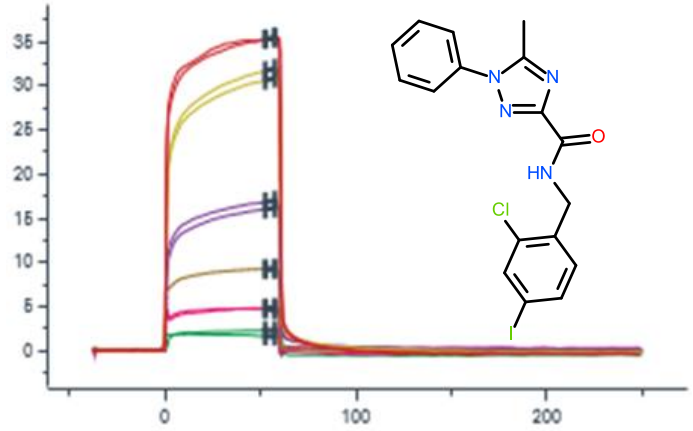




CACHE2-HO_1419_28

K_D _1 = 41 µM – 81% binding
K_D _2 = 17 µM – 85% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 14

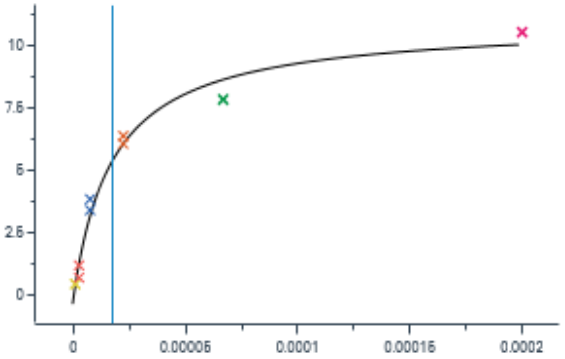


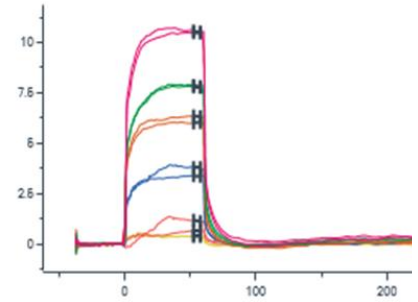


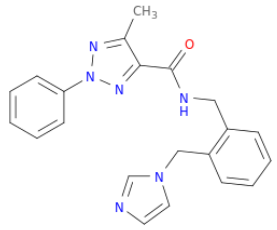
CACHE2-HO_1419_29

K_D _1 = 51 µM – 157% binding
K_D _2 = 55 µM – 177% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 13

PARENT MOLECULE







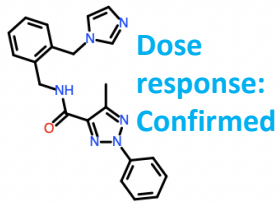
CACHE_1419_42

K_D = 18 µM – 39% binding

Selectivity (unrelated WDR5 protein) – 67% binding

%inhibition@50 µM_ATPase = 3

Tested analogs



Dose response: Confirmed

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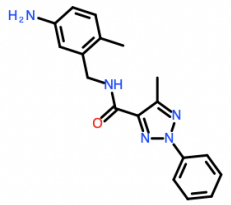
Parent CACHE_1419_42
distance_to_pai 0



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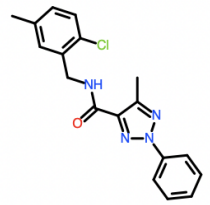
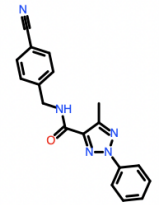
Parent CACHE_1419_42
distance_to_pai 0.1991



CACHE_ID CACHE2-HO_1419_3
Parent CACHE_1419_42
distance_to_pai 0.2045



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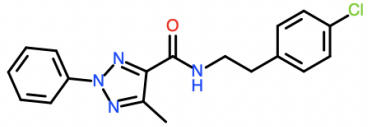
Parent CACHE_1419_42
distance_to_pai 0.2262



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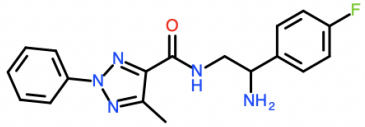
distance_to_pai 0.2576



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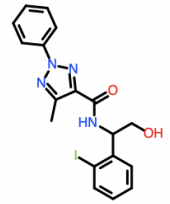
distance_to_pai 0.2845



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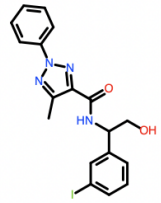
distance_to_pai 0.2955



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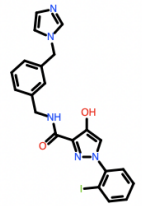

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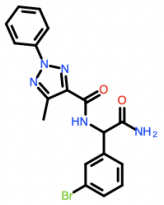

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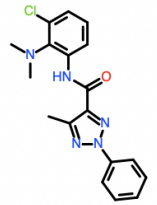
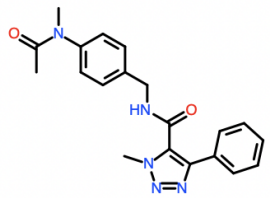
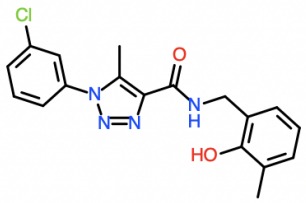


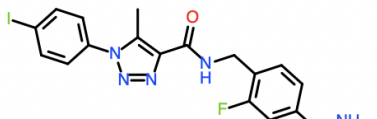
CACHE_ID CACHE2-HO_1419_11
Parent CACHE_1419_42
distance_to_pai 0.332



CACHE_ID CACHE2-HO_1419_12
Parent CACHE_1419_42
distance_to_pai 0.3415



CACHE_ID CACHE2-HO_1419_13
Parent CACHE_1419_42
distance_to_pai 0.3439



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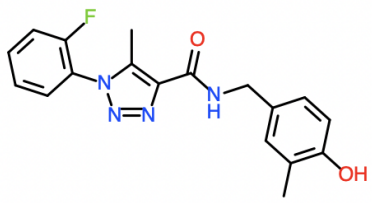
Parent CACHE_1419_42
distance_to_pai 0.3451



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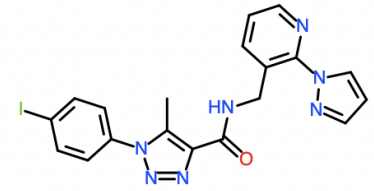
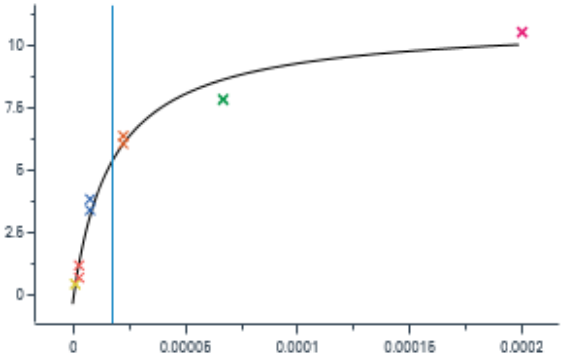
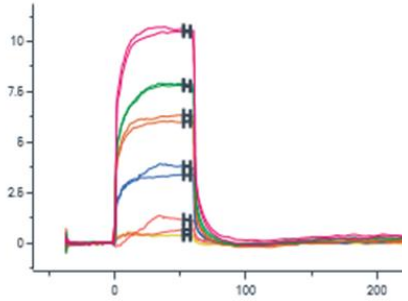
Parent CACHE_1419_42
distance_to_pai 0.3516

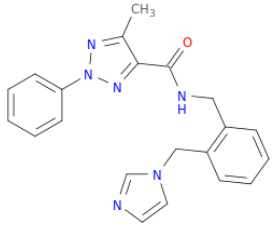


CACHE_ID CACHE2-HO_1419_16
Parent CACHE_1419_42
distance_to_pai 0.3574

PARENT MOLECULE







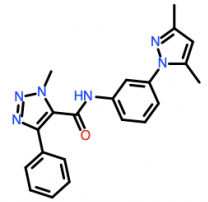
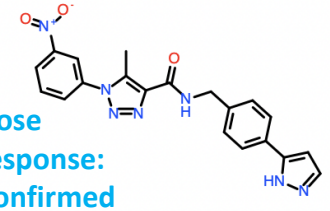
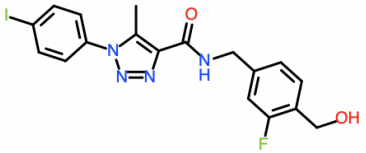
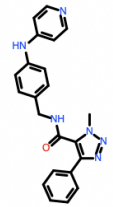
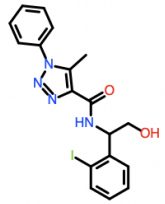
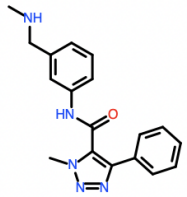
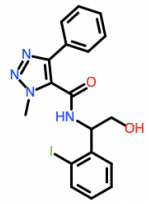
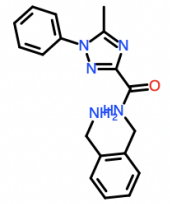
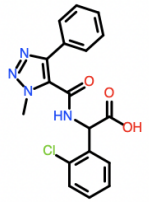
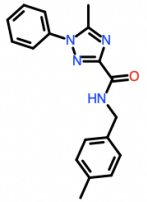
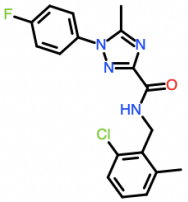
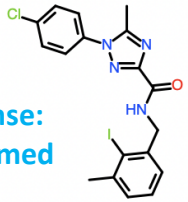
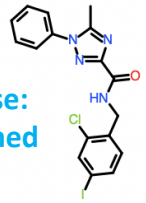
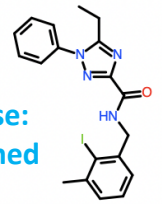
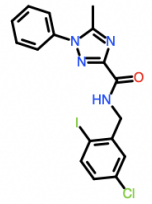
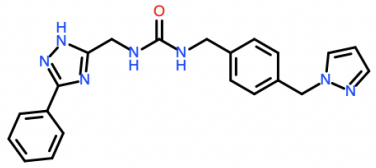
CACHE_1419_42

K_D = 18 µM – 39% binding

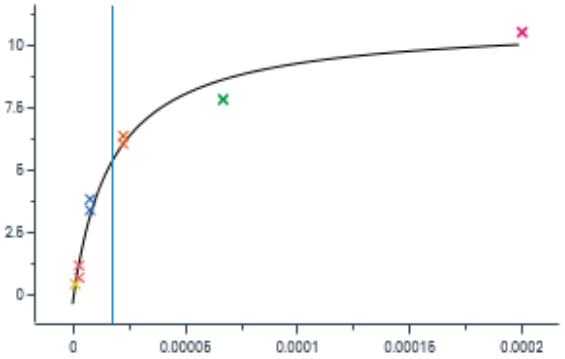
Selectivity (unrelated WDR5 protein) – 67% binding

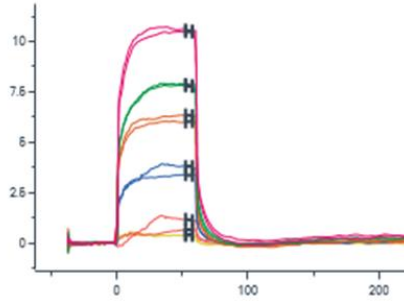
%inhibition@50 µM_ATPase = 3

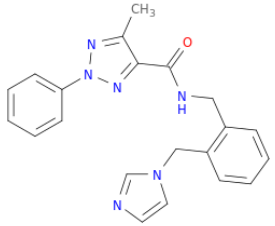
Tested analogs

 CACHE_ID CACHE2-HO_1419_17 Parent CACHE_1419_42 distance_to_pai 0.3574	 Dose response: Confirmed CACHE_ID CACHE2-HO_1419_18 Parent CACHE_1419_42 distance_to_pai 0.3609	 CACHE_ID CACHE2-HO_1419_19 Parent CACHE_1419_42 distance_to_pai 0.3668	 CACHE_ID CACHE2-HO_1419_20 Parent CACHE_1419_42 distance_to_pai 0.368
 CACHE_ID CACHE2-HO_1419_21 Parent CACHE_1419_42 distance_to_pai 0.3688	 CACHE_ID CACHE2-HO_1419_22 Parent CACHE_1419_42 distance_to_pai 0.375	 CACHE_ID CACHE2-HO_1419_23 Parent CACHE_1419_42 distance_to_pai 0.4082	 CACHE_ID CACHE2-HO_1419_24 Parent CACHE_1419_42 distance_to_pai 0.4302
 CACHE_ID CACHE2-HO_1419_25 Parent CACHE_1419_42 distance_to_pai 0.4327	 CACHE_ID CACHE2-HO_1419_26 Parent CACHE_1419_42 distance_to_pai 0.4466	 CACHE_ID CACHE2-HO_1419_27 Parent CACHE_1419_42 distance_to_pai 0.4596	 Dose response: Confirmed CACHE_ID CACHE2-HO_1419_28 Parent CACHE_1419_42 distance_to_pai 0.4613
Dose response: Confirmed  CACHE_ID CACHE2-HO_1419_29 Parent CACHE_1419_42 distance_to_pai 0.4667	Dose response: Confirmed  CACHE_ID CACHE2-HO_1419_30 Parent CACHE_1419_42 distance_to_pai 0.4672	 CACHE_ID CACHE2-HO_1419_31 Parent CACHE_1419_42 distance_to_pai 0.4689	 CACHE_ID CACHE2-HO_1419_32 Parent CACHE_1419_42 distance_to_pai 0.4725

PARENT MOLECULE



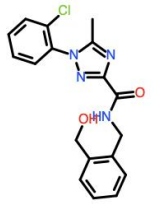
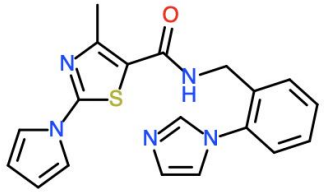
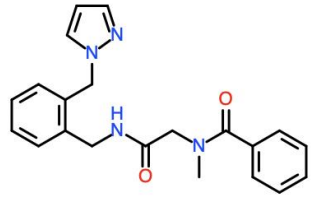
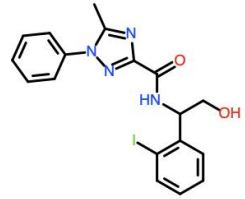
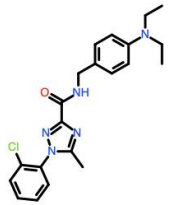
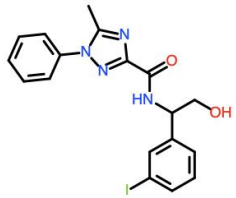
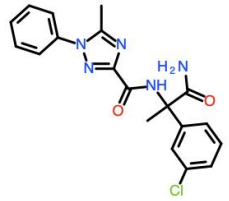
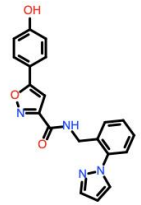
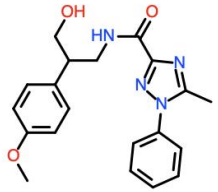
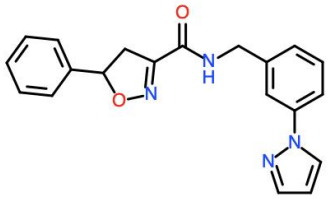
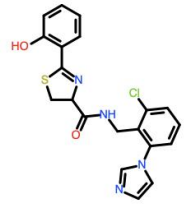
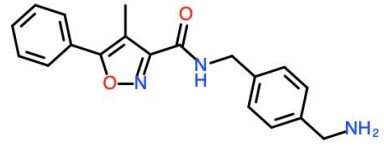
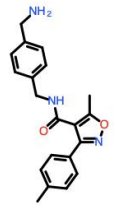
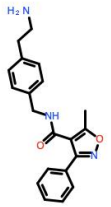
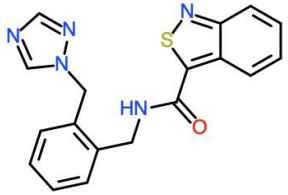
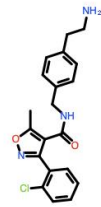




CACHE_1419_42

K_D = 18 µM – 39% binding
Selectivity (unrelated WDR5 protein) – 67% binding
%inhibition@50 µM_ATPase = 3

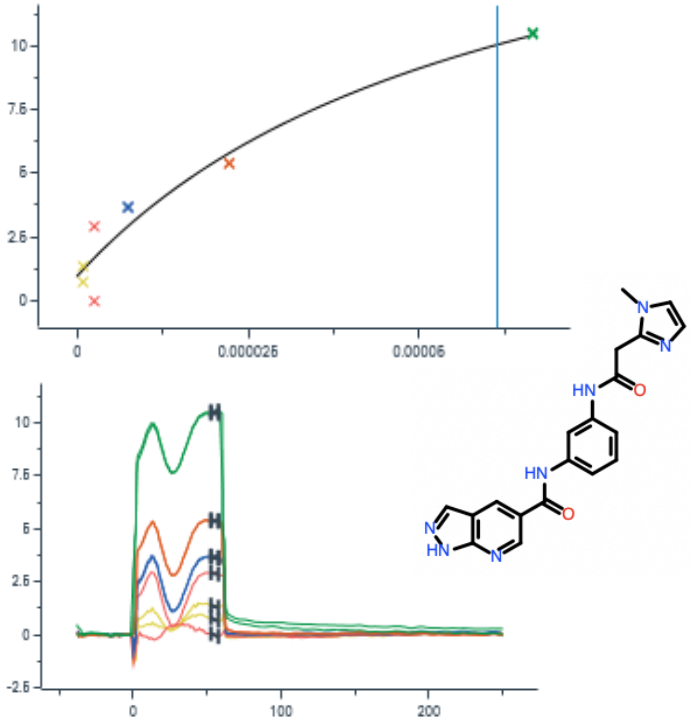
Tested analogs

 CACHE_ID CACHE2-HO_1419_33 Parent CACHE_1419_42 distance_to_pai 0.4894	 CACHE_ID CACHE2-HO_1419_34 Parent CACHE_1419_42 distance_to_pai 0.4932	 CACHE_ID CACHE2-HO_1419_35 Parent CACHE_1419_42 distance_to_pai 0.494	 CACHE_ID CACHE2-HO_1419_36 Parent CACHE_1419_42 distance_to_pai 0.4983
 CACHE_ID CACHE2-HO_1419_37 Parent CACHE_1419_42 distance_to_pai 0.5	 CACHE_ID CACHE2-HO_1419_38 Parent CACHE_1419_42 distance_to_pai 0.5088	 CACHE_ID CACHE2-HO_1419_39 Parent CACHE_1419_42 distance_to_pai 0.519	 CACHE_ID CACHE2-HO_1419_40 Parent CACHE_1419_42 distance_to_pai 0.527
 CACHE_ID CACHE2-HO_1419_41 Parent CACHE_1419_42 distance_to_pai 0.5329	 CACHE_ID CACHE2-HO_1419_42 Parent CACHE_1419_42 distance_to_pai 0.5631	 CACHE_ID CACHE2-HO_1419_43 Parent CACHE_1419_42 distance_to_pai 0.5684	 CACHE_ID CACHE2-HO_1419_44 Parent CACHE_1419_42 distance_to_pai 0.578
 CACHE_ID CACHE2-HO_1419_45 Parent CACHE_1419_42 distance_to_pai 0.5791	 CACHE_ID CACHE2-HO_1419_46 Parent CACHE_1419_42 distance_to_pai 0.5944	 CACHE_ID CACHE2-HO_1419_47 Parent CACHE_1419_42 distance_to_pai 0.6037	 CACHE_ID CACHE2-HO_1419_48 Parent CACHE_1419_42 distance_to_pai 0.6113

CACHE#2 – NSP13 SARS2

Participant 1421

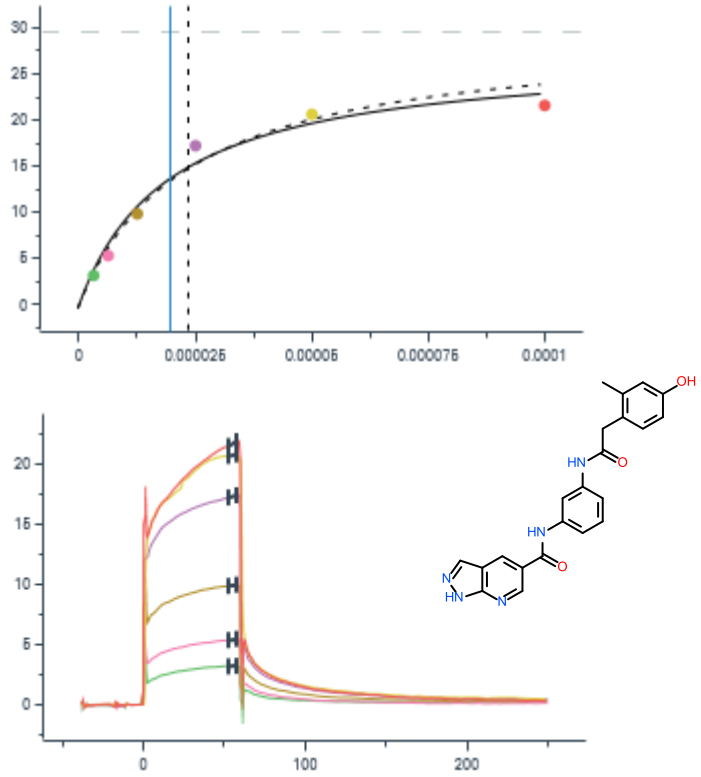
PARENT MOLECULE



CACHE_1421_62

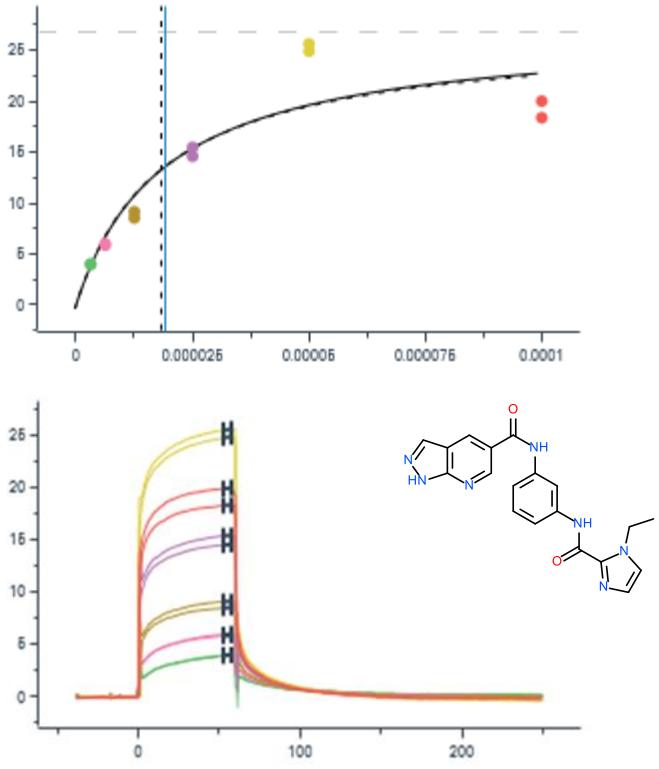
K_D = 62 µM – 70% binding
%inhibition@50 µM_ATPase = 13

11 analogs of CACHE_1421_62 were submitted for round 2. 2 compounds confirmed a selective dose dependent binding response by SPR.



CACHE2-HO_1421_29

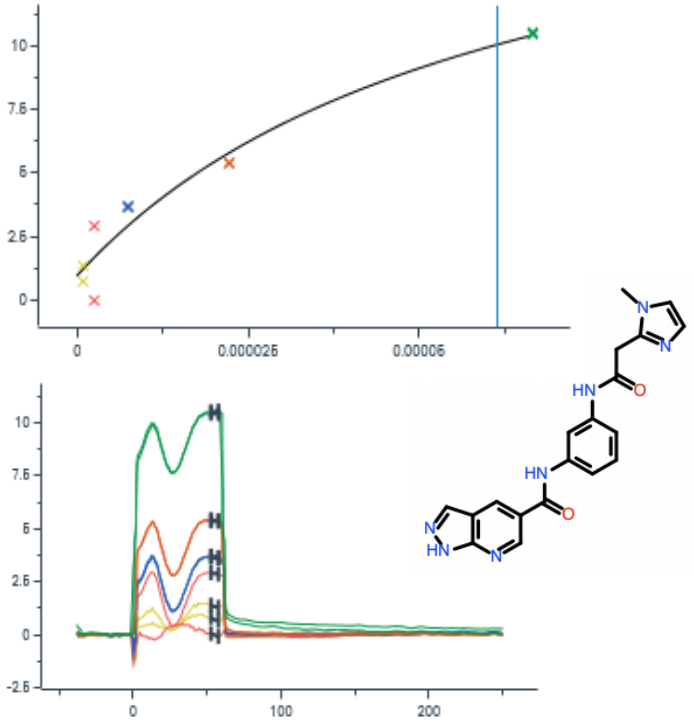
K_D (3%DMSO) = 18±2 µM – 94±1% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = -5



CACHE2-HO_1421_27

K_D (3% DMSO) = 19 µM (poor fit) – 101% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = -5

PARENT MOLECULE

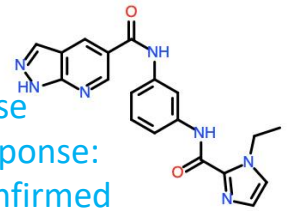
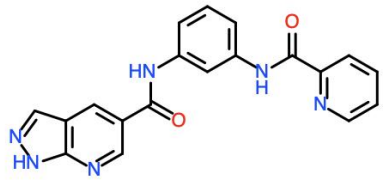
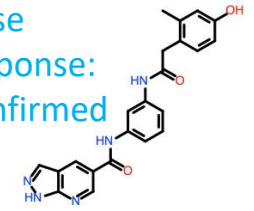
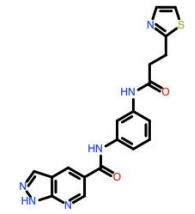
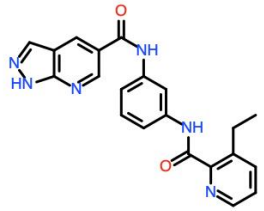
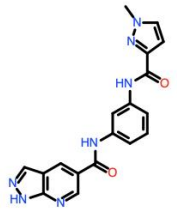
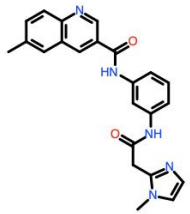
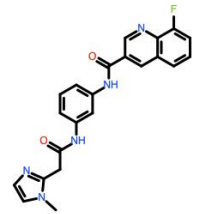
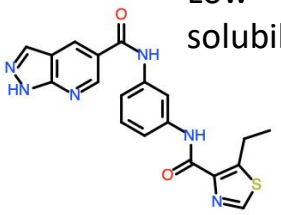
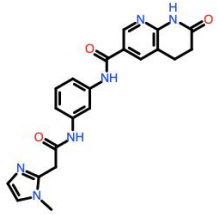
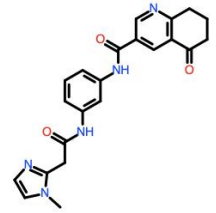


CACHE_1421_62

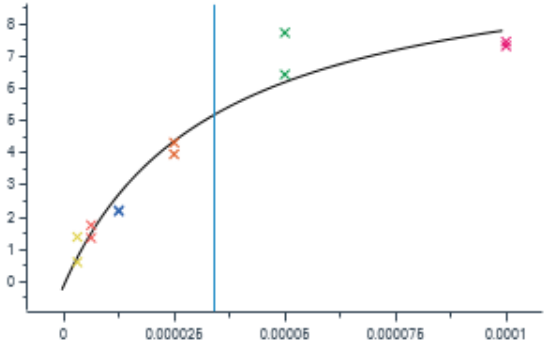
K_D = 62 µM – 70% binding

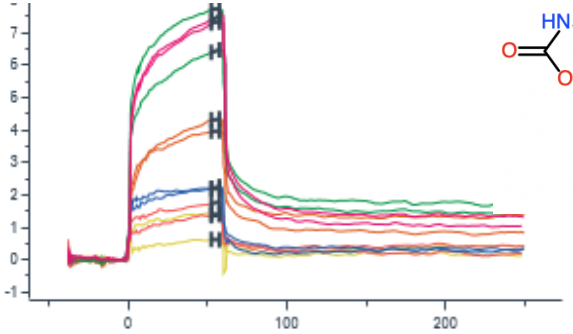
%inhibition@50 µM_ATPase = 13

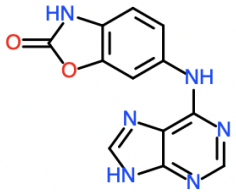
Tested analogs

 Dose response: Confirmed CACHE_ID CACHE2-HO_1421_27 Parent CACHE_1421_62 distance_to_pai 0.1477	 CACHE_ID CACHE2-HO_1421_28 Parent CACHE_1421_62 distance_to_pai 0.2266	 Dose response: Confirmed CACHE_ID CACHE2-HO_1421_29 Parent CACHE_1421_62 distance_to_pai 0.2285	 CACHE_ID CACHE2-HO_1421_30 Parent CACHE_1421_62 distance_to_pai 0.2404
 CACHE_ID CACHE2-HO_1421_31 Parent CACHE_1421_62 distance_to_pai 0.2481	 CACHE_ID CACHE2-HO_1421_32 Parent CACHE_1421_62 distance_to_pai 0.277	 CACHE_ID CACHE2-HO_1421_33 Parent CACHE_1421_62 distance_to_pai 0.2782	 CACHE_ID CACHE2-HO_1421_34 Parent CACHE_1421_62 distance_to_pai 0.2971
 Low solubility CACHE_ID CACHE2-HO_1421_35 Parent CACHE_1421_62 distance_to_pai 0.3036	 CACHE_ID CACHE2-HO_1421_36 Parent CACHE_1421_62 distance_to_pai 0.3299	 CACHE_ID CACHE2-HO_1421_37 Parent CACHE_1421_62 distance_to_pai 0.3412	

PARENT MOLECULE







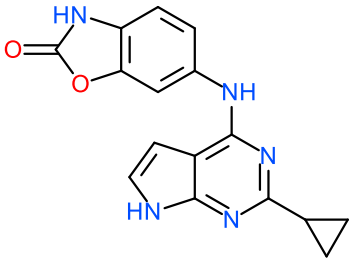
CACHE_1421_1

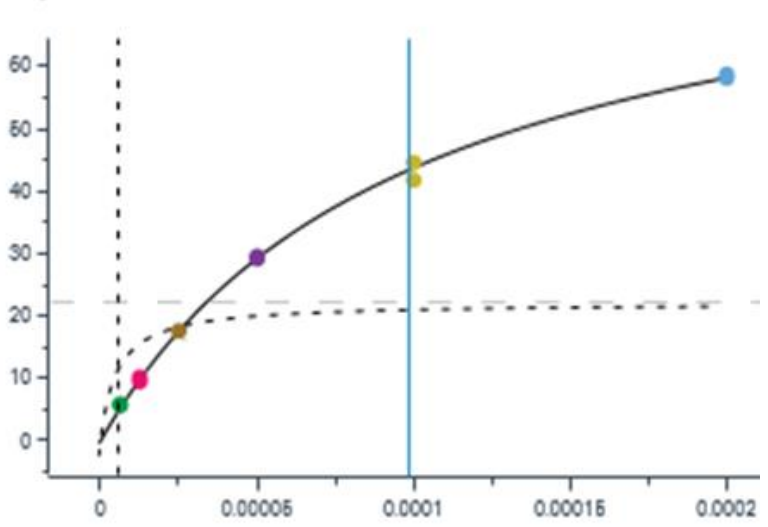
K_D = 39±18 µM – 67±1% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 14

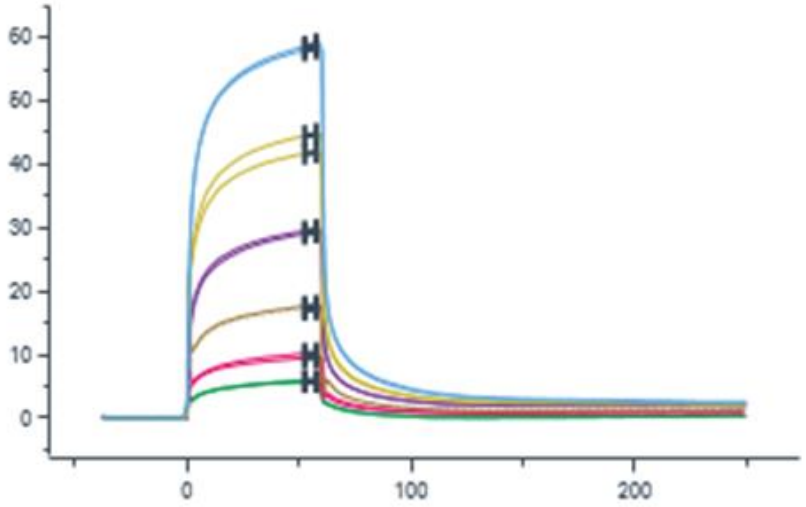
9 analogs of CACHE_1421_1 were submitted for round 2.
1 compound showed a superstoichiometric binding response with mild binding affinity to unrelated negative control protein.

CACHE2-HO_1421_3

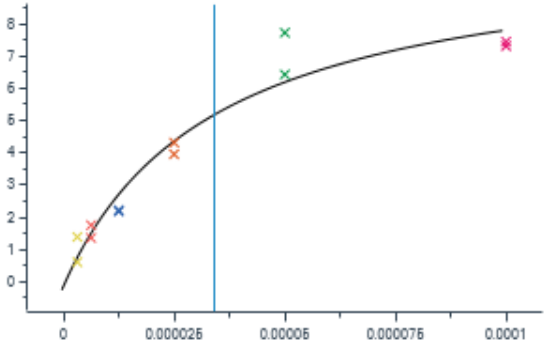
K_D _1 = 104 µM – 395% binding
K_D _2 = 98 µM – 392% binding
Selectivity (unrelated WDR5 protein) – mild binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 40

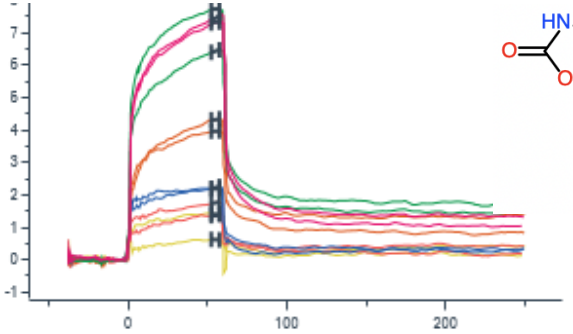


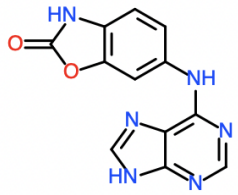




PARENT MOLECULE



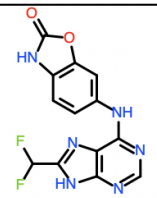




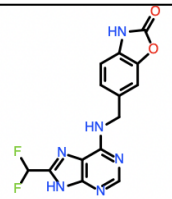
CACHE_1421_1

K_D = 39±18 µM – 67±1% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 14

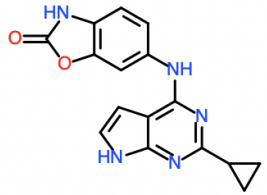
Tested analogs



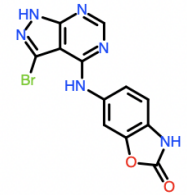
CACHE_ID CACHE2-HO_1421_1
Parent CACHE_1421_1
distance_to_pai 0.1155



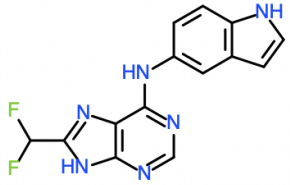
CACHE_ID CACHE2-HO_1421_2
Parent CACHE_1421_1
distance_to_pai 0.2174



CACHE_ID CACHE2-HO_1421_3
Parent CACHE_1421_1
distance_to_pai 0.2508

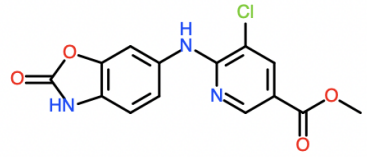


CACHE_ID CACHE2-HO_1421_4
Parent CACHE_1421_1
distance_to_pai 0.2593

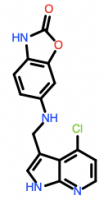


CACHE_ID CACHE2-HO_1421_5
Parent CACHE_1421_1
distance_to_pai 0.3831

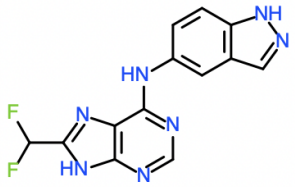
CACHE_ID CACHE2-HO_1421_6
Parent CACHE_1421_1
distance_to_pai 0.3921



CACHE_ID CACHE2-HO_1421_7
Parent CACHE_1421_1
distance_to_pai 0.3968

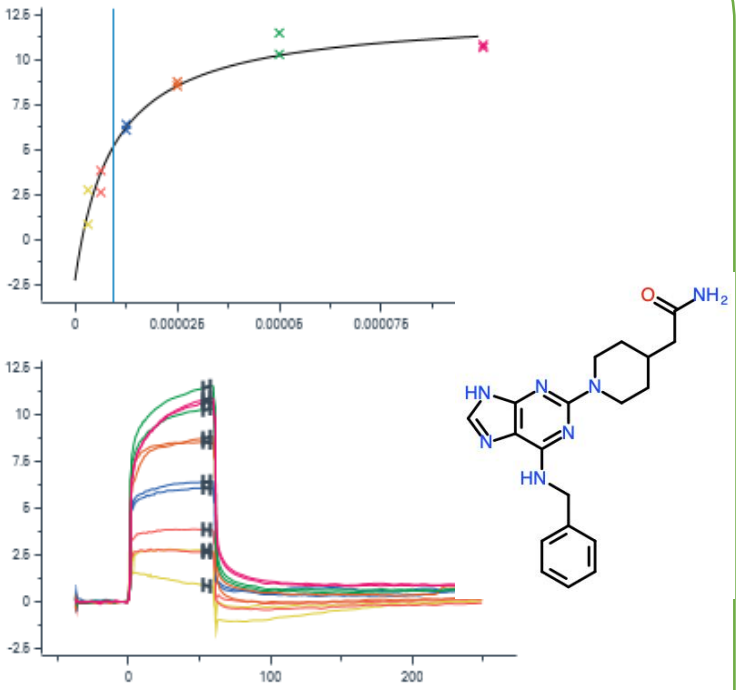


CACHE_ID CACHE2-HO_1421_8
Parent CACHE_1421_1
distance_to_pai 0.4177



CACHE_ID CACHE2-HO_1421_9
Parent CACHE_1421_1
distance_to_pai 0.4244

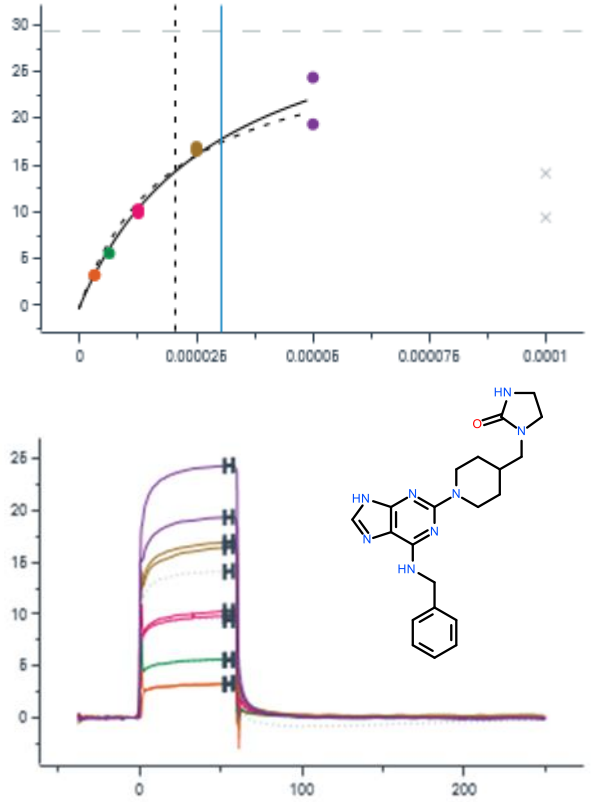
PARENT MOLECULE



CACHE_1421_21

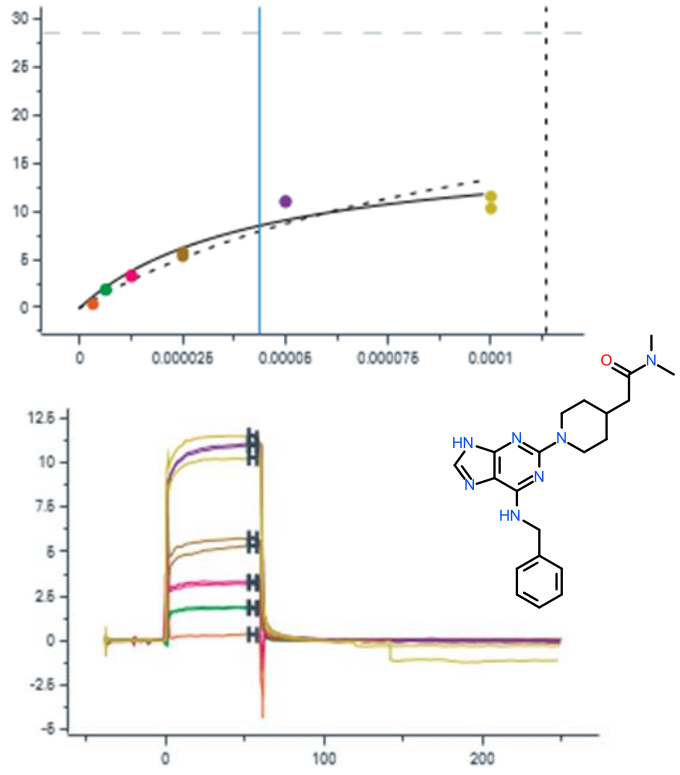
K_D = 10± 1µM – 65±13% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
%inhibition@50 µM_ATPase = 12

14 analogs of CACHE_1421_21 were submitted for round 2.
2 compound showed a binding response.



CACHE2-HO_1421_16

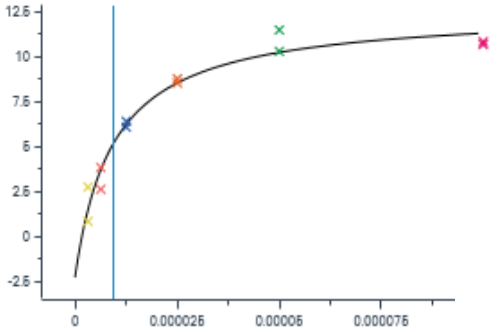
K_D = 30 µM – 122% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 13

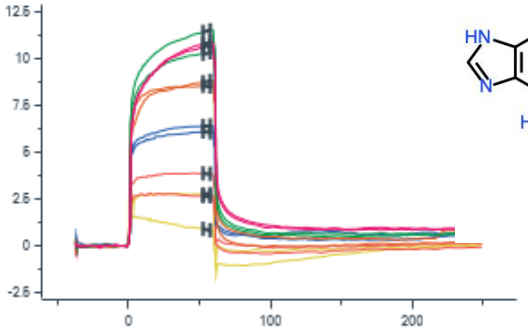


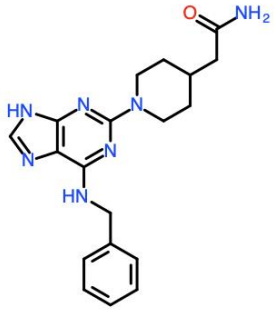
CACHE2-HO_1421_12

K_D (3% DMSO) = 43 µM – 60% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
%inhibition@50 µM_ATPase = 16

PARENT MOLECULE



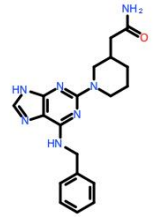




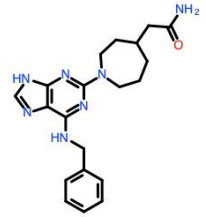
CACHE_1421_21

K_D = 10± 1µM – 65±13% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
%inhibition@50 µM_ATPase = 12

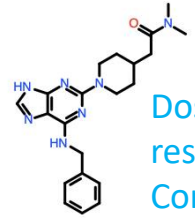
Tested analogs



CACHE_ID CACHE2-HO_1421_10
Parent CACHE_1421_21
distance_to_pai 0.01293

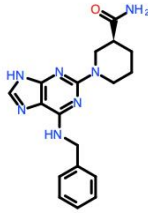


CACHE_ID CACHE2-HO_1421_11
Parent CACHE_1421_21
distance_to_pai 0.01299

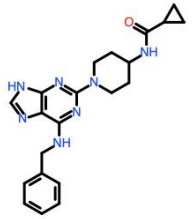


Dose response: Confirmed

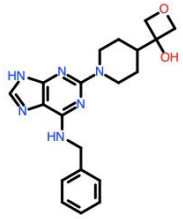
CACHE_ID CACHE2-HO_1421_12
Parent CACHE_1421_21
distance_to_pai 0.02155



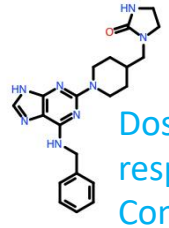
CACHE_ID CACHE2-HO_1421_13
Parent CACHE_1421_21
distance_to_pai 0.04219



CACHE_ID CACHE2-HO_1421_14
Parent CACHE_1421_21
distance_to_pai 0.09274

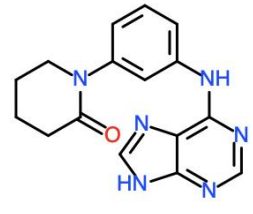


CACHE_ID CACHE2-HO_1421_15
Parent CACHE_1421_21
distance_to_pai 0.1333

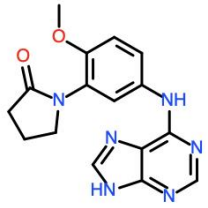


Dose response: Confirmed

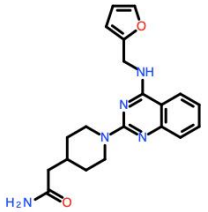
CACHE_ID CACHE2-HO_1421_16
Parent CACHE_1421_21
distance_to_pai 0.1654



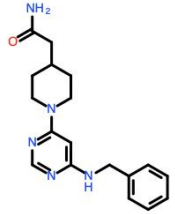
CACHE_ID CACHE2-HO_1421_17
Parent CACHE_1421_21
distance_to_pai 0.252



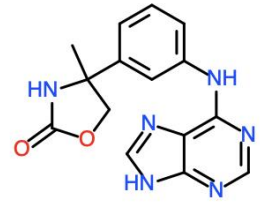
CACHE_ID CACHE2-HO_1421_18
Parent CACHE_1421_21
distance_to_pai 0.3345



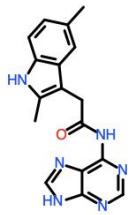
CACHE_ID CACHE2-HO_1421_19
Parent CACHE_1421_21
distance_to_pai 0.3552



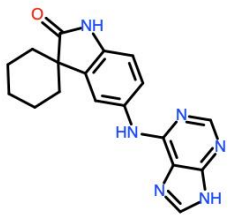
CACHE_ID CACHE2-HO_1421_20
Parent CACHE_1421_21
distance_to_pai 0.3651



CACHE_ID CACHE2-HO_1421_21
Parent CACHE_1421_21
distance_to_pai 0.3677

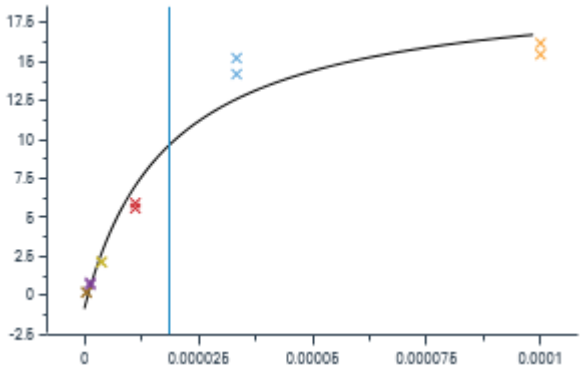


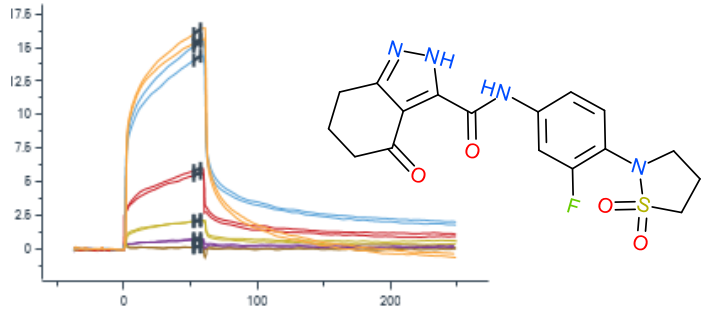
CACHE_ID CACHE2-HO_1421_22
Parent CACHE_1421_21
distance_to_pai 0.4153



CACHE_ID CACHE2-HO_1421_23
Parent CACHE_1421_21
distance_to_pai 0.4211

PARENT MOLECULE

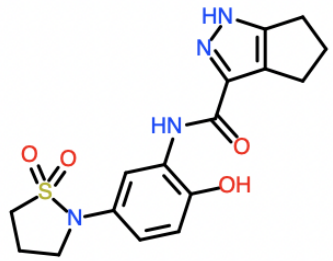




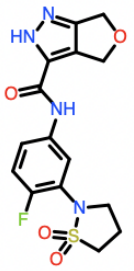
CACHE_1421_33

K_D = 18 µM – 73% binding
Selectivity (unrelated WDR5 protein) – 25% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 86

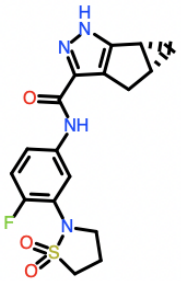
Tested analogs



CACHE_ID	CACHE2-HO_1421_24
Parent	CACHE_1421_33
distance_to_pai	0.2322



CACHE_ID	CACHE2-HO_1421_25
Parent	CACHE_1421_33
distance_to_pai	0.2358

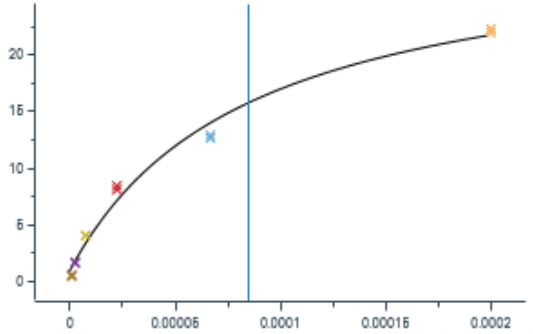


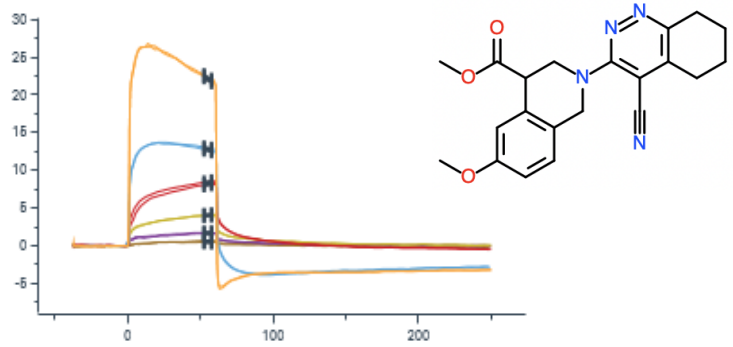
CACHE_ID	CACHE2-HO_1421_26
Parent	CACHE_1421_33
distance_to_pai	0.2857

CACHE#2 – NSP13 SARS2

Participant 1422

PARENT MOLECULE

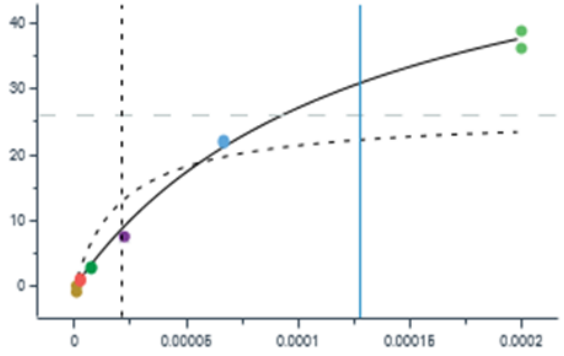


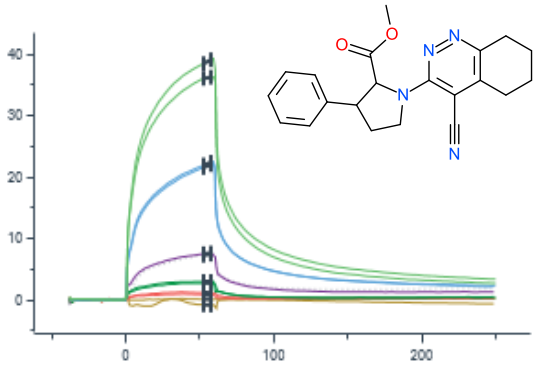


CACHE_1422_15

K_D = 85 µM – 91% binding
DLS (solub@200 µM)
IC_{50}_1 ATPase = 39 µM, Hill slope -1.2
IC_{50}_2 ATPase = 96 µM, Hill slope -0.7
IC_{50} no DNA _ ATPase = 43 µM, Hill slope -1.0

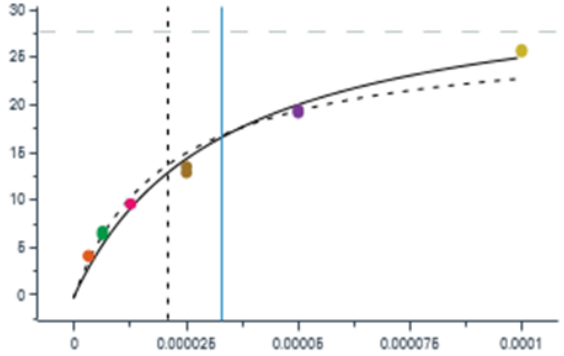
36 analogs of CACHE_1422_15 were submitted for round 2.
2 compounds showed a binding response by SPR with a tendency to saturation.

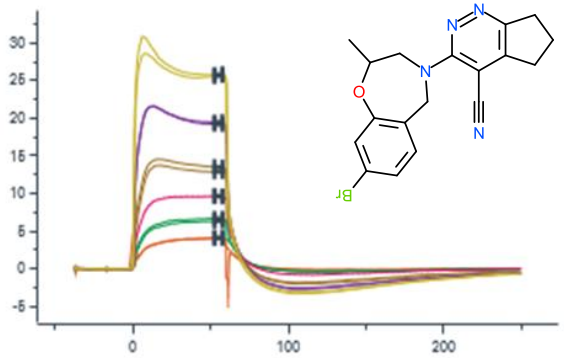




CACHE2-HO_1422_6

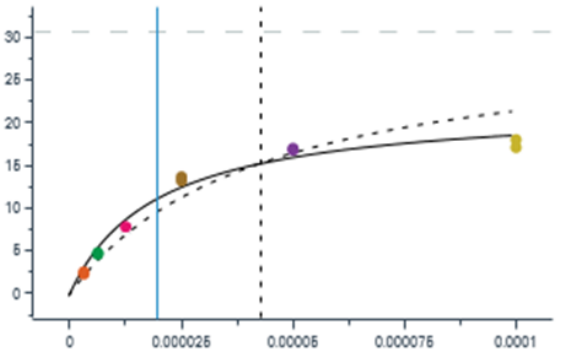
K_D = 128 µM (baseline difference) – 238% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 11

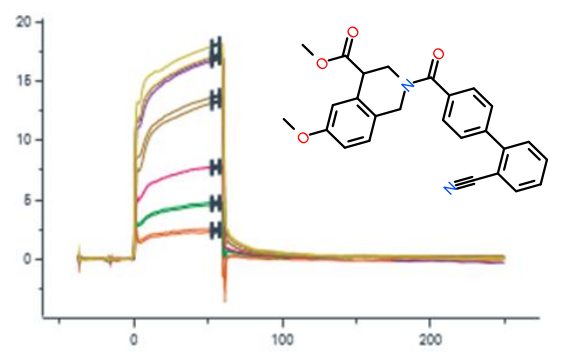




CACHE2-HO_1422_13

K_D _1 = 41 µM – 110% binding
K_D _2 = 33 µM – 120% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 6

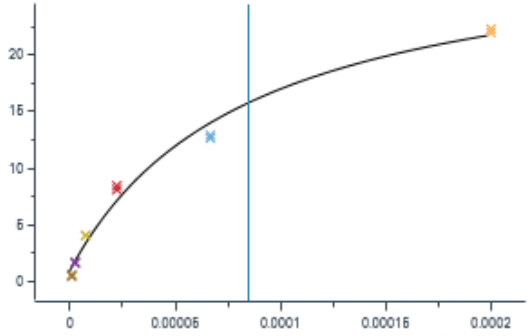


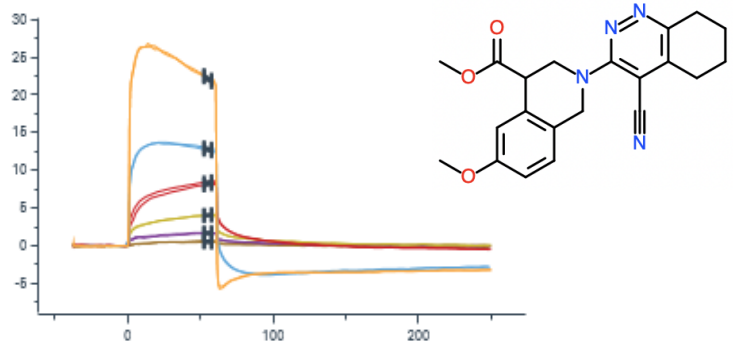


CACHE2-HO_1422_23

K_D = 19 µM – 72% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
%inhibition@50 µM_ATPase = 11

PARENT MOLECULE





CACHE_1422_15

K_D = 85 µM – 91% binding

DLS (solub@200 µM)

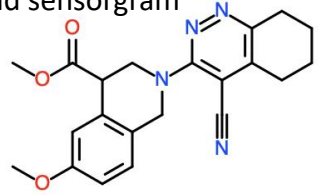
IC_{50}_1 ATPase = 39 µM, Hill slope -1.2

IC_{50}_2 ATPase = 96 µM, Hill slope -0.7

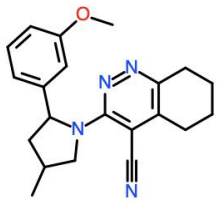
IC_{50} no DNA _ ATPase = 43 µM, Hill slope -1.0

Tested analogs

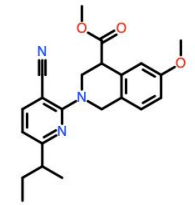
Bad sensorgram



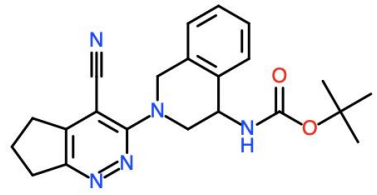
CACHE_ID	CACHE2-HO_1422_1
Parent	CACHE_1422_15
distance_to_pai	0



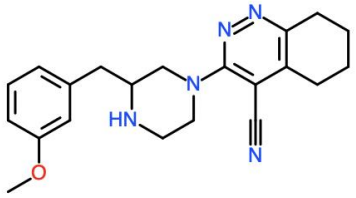
CACHE_ID	CACHE2-HO_1422_2
Parent	CACHE_1422_15
distance_to_pai	0.2364



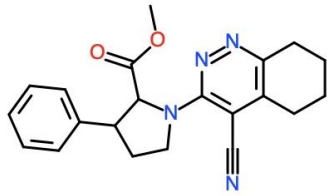
CACHE_ID	CACHE2-HO_1422_3
Parent	CACHE_1422_15
distance_to_pai	0.2445



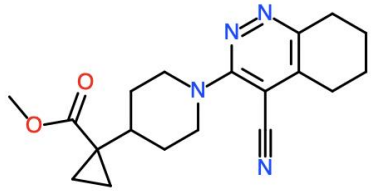
CACHE_ID	CACHE2-HO_1422_4
Parent	CACHE_1422_15
distance_to_pai	0.2463



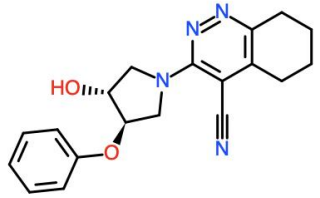
CACHE_ID	CACHE2-HO_1422_5
Parent	CACHE_1422_15
distance_to_pai	0.2617



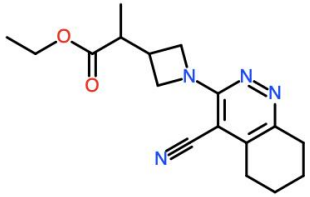
CACHE_ID	CACHE2-HO_1422_6
Parent	CACHE_1422_15
distance_to_pai	0.2652



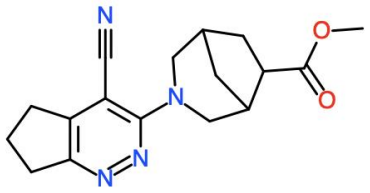
CACHE_ID	CACHE2-HO_1422_7
Parent	CACHE_1422_15
distance_to_pai	0.2675



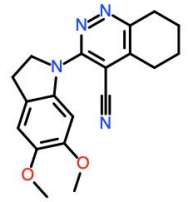
CACHE_ID	CACHE2-HO_1422_8
Parent	CACHE_1422_15
distance_to_pai	0.2796



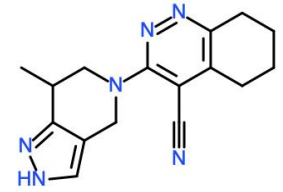
CACHE_ID	CACHE2-HO_1422_9
Parent	CACHE_1422_15
distance_to_pai	0.2816



CACHE_ID	CACHE2-HO_1422_10
Parent	CACHE_1422_15
distance_to_pai	0.2835

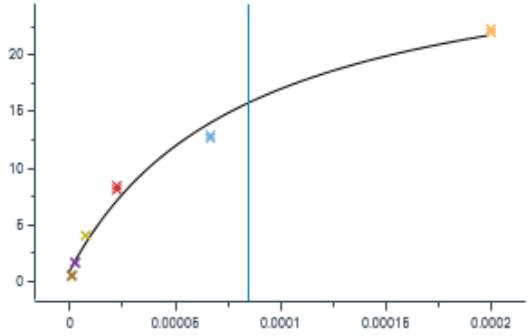


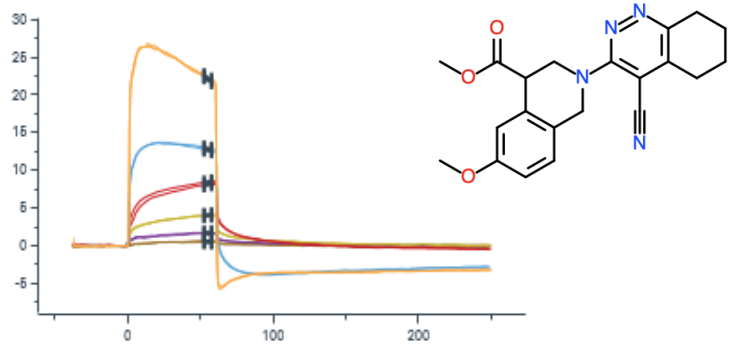
CACHE_ID	CACHE2-HO_1422_11
Parent	CACHE_1422_15
distance_to_pai	0.2849



CACHE_ID	CACHE2-HO_1422_12
Parent	CACHE_1422_15
distance_to_pai	0.2866

PARENT MOLECULE





CACHE_1422_15

K_D = 85 µM – 91% binding

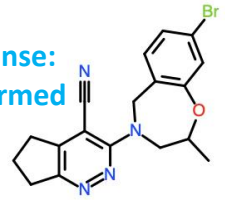
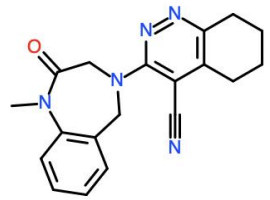
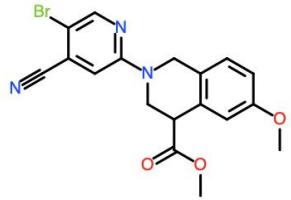
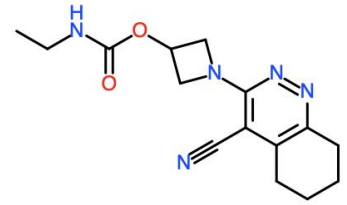
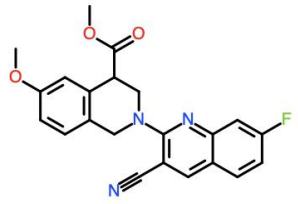
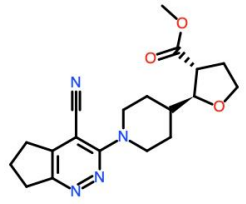
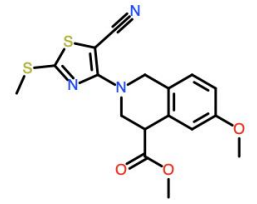
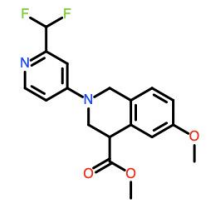
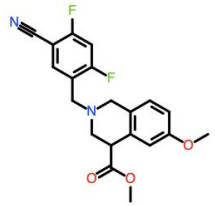
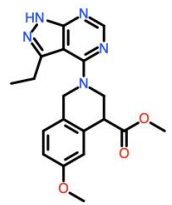
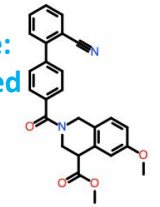
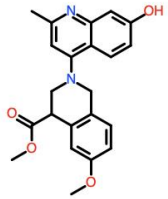
DLS (solub@200 µM)

IC_{50}_1 ATPase = 39 µM, Hill slope -1.2

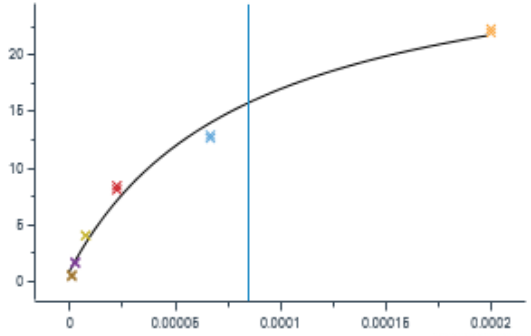
IC_{50}_2 ATPase = 96 µM, Hill slope -0.7

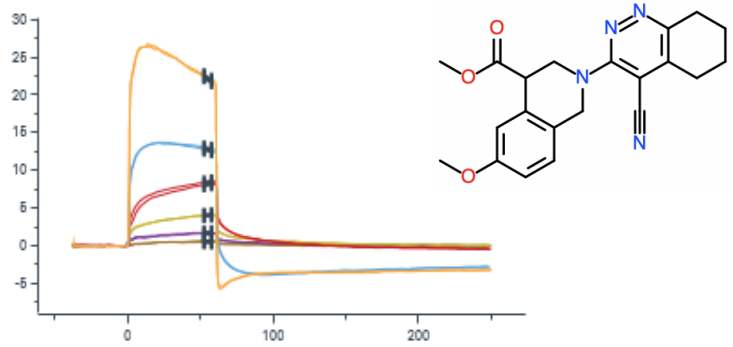
IC_{50} no DNA _ ATPase = 43 µM, Hill slope -1.0

Tested analogs

Dose response: Confirmed  CACHE_ID CACHE2-HO_1422_13 Parent CACHE_1422_15 distance_to_pai 0.2963	 CACHE_ID CACHE2-HO_1422_14 Parent CACHE_1422_15 distance_to_pai 0.3038	 CACHE_ID CACHE2-HO_1422_15 Parent CACHE_1422_15 distance_to_pai 0.3089	 CACHE_ID CACHE2-HO_1422_16 Parent CACHE_1422_15 distance_to_pai 0.3252
 CACHE_ID CACHE2-HO_1422_17 Parent CACHE_1422_15 distance_to_pai 0.3296	 CACHE_ID CACHE2-HO_1422_18 Parent CACHE_1422_15 distance_to_pai 0.3303	 CACHE_ID CACHE2-HO_1422_19 Parent CACHE_1422_15 distance_to_pai 0.3775	 CACHE_ID CACHE2-HO_1422_20 Parent CACHE_1422_15 distance_to_pai 0.3872
 CACHE_ID CACHE2-HO_1422_21 Parent CACHE_1422_15 distance_to_pai 0.3887	 CACHE_ID CACHE2-HO_1422_22 Parent CACHE_1422_15 distance_to_pai 0.3896	Dose response: Confirmed  CACHE_ID CACHE2-HO_1422_23 Parent CACHE_1422_15 distance_to_pai 0.3908	 CACHE_ID CACHE2-HO_1422_24 Parent CACHE_1422_15 distance_to_pai 0.3918

PARENT MOLECULE





CACHE_1422_15

K_D = 85 µM – 91% binding

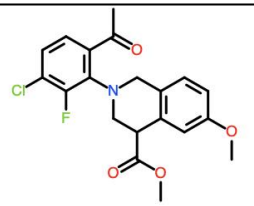
DLS (solub@200 µM)

IC_{50}_1 ATPase = 39 µM, Hill slope -1.2

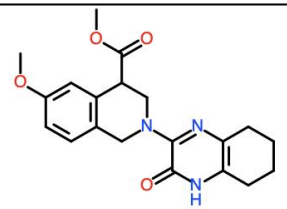
IC_{50}_2 ATPase = 96 µM, Hill slope -0.7

IC_{50} no DNA _ ATPase = 43 µM, Hill slope -1.0

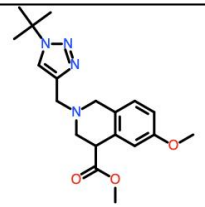
Tested analogs



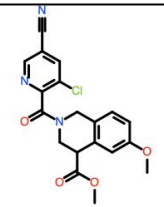
CACHE_ID CACHE2-HO_1422_25
Parent CACHE_1422_15
distance_to_pai 0.3982



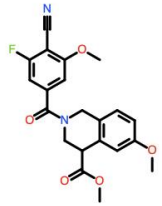
CACHE_ID CACHE2-HO_1422_26
Parent CACHE_1422_15
distance_to_pai 0.4074



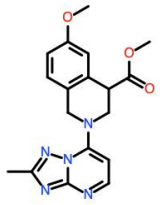
CACHE_ID CACHE2-HO_1422_27
Parent CACHE_1422_15
distance_to_pai 0.4142



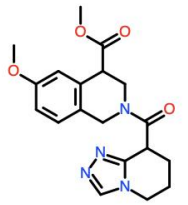
CACHE_ID CACHE2-HO_1422_28
Parent CACHE_1422_15
distance_to_pai 0.419



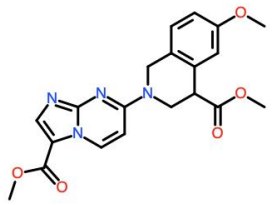
CACHE_ID CACHE2-HO_1422_29
Parent CACHE_1422_15
distance_to_pai 0.4294



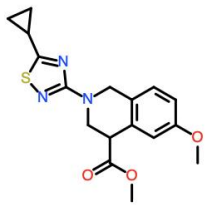
CACHE_ID CACHE2-HO_1422_30
Parent CACHE_1422_15
distance_to_pai 0.4312



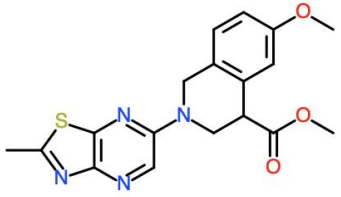
CACHE_ID CACHE2-HO_1422_31
Parent CACHE_1422_15
distance_to_pai 0.4368



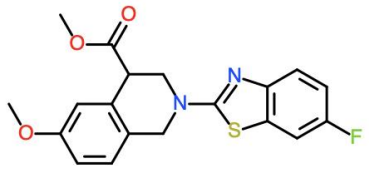
CACHE_ID CACHE2-HO_1422_32
Parent CACHE_1422_15
distance_to_pai 0.4378



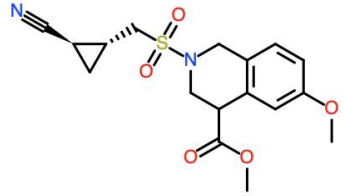
CACHE_ID CACHE2-HO_1422_33
Parent CACHE_1422_15
distance_to_pai 0.446



CACHE_ID CACHE2-HO_1422_34
Parent CACHE_1422_15
distance_to_pai 0.4583



CACHE_ID CACHE2-HO_1422_35
Parent CACHE_1422_15
distance_to_pai 0.4697

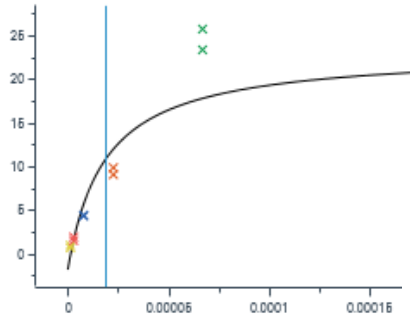


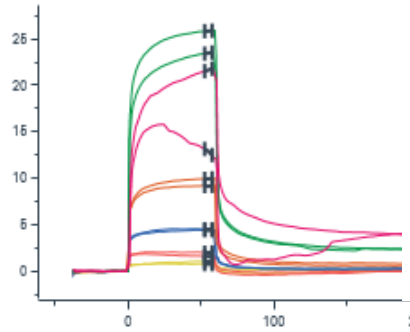
CACHE_ID CACHE2-HO_1422_36
Parent CACHE_1422_15
distance_to_pai 0.478

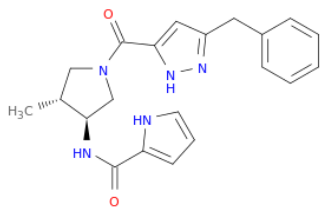
CACHE#2 – NSP13 SARS2

Participant 1425

PARENT MOLECULE



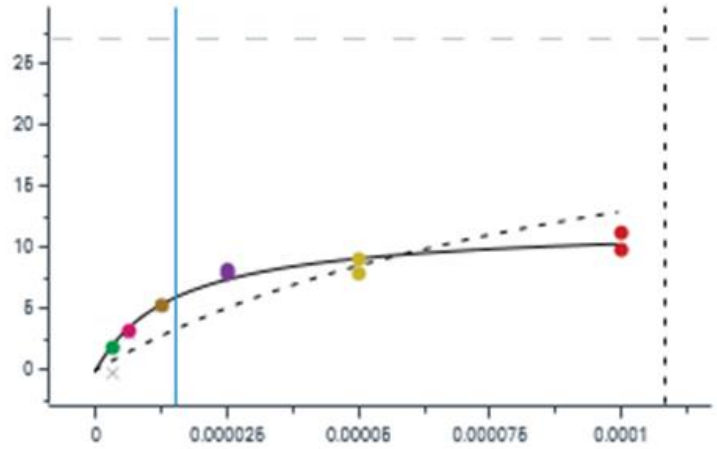


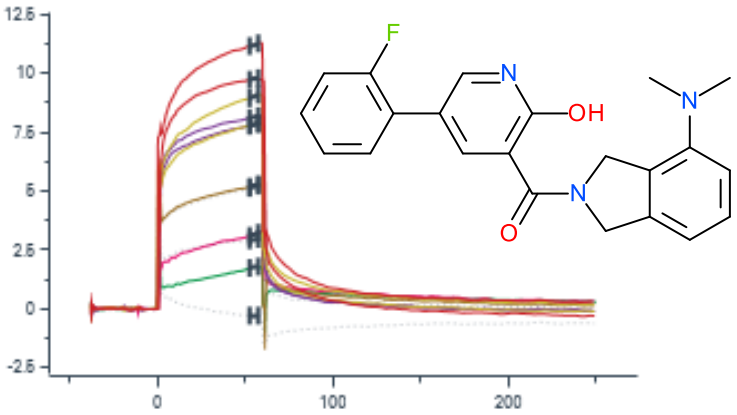


CACHE_1425_80

K_D = 19 µM (baseline difference/poor fit) – 95% binding
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = no inhibition

12 follow-ups of CACHE_1425_80 were submitted for round 2.
1 compound showed a mild binding response reaching saturation.



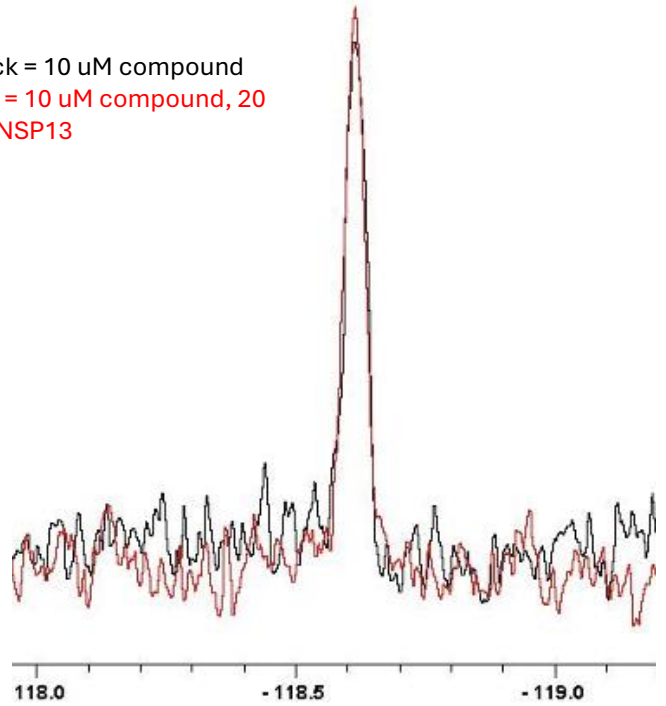


CACHE2-HO_1425_9

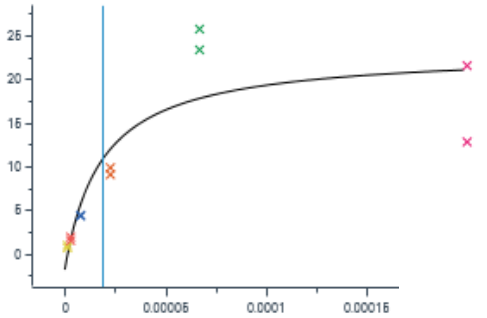
K_D = 15 µM – 44% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 10

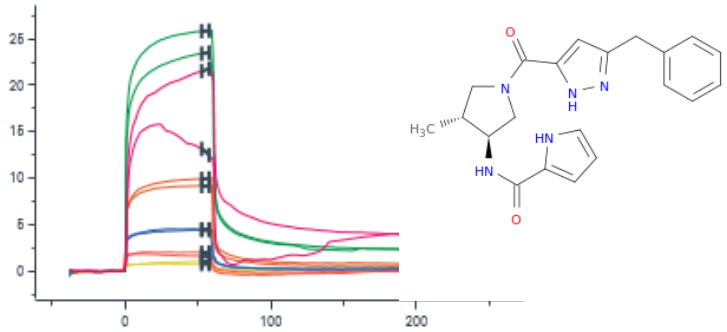
^{19}F NMR
Did not confirm binding

Black = 10 uM compound
Red = 10 uM compound, 20 uM NSP13



PARENT MOLECULE

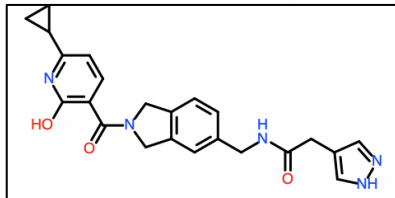




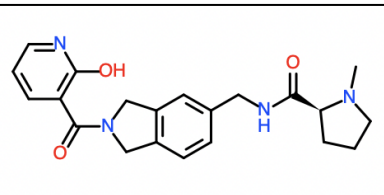
CACHE_1425_80

K_D = 19 µM (baseline difference/poor fit) – 95% binding
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = no inhibition

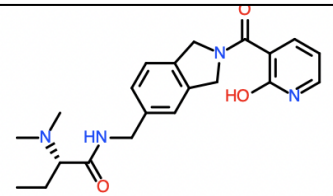
Tested follow-ups



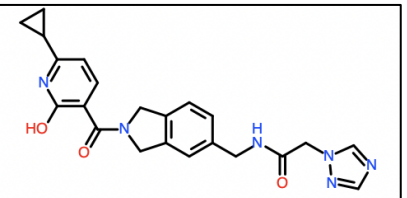
CACHE_ID CACHE2-HO_1425_1
Parent CACHE_1425_80
distance_to_pai 0.4792



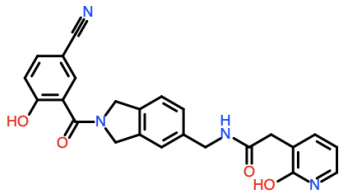
CACHE_ID CACHE2-HO_1425_2
Parent CACHE_1425_80
distance_to_pai 0.544



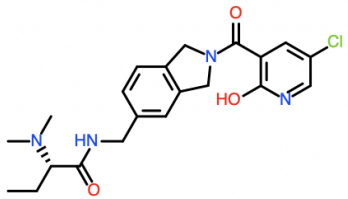
CACHE_ID CACHE2-HO_1425_3
Parent CACHE_1425_80
distance_to_pai 0.5574



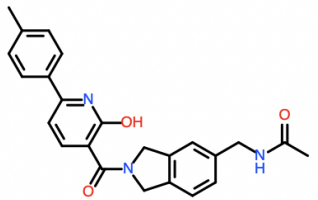
CACHE_ID CACHE2-HO_1425_4
Parent CACHE_1425_80
distance_to_pai 0.5594



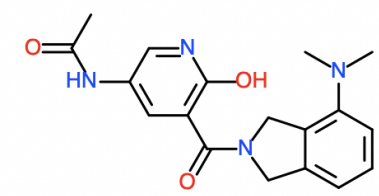
CACHE_ID CACHE2-HO_1425_5
Parent CACHE_1425_80
distance_to_pai 0.5682



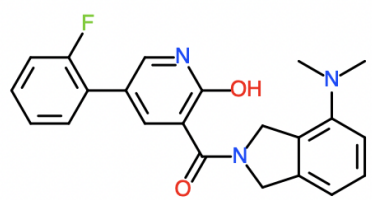
CACHE_ID CACHE2-HO_1425_6
Parent CACHE_1425_80
distance_to_pai 0.5789



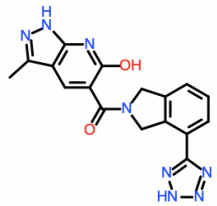
CACHE_ID CACHE2-HO_1425_7
Parent CACHE_1425_80
distance_to_pai 0.5809



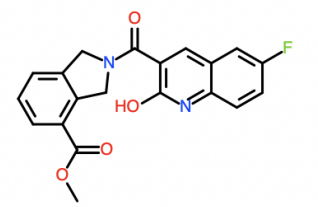
CACHE_ID CACHE2-HO_1425_8
Parent CACHE_1425_80
distance_to_pai 0.607



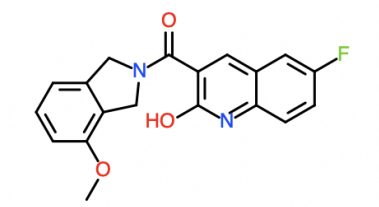
CACHE_ID CACHE2-HO_1425_9
Parent CACHE_1425_80
distance_to_pai 0.6246



CACHE_ID CACHE2-HO_1425_10
Parent CACHE_1425_80
distance_to_pai 0.6283



CACHE_ID CACHE2-HO_1425_11
Parent CACHE_1425_80
distance_to_pai 0.6744

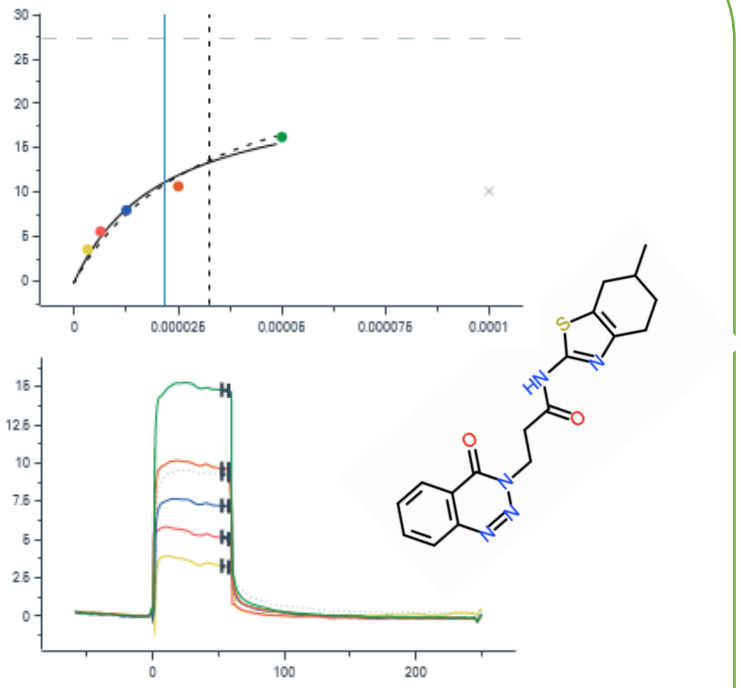


CACHE_ID CACHE2-HO_1425_12
Parent CACHE_1425_80
distance_to_pai 0.6989

CACHE#2 – NSP13 SARS2

Participant 1430

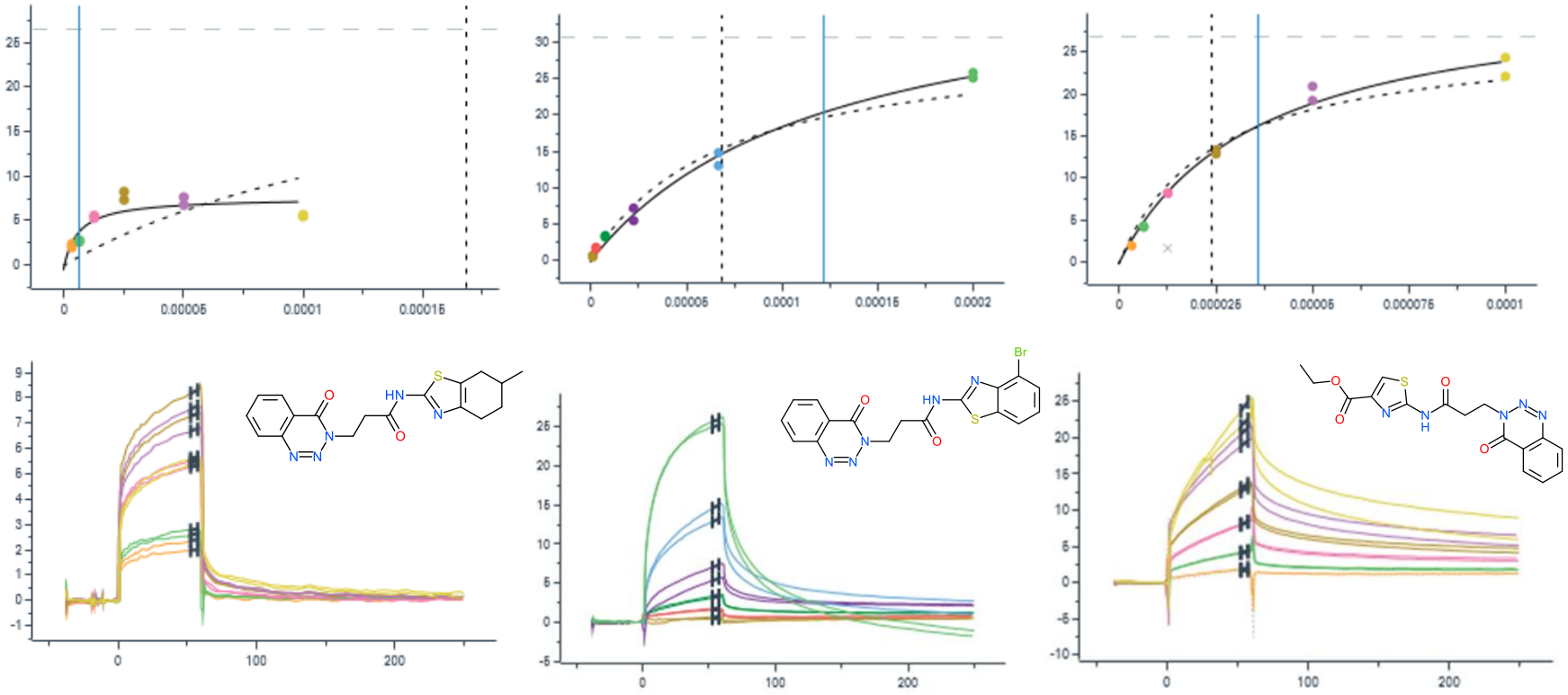
PARENT MOLECULE



CACHE_1430_25

K_D = 22 µM (solubility issues) – 81% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
IC_{50}_ATPase >100 µM

48 analogs of CACHE_1430_25 were submitted for round 2.
2 compounds showed a weak binding response by SPR.



CACHE2-HO_1430_1

K_D (3%DMSO) = 6 µM (poor fit) – 29% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
%inhibition@50 µM_ATPase = 11

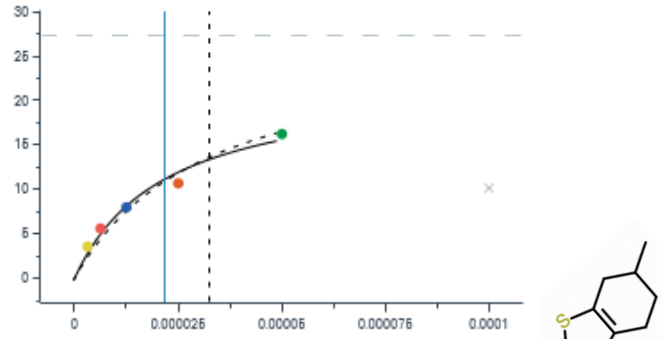
CACHE2-HO_1430_16

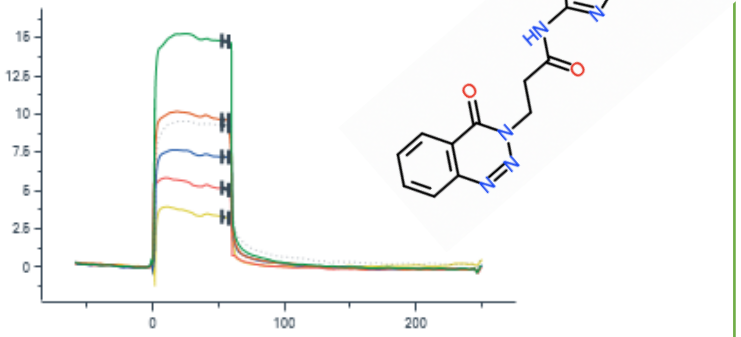
K_D = 122 µM – 133% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 25

CACHE2-HO_1430_33

K_D (3% DMSO) = 36 µM (baseline difference) – 121% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 10

PARENT MOLECULE

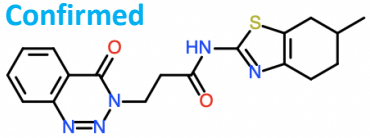
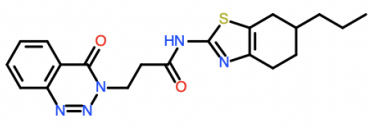
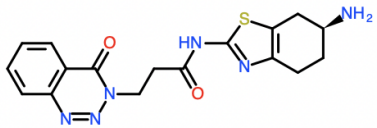
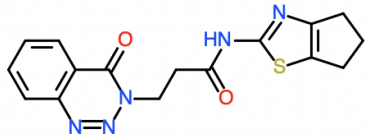
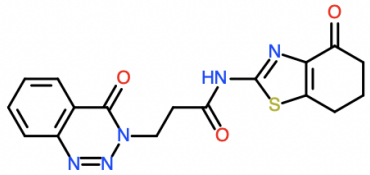
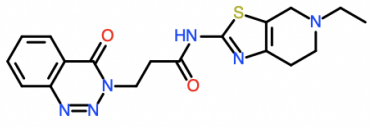
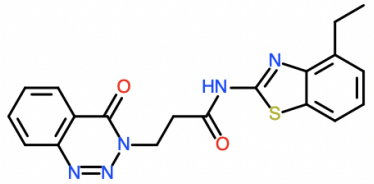
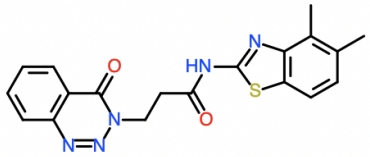
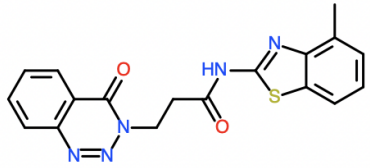
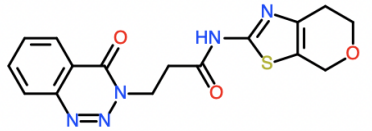
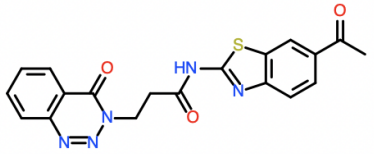
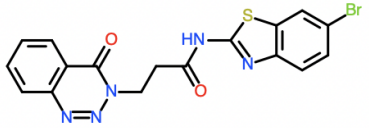
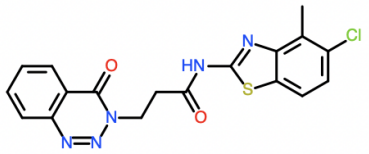
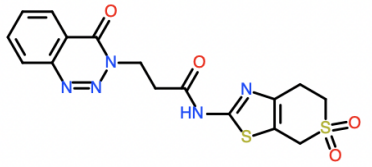
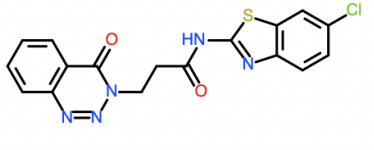
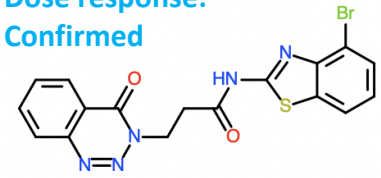




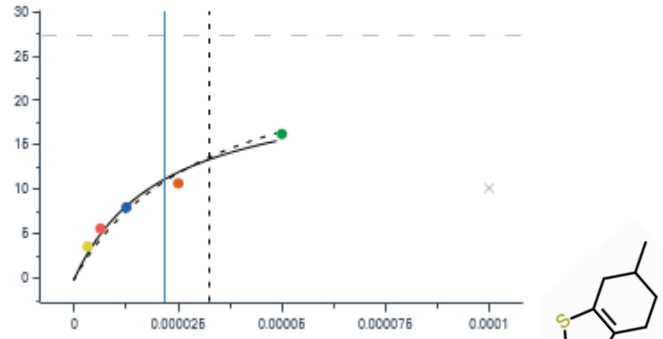
CACHE_1430_25

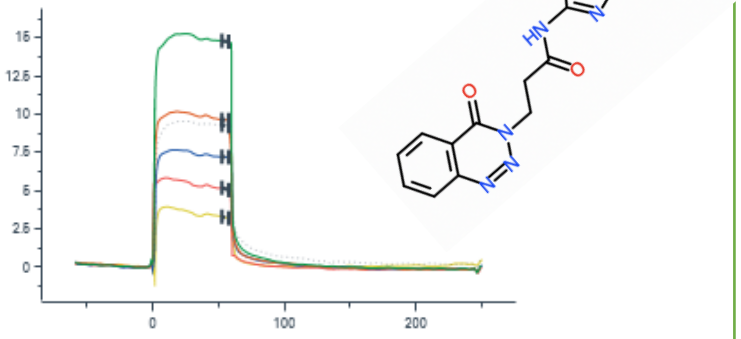
K_D = 22 µM (solubility issues) – 81% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
IC_{50}_ATPase >100 µM

Tested analogs

Dose response: Confirmed  CACHE_ID CACHE2-HO_1430_1 Parent CACHE_1430_25 distance_to_pai 0	 CACHE_ID CACHE2-HO_1430_2 Parent CACHE_1430_25 distance_to_pai 0.01749	 CACHE_ID CACHE2-HO_1430_3 Parent CACHE_1430_25 distance_to_pai 0.04274	 CACHE_ID CACHE2-HO_1430_4 Parent CACHE_1430_25 distance_to_pai 0.04651
 CACHE_ID CACHE2-HO_1430_5 Parent CACHE_1430_25 distance_to_pai 0.07042	 CACHE_ID CACHE2-HO_1430_6 Parent CACHE_1430_25 distance_to_pai 0.1444	 CACHE_ID CACHE2-HO_1430_7 Parent CACHE_1430_25 distance_to_pai 0.1519	 CACHE_ID CACHE2-HO_1430_8 Parent CACHE_1430_25 distance_to_pai 0.1738
 CACHE_ID CACHE2-HO_1430_9 Parent CACHE_1430_25 distance_to_pai 0.1771	 CACHE_ID CACHE2-HO_1430_10 Parent CACHE_1430_25 distance_to_pai 0.1782	 CACHE_ID CACHE2-HO_1430_11 Parent CACHE_1430_25 distance_to_pai 0.1933	 CACHE_ID CACHE2-HO_1430_12 Parent CACHE_1430_25 distance_to_pai 0.2039
 CACHE_ID CACHE2-HO_1430_13 Parent CACHE_1430_25 distance_to_pai 0.2082	 CACHE_ID CACHE2-HO_1430_14 Parent CACHE_1430_25 distance_to_pai 0.2087	 CACHE_ID CACHE2-HO_1430_15 Parent CACHE_1430_25 distance_to_pai 0.2089	**Dose response: Confirmed**  CACHE_ID CACHE2-HO_1430_16 Parent CACHE_1430_25 distance_to_pai 0.2105

PARENT MOLECULE

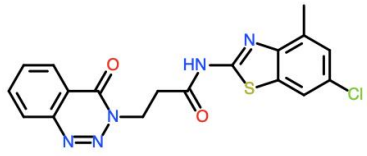




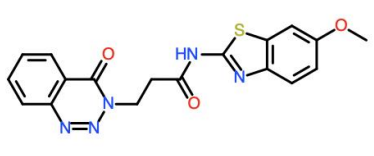
CACHE_1430_25

K_D = 22 µM (solubility issues) – 81% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
IC_{50}_ATPase >100 µM

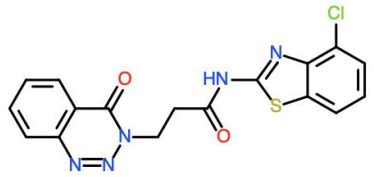
Tested analogs



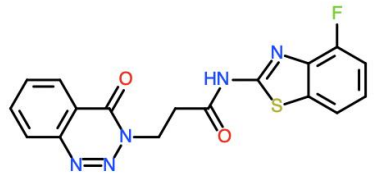
CACHE_ID CACHE2-HO_1430_17
Parent CACHE_1430_25
distance_to_pai 0.2125



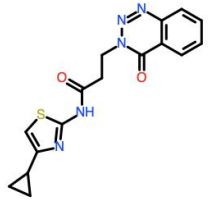
CACHE_ID CACHE2-HO_1430_18
Parent CACHE_1430_25
distance_to_pai 0.2143



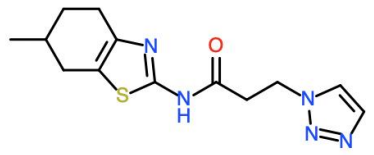
CACHE_ID CACHE2-HO_1430_19
Parent CACHE_1430_25
distance_to_pai 0.2155



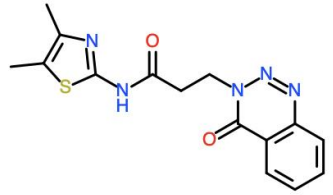
CACHE_ID CACHE2-HO_1430_20
Parent CACHE_1430_25
distance_to_pai 0.2176



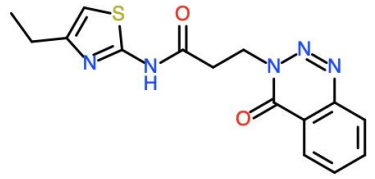
CACHE_ID CACHE2-HO_1430_21
Parent CACHE_1430_25
distance_to_pai 0.2351



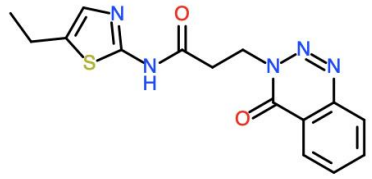
CACHE_ID CACHE2-HO_1430_22
Parent CACHE_1430_25
distance_to_pai 0.2407



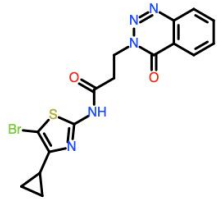
CACHE_ID CACHE2-HO_1430_23
Parent CACHE_1430_25
distance_to_pai 0.2636



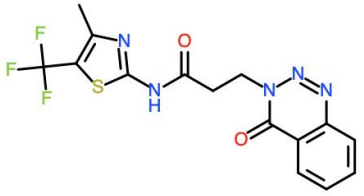
CACHE_ID CACHE2-HO_1430_24
Parent CACHE_1430_25
distance_to_pai 0.2644



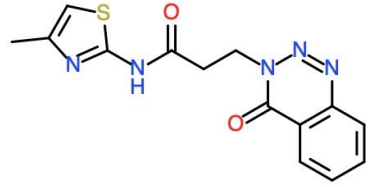
CACHE_ID CACHE2-HO_1430_25
Parent CACHE_1430_25
distance_to_pai 0.2693



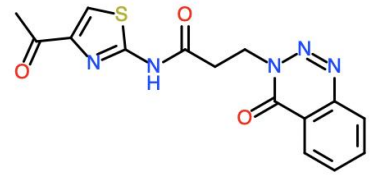
CACHE_ID CACHE2-HO_1430_26
Parent CACHE_1430_25
distance_to_pai 0.2727



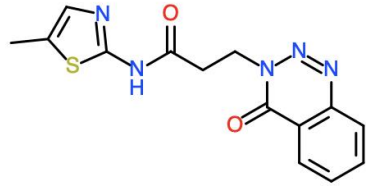
CACHE_ID CACHE2-HO_1430_27
Parent CACHE_1430_25
distance_to_pai 0.279



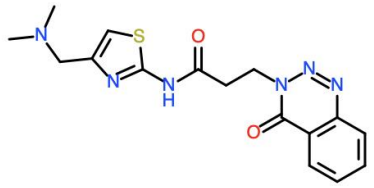
CACHE_ID CACHE2-HO_1430_28
Parent CACHE_1430_25
distance_to_pai 0.2923



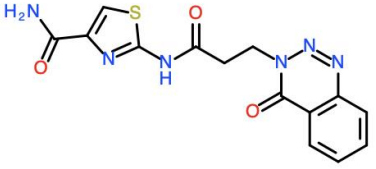
CACHE_ID CACHE2-HO_1430_29
Parent CACHE_1430_25
distance_to_pai 0.2944



CACHE_ID CACHE2-HO_1430_30
Parent CACHE_1430_25
distance_to_pai 0.2989

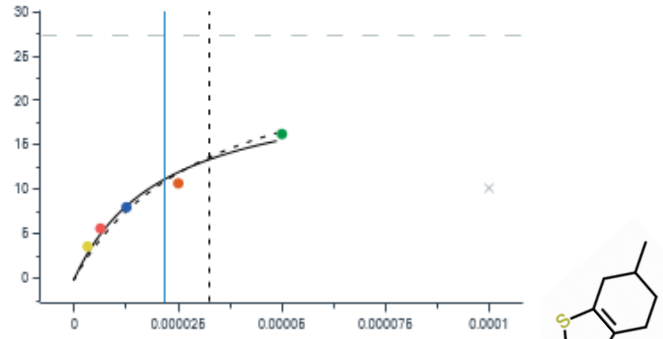


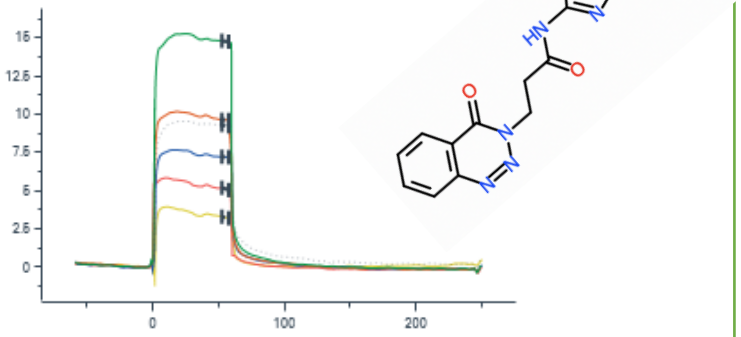
CACHE_ID CACHE2-HO_1430_31
Parent CACHE_1430_25
distance_to_pai 0.3132



CACHE_ID CACHE2-HO_1430_32
Parent CACHE_1430_25
distance_to_pai 0.3215

PARENT MOLECULE

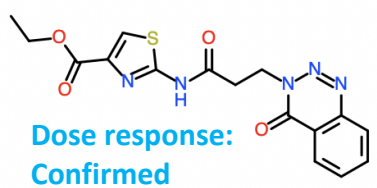




CACHE_1430_25

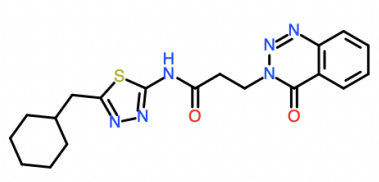
K_D = 22 µM (solubility issues) – 81% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
IC_{50}_ATPase >100 µM

Tested analogs

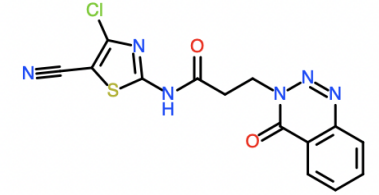


Dose response: Confirmed

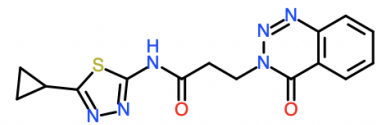
CACHE_ID CACHE2-HO_1430_33
Parent CACHE_1430_25
distance_to_pai 0.3227



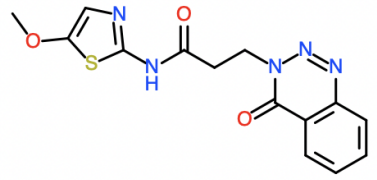
CACHE_ID CACHE2-HO_1430_34
Parent CACHE_1430_25
distance_to_pai 0.3378



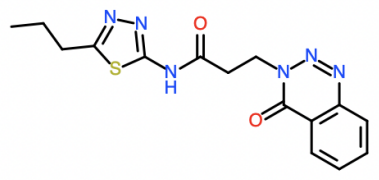
CACHE_ID CACHE2-HO_1430_35
Parent CACHE_1430_25
distance_to_pai 0.3404



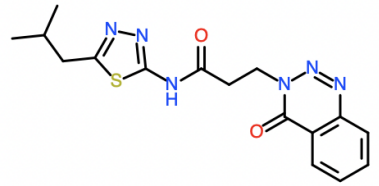
CACHE_ID CACHE2-HO_1430_36
Parent CACHE_1430_25
distance_to_pai 0.3449



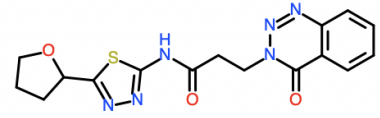
CACHE_ID CACHE2-HO_1430_37
Parent CACHE_1430_25
distance_to_pai 0.3542



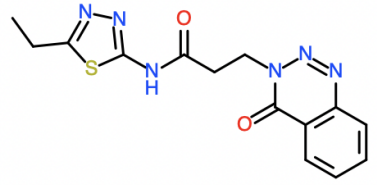
CACHE_ID CACHE2-HO_1430_38
Parent CACHE_1430_25
distance_to_pai 0.3612



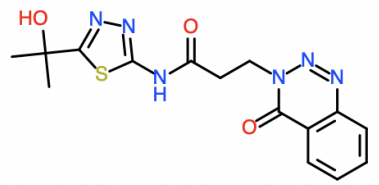
CACHE_ID CACHE2-HO_1430_39
Parent CACHE_1430_25
distance_to_pai 0.3619



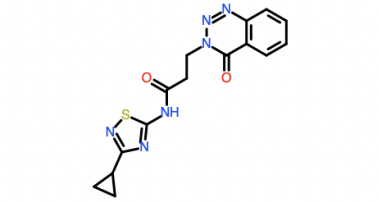
CACHE_ID CACHE2-HO_1430_40
Parent CACHE_1430_25
distance_to_pai 0.3636



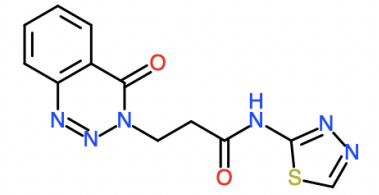
CACHE_ID CACHE2-HO_1430_41
Parent CACHE_1430_25
distance_to_pai 0.3696



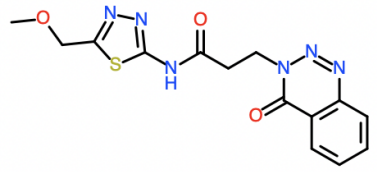
CACHE_ID CACHE2-HO_1430_42
Parent CACHE_1430_25
distance_to_pai 0.3858



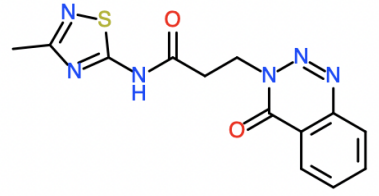
CACHE_ID CACHE2-HO_1430_43
Parent CACHE_1430_25
distance_to_pai 0.3953



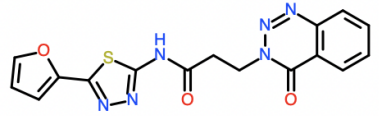
CACHE_ID CACHE2-HO_1430_44
Parent CACHE_1430_25
distance_to_pai 0.3955



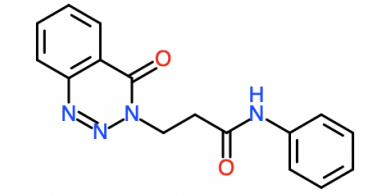
CACHE_ID CACHE2-HO_1430_45
Parent CACHE_1430_25
distance_to_pai 0.4042



CACHE_ID CACHE2-HO_1430_46
Parent CACHE_1430_25
distance_to_pai 0.4259

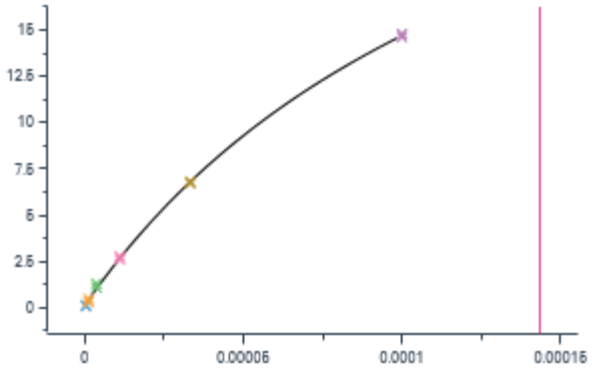


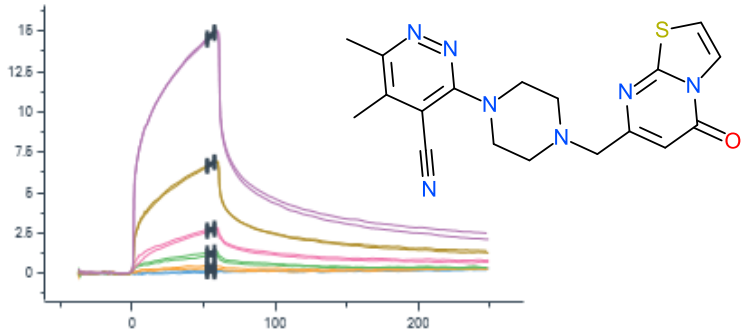
CACHE_ID CACHE2-HO_1430_47
Parent CACHE_1430_25
distance_to_pai 0.4387



CACHE_ID CACHE2-HO_1430_48
Parent CACHE_1430_25
distance_to_pai 0.4574

Round 1 HIT MOLECULE





CACHE_1430_47

K_D = 144 µM (does not reach saturation) – 125% binding

DLS (solub@100 µM)

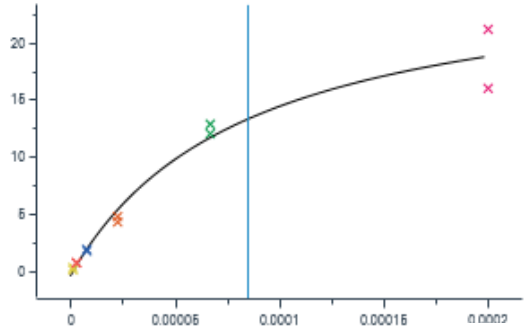
%inhibition@50 µM_ATPase = 91

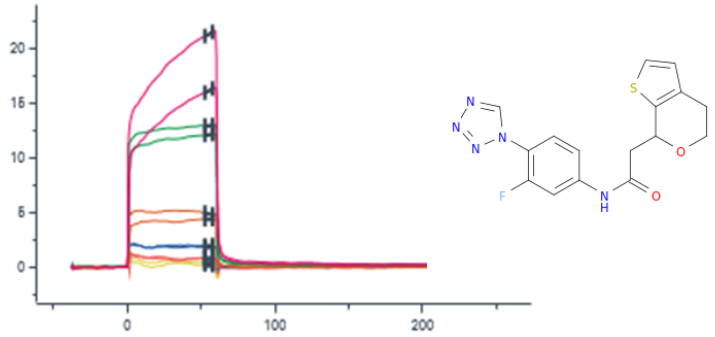
No analog in Round 2

CACHE#2 – NSP13 SARS2

Participant 1431

PARENT MOLECULE



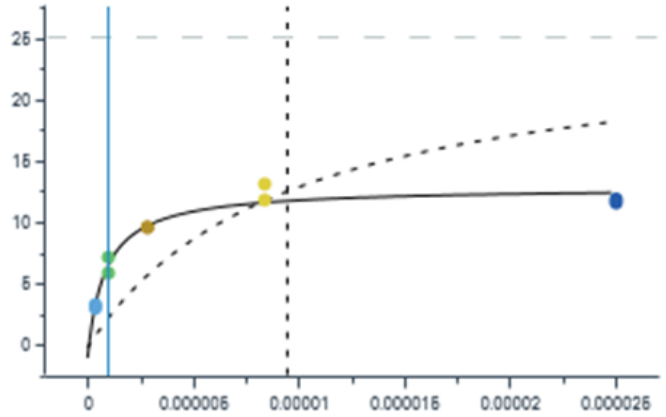


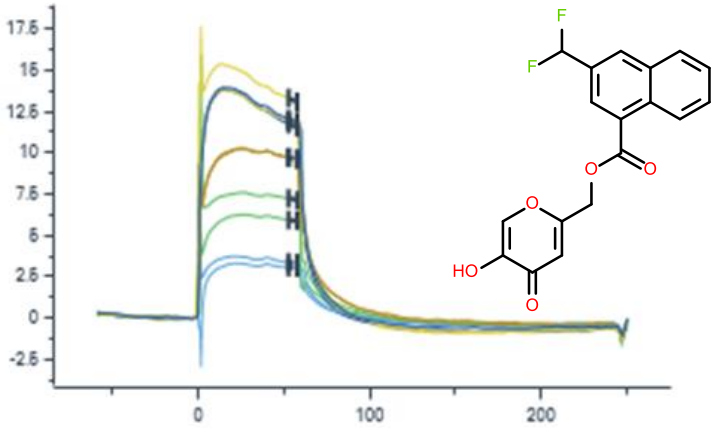
CACHE_1431_64

K_D = 85 µM – 111% binding

%inhibition@50 µM_ATPase = 9

11 non-analog follow-ups of CACHE_1431_64 were submitted for round 2. One compound showed a high binding affinity by SPR that was confirmed by ^{19}F NMR.





CACHE2-HO_1431_6

K_D _1 = 0.65 µM – 72% binding

K_D _2 (3% DMSO) = 0.9 µM – 51% binding

Selectivity (unrelated WDR5 protein) – Yes

DLS (solub@100 µM)

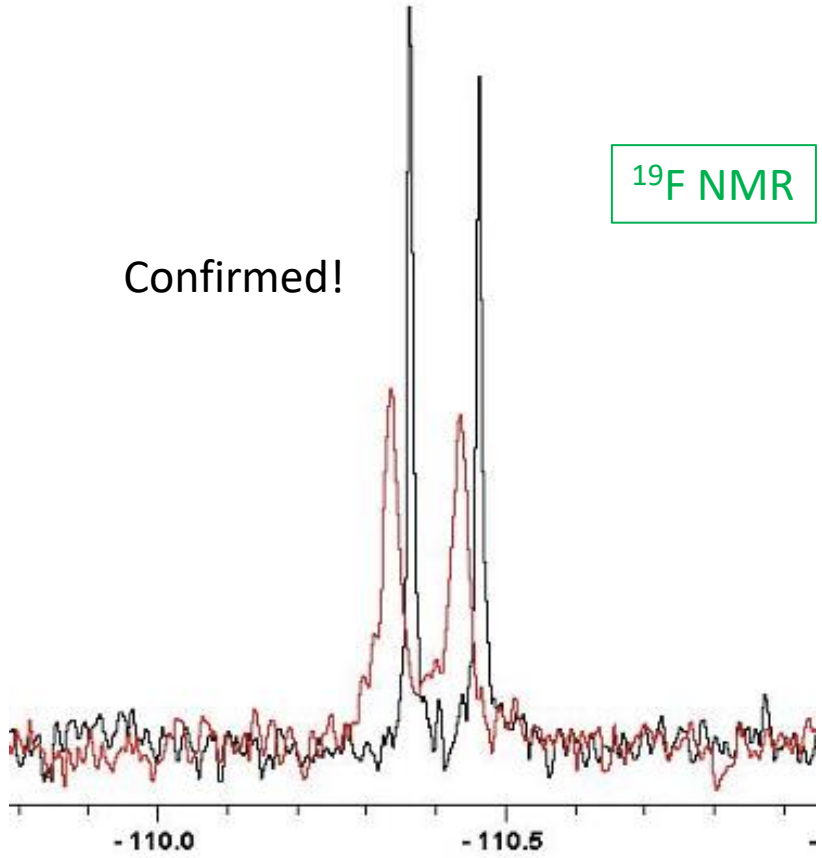
%inhibition@50 µM_ATPase = 11

Black = 10 uM compound

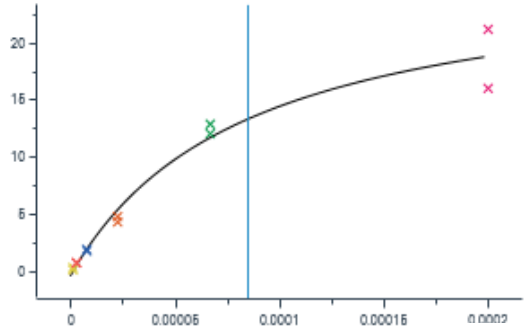
Red = 10 uM compound, 20 uM NSP13

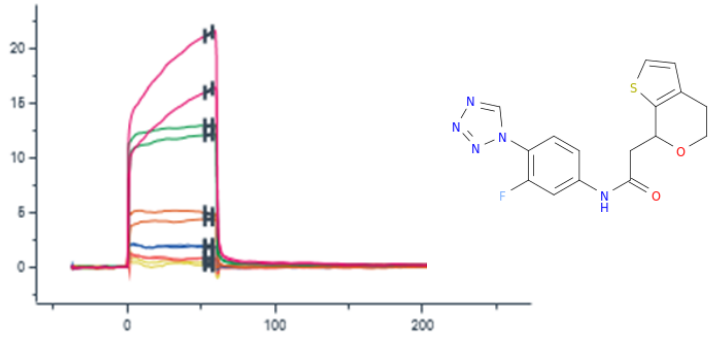
^{19}F NMR

Confirmed!



PARENT MOLECULE



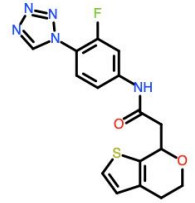


CACHE_1431_64

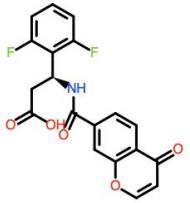
K_D = 85 µM – 111% binding

%inhibition@50 µM_ATPase = 9

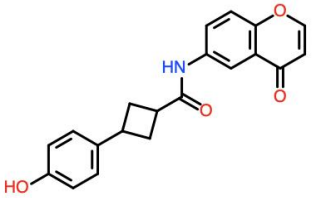
Tested analogs



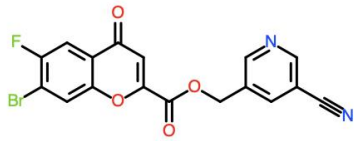
CACHE_ID CACHE2-HO_1431_1
Parent CACHE_1431_64
distance_to_pai 0



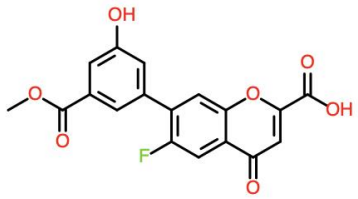
CACHE_ID CACHE2-HO_1431_2
Parent CACHE_1431_64
distance_to_pai 0.5989



CACHE_ID CACHE2-HO_1431_3
Parent CACHE_1431_64
distance_to_pai 0.5994

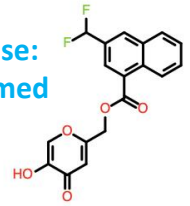


CACHE_ID CACHE2-HO_1431_4
Parent CACHE_1431_64
distance_to_pai 0.6849

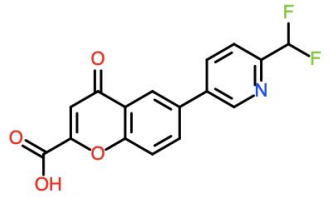


CACHE_ID CACHE2-HO_1431_5
Parent CACHE_1431_64
distance_to_pai 0.7005

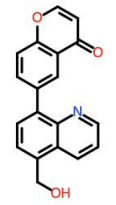
Dose response: Confirmed



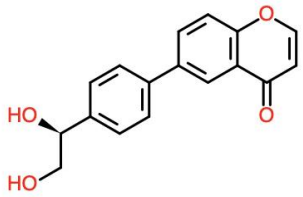
CACHE_ID CACHE2-HO_1431_6
Parent CACHE_1431_64
distance_to_pai 0.7059



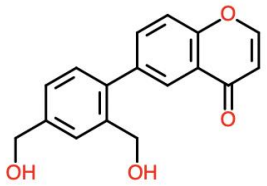
CACHE_ID CACHE2-HO_1431_7
Parent CACHE_1431_64
distance_to_pai 0.7203



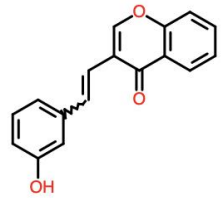
CACHE_ID CACHE2-HO_1431_8
Parent CACHE_1431_64
distance_to_pai 0.7225



CACHE_ID CACHE2-HO_1431_9
Parent CACHE_1431_64
distance_to_pai 0.727

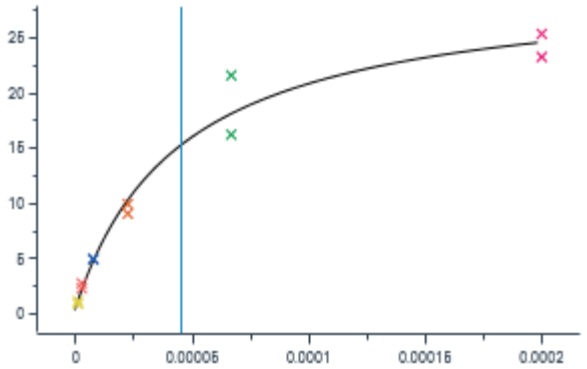


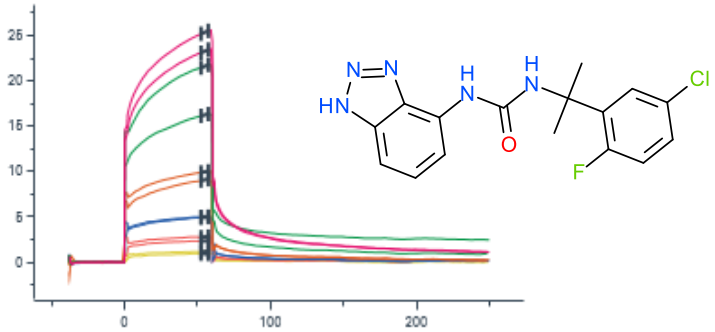
CACHE_ID CACHE2-HO_1431_10
Parent CACHE_1431_64
distance_to_pai 0.7478



CACHE_ID CACHE2-HO_1431_11
Parent CACHE_1431_64
distance_to_pai 0.7686

PARENT MOLECULE





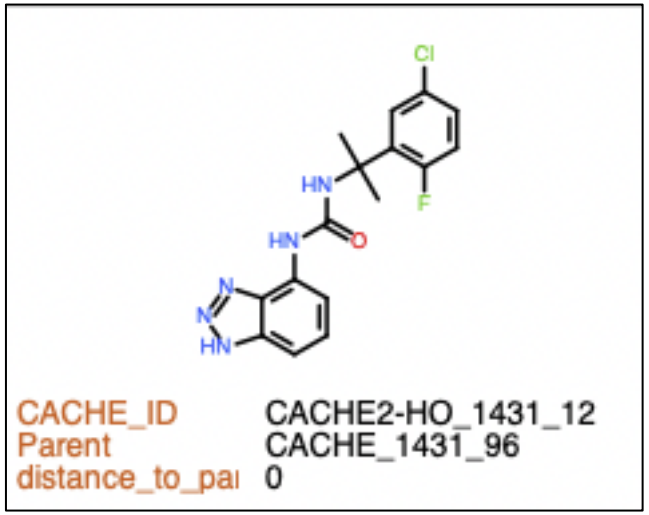
CACHE_1431_96

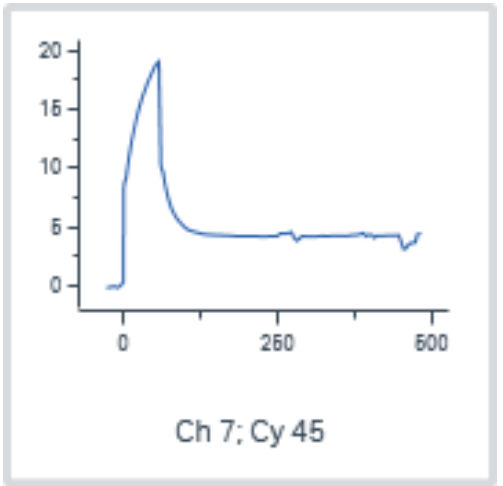
K_D = 46 µM (slow on/off)– 124% binding

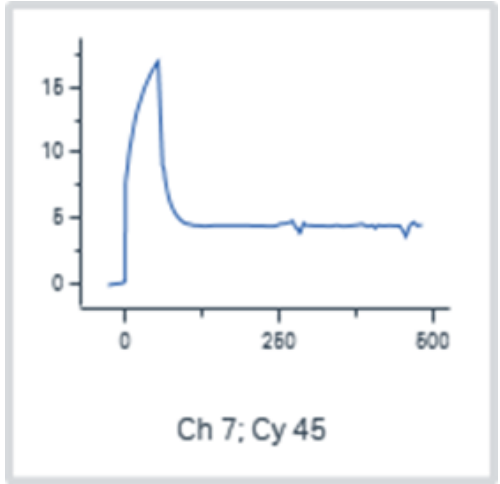
Selectivity (unrelated WDR5 protein) – mild binding to WDR5

%inhibition@50 µM_ATPase = 18

Resupply – showed baseline difference and was not included for a dose - response



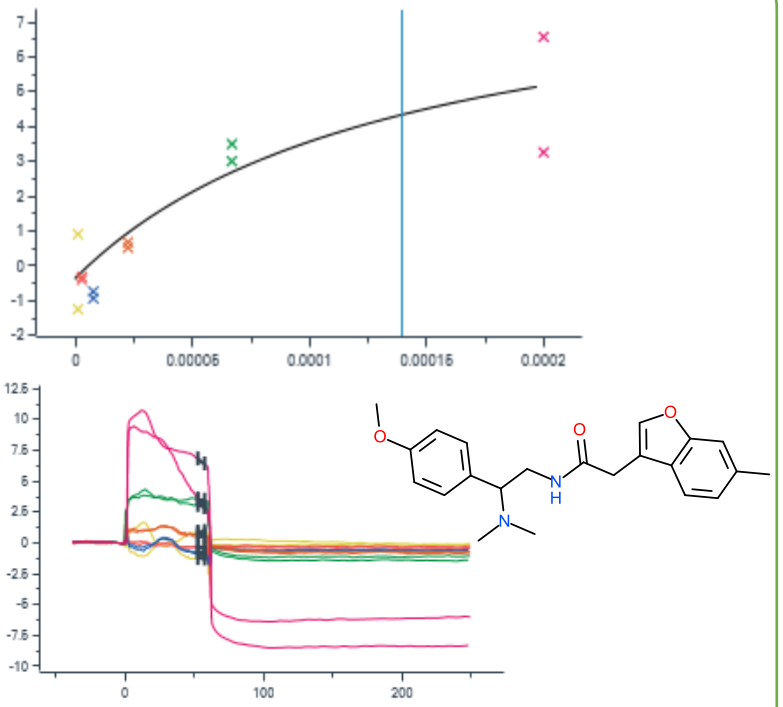




CACHE#2 – NSP13 SARS2

Participant 1434

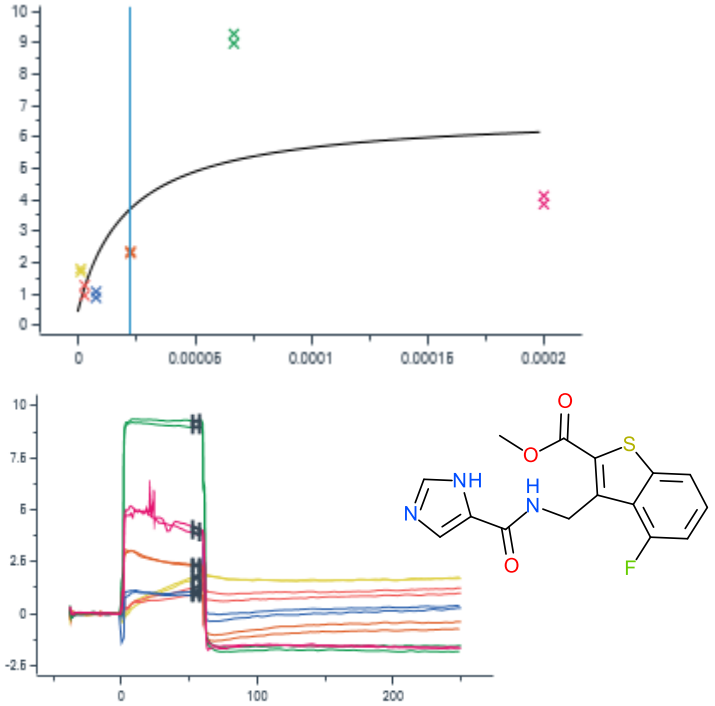
Round 1 HIT MOLECULE



CACHE_1434_50

K_D = 140 µM (poor fit) – 39% binding
%inhibition@50 µM_ATPase = no binding

Round 1 HIT MOLECULE



CACHE_1434_57

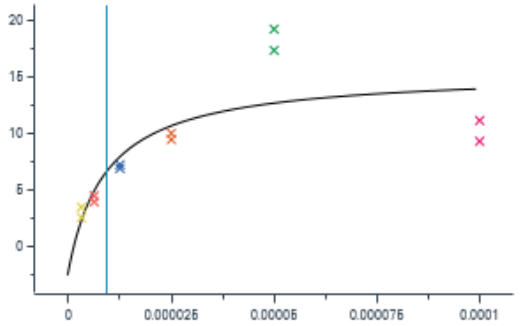
K_D = 22 µM (poor fit/low binding) – 24% binding
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 2

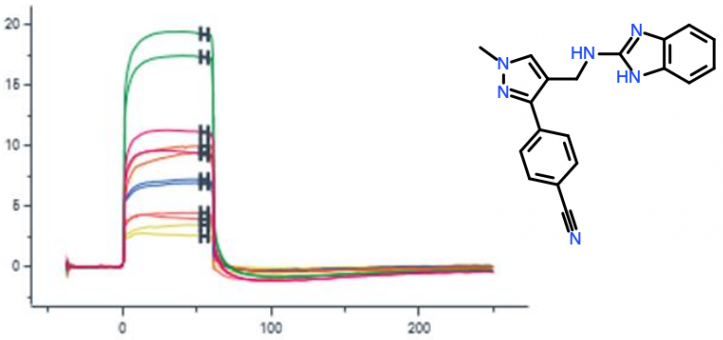
No analogs in Round 2

CACHE#2 – NSP13 SARS2

Participant 1438

PARENT MOLECULE

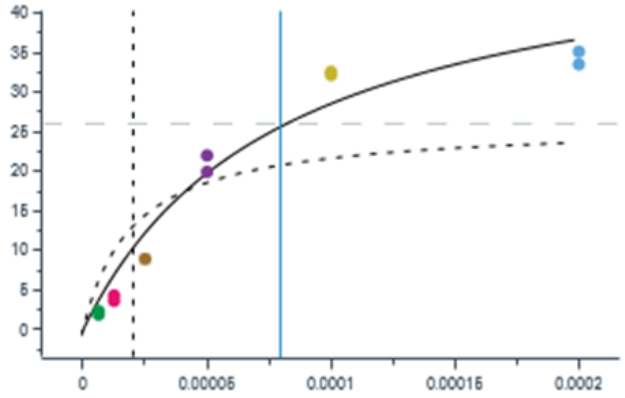


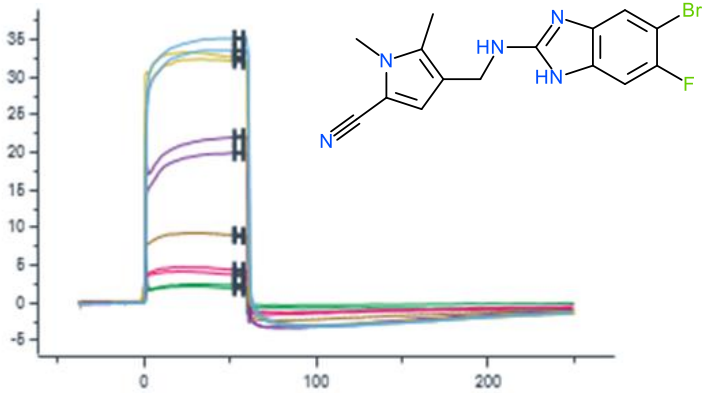


CACHE_1438_39

K_D = 10±0 µM (poor fit) – 85±12% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 8

45 analogs of CACHE_1438_39 were submitted for round 2. Three compounds (including re-supplied parent molecule) showed a binding response by SPR with a tendency to reach saturation. 1 compound confirmed binding affinity by ^{19}F NMR.





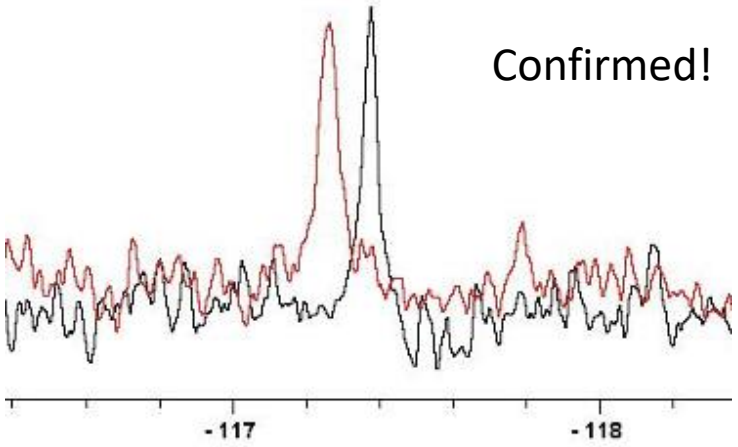
CACHE2-HO_1438_19

K_D _1 = 90 µM – 166% binding
K_D _2 = 80 µM – 198% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 11

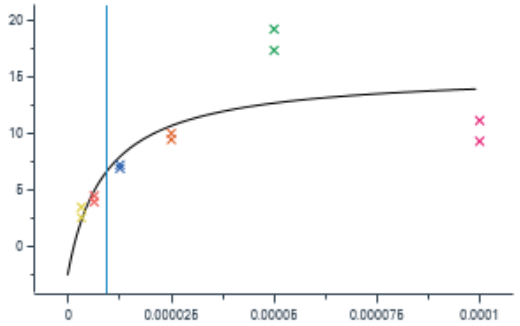
Black = 10 uM compound
Red = 10 uM compound, 20 uM NSP13

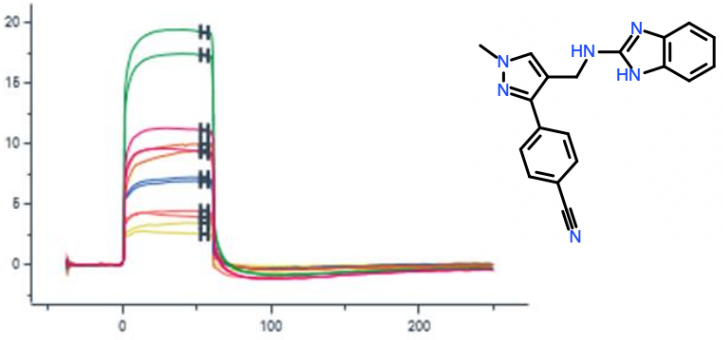
^{19}F NMR

Confirmed!



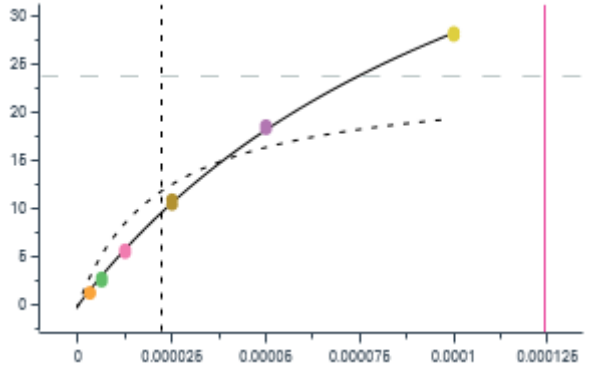
PARENT MOLECULE

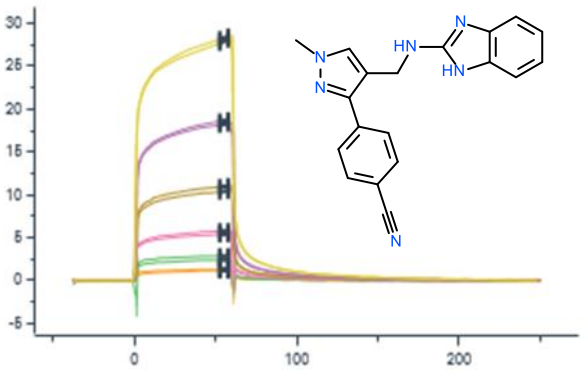




CACHE_1438_39

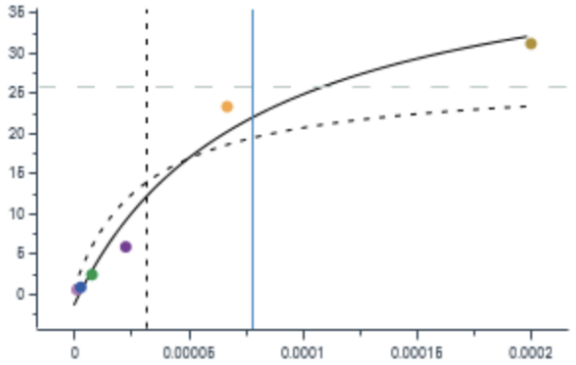
K_D = 10±0 µM (poor fit) – 85±12% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 8

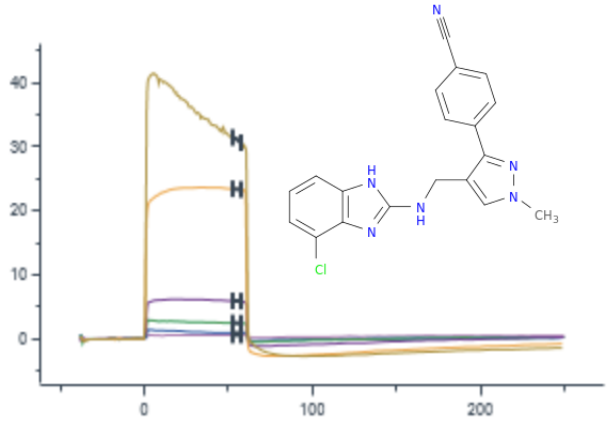




CACHE2-HO_1438_1

K_D (3% DMSO) = 124 µM (does not reach saturation) – 268% binding
Selectivity (unrelated WDR5 protein) – 31% binding (linear response)
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 11

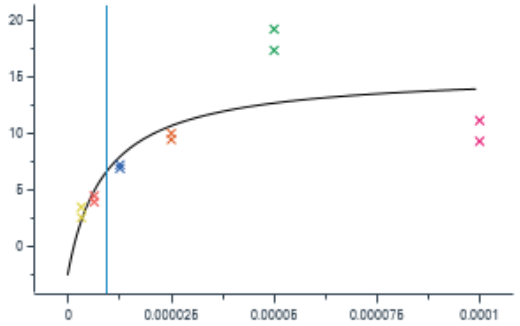


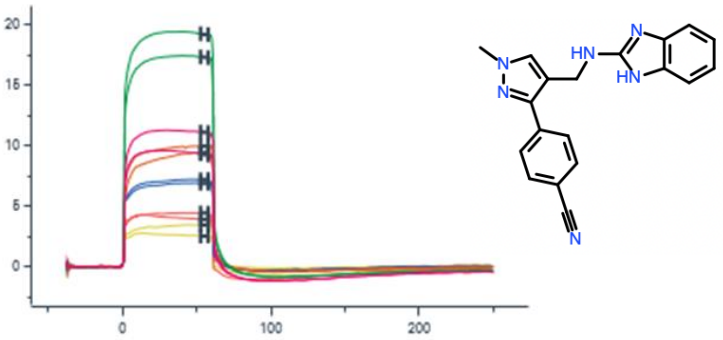


CACHE2-HO_1438_3

K_D = 78 µM – 178% binding
Suspicious sensorgram
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = -3

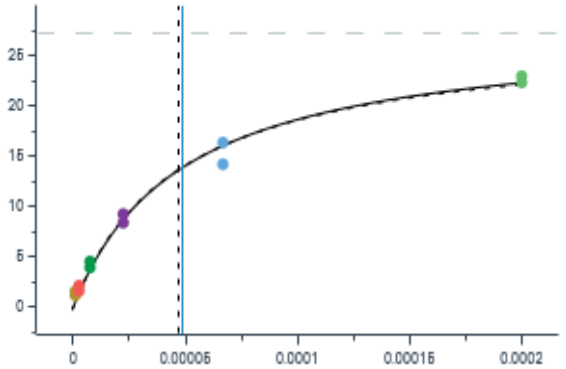
PARENT MOLECULE

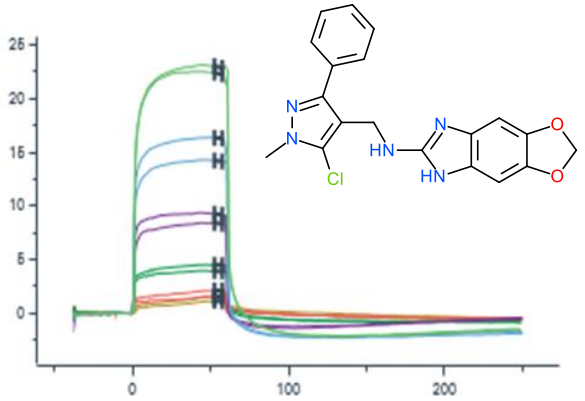




CACHE_1438_39

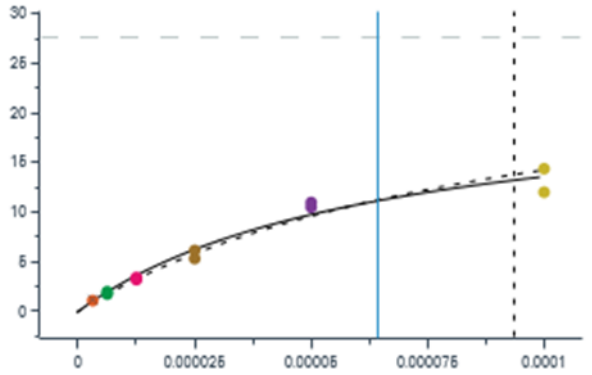
K_D = 10±0 µM (poor fit) – 85±12% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 8

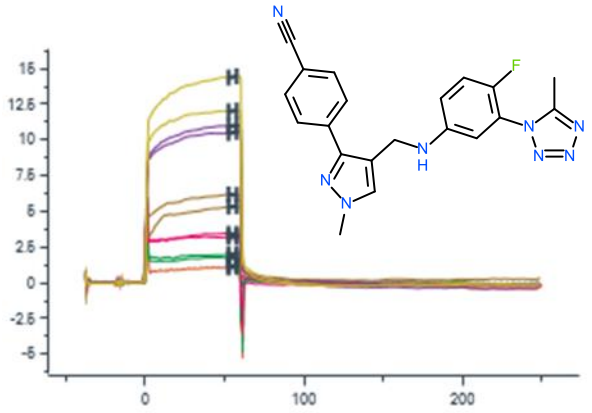




CACHE2-HO_1438_22

K_D = 49 µM – 102% binding
Selectivity (unrelated WDR5 protein) – weak binding (linear response)
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 10

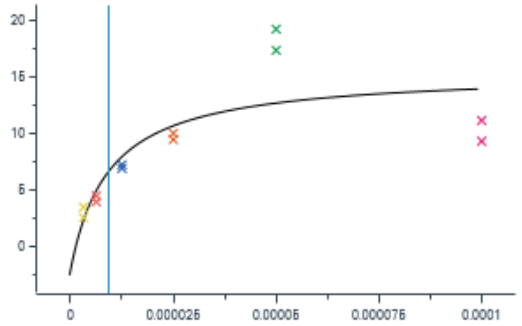


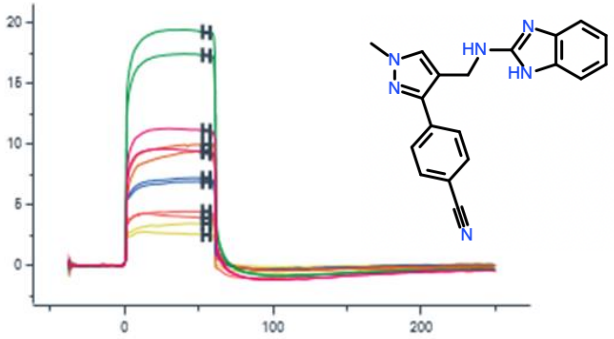


CACHE2-HO_1438_41

K_D = 64 µM – 81% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 8

PARENT MOLECULE

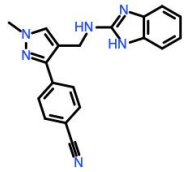
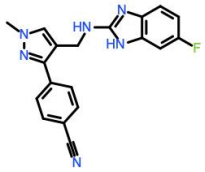
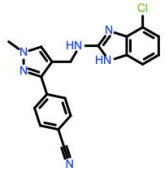
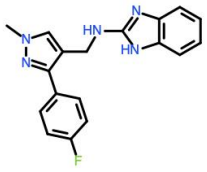
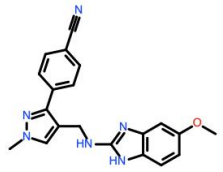
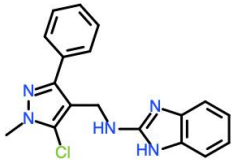
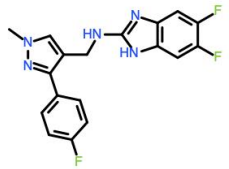
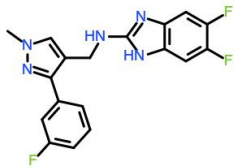
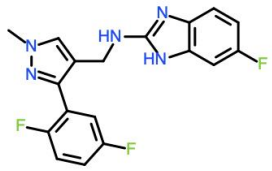
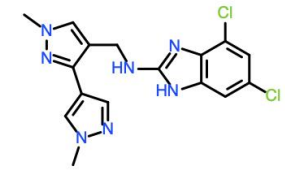
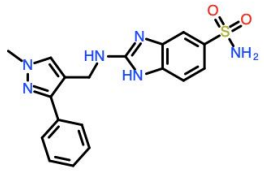
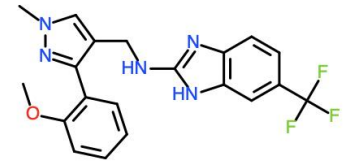
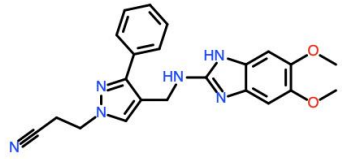
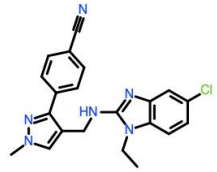
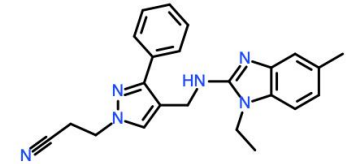
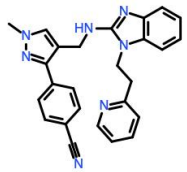
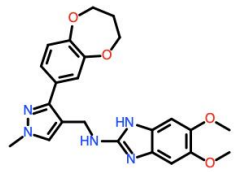
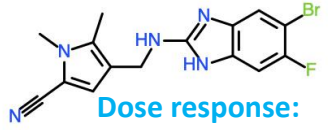
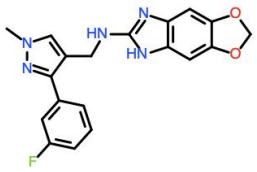




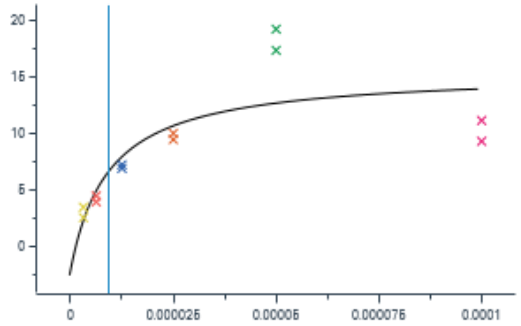
CACHE_1438_39

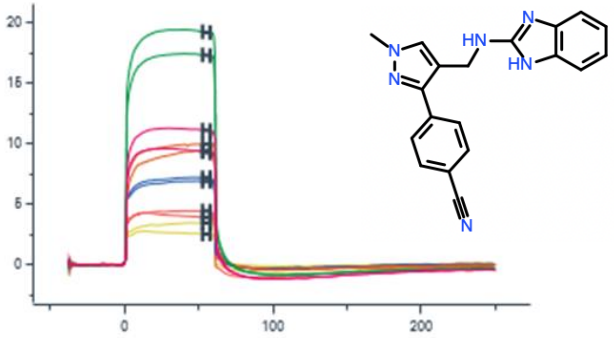
K_D = 10±0 µM (poor fit) – 85±12% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 8

Tested analogs

 CACHE_ID CACHE2-HO_1438_1 Parent CACHE_1438_39 distance_to_pa 0	 CACHE_ID CACHE2-HO_1438_2 Parent CACHE_1438_39 distance_to_pa 0.0793	 CACHE_ID CACHE2-HO_1438_3 Parent CACHE_1438_39 distance_to_pa 0.0793	 CACHE_ID CACHE2-HO_1438_4 Parent CACHE_1438_39 distance_to_pa 0.09589	 CACHE_ID CACHE2-HO_1438_5 Parent CACHE_1438_39 distance_to_pa 0.1292
 CACHE_ID CACHE2-HO_1438_6 Parent CACHE_1438_39 distance_to_pa 0.1429	 CACHE_ID CACHE2-HO_1438_7 Parent CACHE_1438_39 distance_to_pa 0.1502	 CACHE_ID CACHE2-HO_1438_8 Parent CACHE_1438_39 distance_to_pa 0.1646	 CACHE_ID CACHE2-HO_1438_9 Parent CACHE_1438_39 distance_to_pa 0.1674	 CACHE_ID CACHE2-HO_1438_10 Parent CACHE_1438_39 distance_to_pa 0.214
 CACHE_ID CACHE2-HO_1438_11 Parent CACHE_1438_39 distance_to_pa 0.2205	 CACHE_ID CACHE2-HO_1438_12 Parent CACHE_1438_39 distance_to_pa 0.2205	 CACHE_ID CACHE2-HO_1438_13 Parent CACHE_1438_39 distance_to_pa 0.2302	 CACHE_ID CACHE2-HO_1438_14 Parent CACHE_1438_39 distance_to_pa 0.251	 CACHE_ID CACHE2-HO_1438_15 Parent CACHE_1438_39 distance_to_pa 0.2734
 CACHE_ID CACHE2-HO_1438_16 Parent CACHE_1438_39 distance_to_pa 0.2915	 CACHE_ID CACHE2-HO_1438_17 Parent CACHE_1438_39 distance_to_pa 0.3101	 CACHE_ID CACHE2-HO_1438_18 Parent CACHE_1438_39 distance_to_pa 0.3288	 **Dose response: Confirmed** CACHE_ID CACHE2-HO_1438_19 Parent CACHE_1438_39 distance_to_pa 0.3385	 CACHE_ID CACHE2-HO_1438_20 Parent CACHE_1438_39 distance_to_pa 0.3404

PARENT MOLECULE

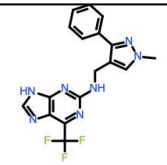
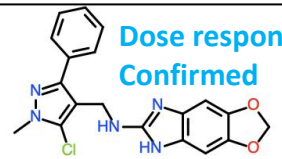
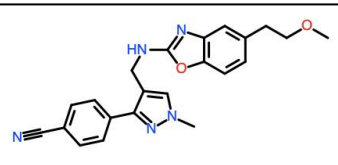
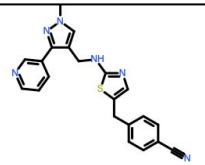
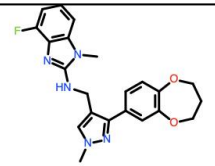
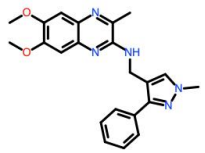
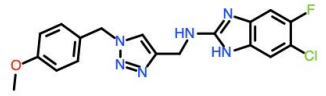
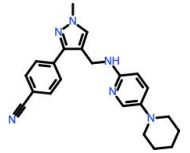
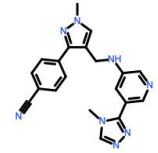
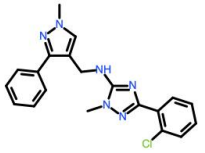
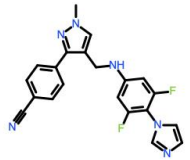
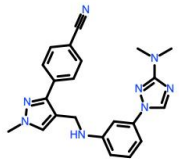
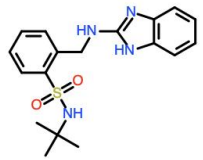
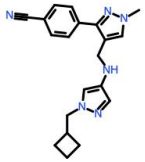
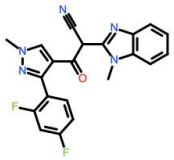
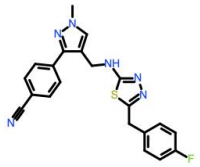
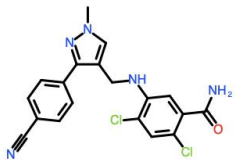
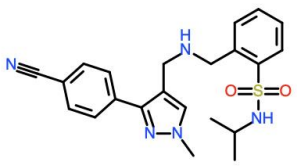
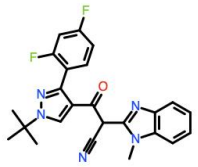
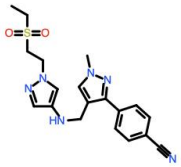
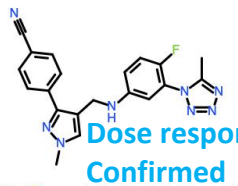
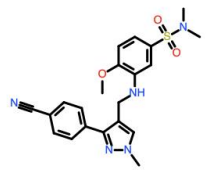
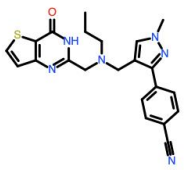
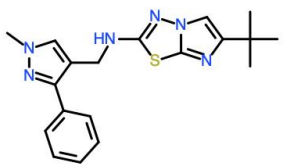
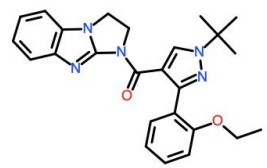




CACHE_1438_39

K_D = 10±0 µM (poor fit) – 85±12% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 8

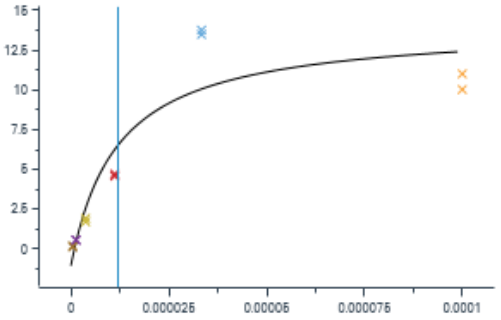
Tested analogs

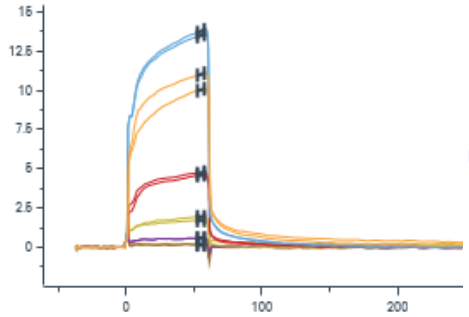
 CACHE_ID CACHE2-HO_1438_21 Parent CACHE_1438_39 distance_to_pa 0.3444	 Dose response: Confirmed CACHE_ID CACHE2-HO_1438_22 Parent CACHE_1438_39 distance_to_pa 0.3552	 CACHE_ID CACHE2-HO_1438_23 Parent CACHE_1438_39 distance_to_pa 0.3946	 CACHE_ID CACHE2-HO_1438_24 Parent CACHE_1438_39 distance_to_pa 0.3993	 CACHE_ID CACHE2-HO_1438_25 Parent CACHE_1438_39 distance_to_pa 0.4007
 CACHE_ID CACHE2-HO_1438_26 Parent CACHE_1438_39 distance_to_pa 0.4007	 CACHE_ID CACHE2-HO_1438_27 Parent CACHE_1438_39 distance_to_pa 0.4034	 CACHE_ID CACHE2-HO_1438_28 Parent CACHE_1438_39 distance_to_pa 0.4053	 CACHE_ID CACHE2-HO_1438_29 Parent CACHE_1438_39 distance_to_pa 0.4167	 CACHE_ID CACHE2-HO_1438_30 Parent CACHE_1438_39 distance_to_pa 0.4363
 CACHE_ID CACHE2-HO_1438_31 Parent CACHE_1438_39 distance_to_pa 0.4424	 CACHE_ID CACHE2-HO_1438_32 Parent CACHE_1438_39 distance_to_pa 0.4465	 CACHE_ID CACHE2-HO_1438_33 Parent CACHE_1438_39 distance_to_pa 0.4515	 CACHE_ID CACHE2-HO_1438_34 Parent CACHE_1438_39 distance_to_pa 0.4577	 CACHE_ID CACHE2-HO_1438_35 Parent CACHE_1438_39 distance_to_pa 0.4585
 CACHE_ID CACHE2-HO_1438_36 Parent CACHE_1438_39 distance_to_pa 0.4629	 CACHE_ID CACHE2-HO_1438_37 Parent CACHE_1438_39 distance_to_pa 0.4697	 CACHE_ID CACHE2-HO_1438_38 Parent CACHE_1438_39 distance_to_pa 0.4799	 CACHE_ID CACHE2-HO_1438_39 Parent CACHE_1438_39 distance_to_pa 0.481	 CACHE_ID CACHE2-HO_1438_40 Parent CACHE_1438_39 distance_to_pa 0.4946
 Dose response: Confirmed CACHE_ID CACHE2-HO_1438_41 Parent CACHE_1438_39 distance_to_pa 0.5017	 CACHE_ID CACHE2-HO_1438_42 Parent CACHE_1438_39 distance_to_pa 0.5035	 CACHE_ID CACHE2-HO_1438_43 Parent CACHE_1438_39 distance_to_pa 0.5265	 CACHE_ID CACHE2-HO_1438_44 Parent CACHE_1438_39 distance_to_pa 0.5373	 CACHE_ID CACHE2-HO_1438_45 Parent CACHE_1438_39 distance_to_pa 0.6266

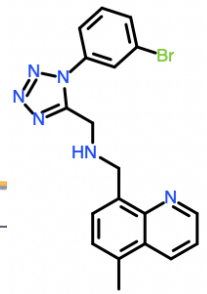
CACHE#2 – NSP13 SARS2

Participant 1439

PARENT MOLECULE







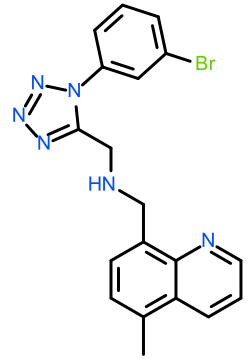
CACHE_1439_43

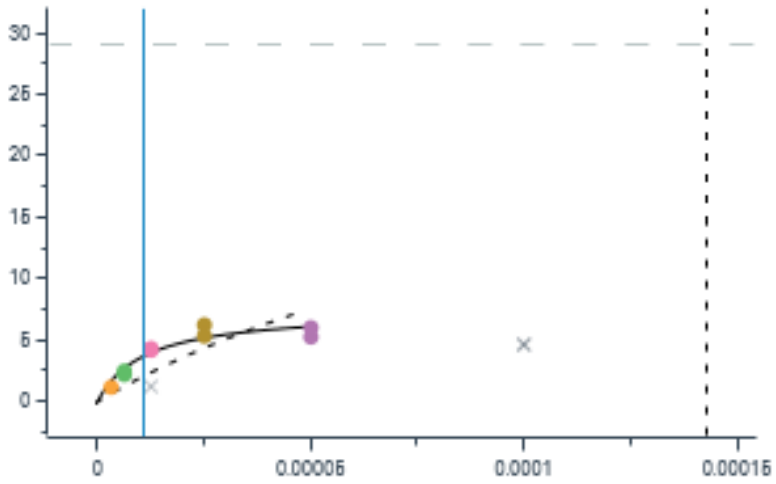
K_D = 12 µM (poor fit) – 49% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 11

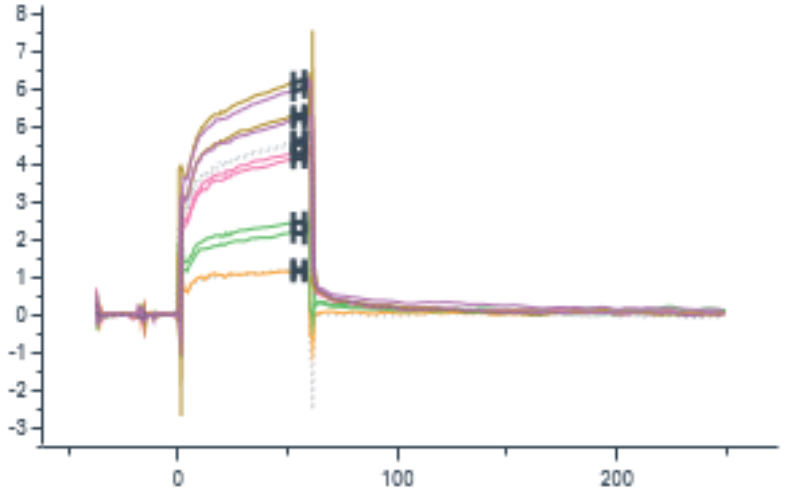
25 analogues of CACHE_1439_43, including re-supplied parent molecule, were submitted for round 2.
Re-supplied hit showed a very weak dose dependent binding response.

CACHE2-HO_1439_21

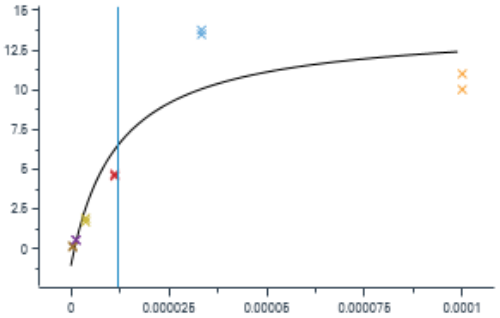
K_D (3% DMSO) = 11 µM (low binding) – 25% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 32

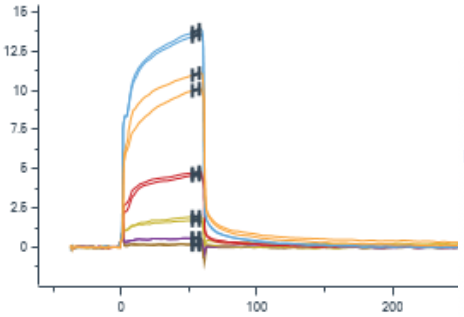


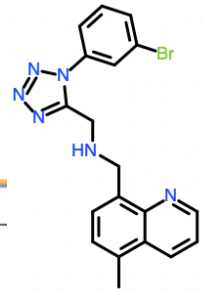




PARENT MOLECULE





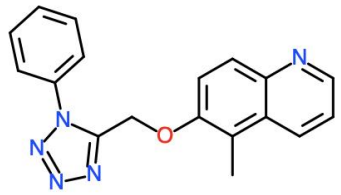


CACHE_1439_43

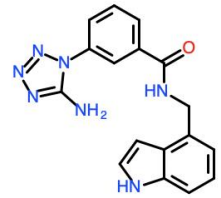
K_D = 12 µM (poor fit) – 49% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 11

Tested follow-ups

CACHE_ID CACHE2-HO_1439_21
Parent CACHE_1439_43
distance_to_pai 0



CACHE_ID CACHE2-HO_1439_22
Parent CACHE_1439_43
distance_to_pai 0.3659



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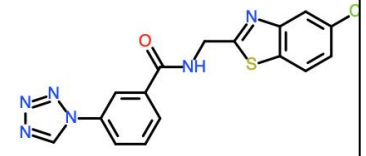
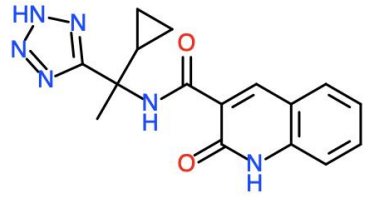
Parent CACHE_1439_43
distance_to_pai 0.4036



CACHE_ID CACHE2-HO_1439_24
Parent CACHE_1439_43
distance_to_pai 0.4985



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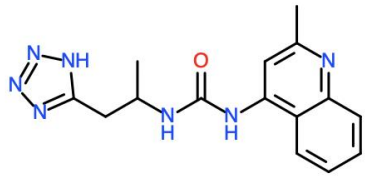
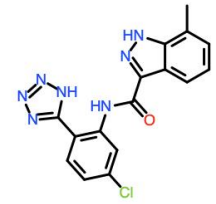
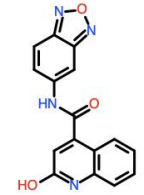
Parent CACHE_1439_43
distance_to_pai 0.5176



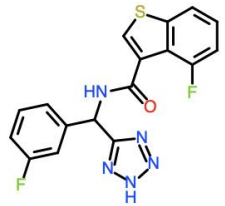
CACHE_ID CACHE2-HO_1439_26
Parent CACHE_1439_43
distance_to_pai 0.5294



CACHE_ID CACHE2-HO_1439_27
Parent CACHE_1439_43
distance_to_pai 0.5549



CACHE_ID CACHE2-HO_1439_28
Parent CACHE_1439_43
distance_to_pai 0.5757



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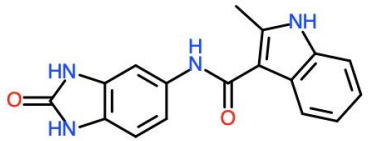
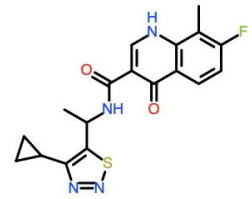
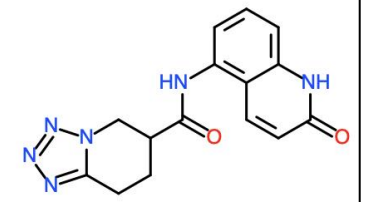
Parent CACHE_1439_43
distance_to_pai 0.5831



CACHE_ID CACHE2-HO_1439_30
Parent CACHE_1439_43
distance_to_pai 0.5911

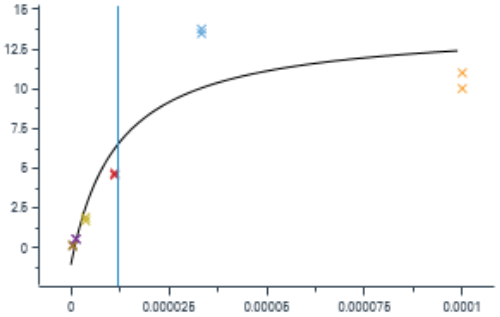


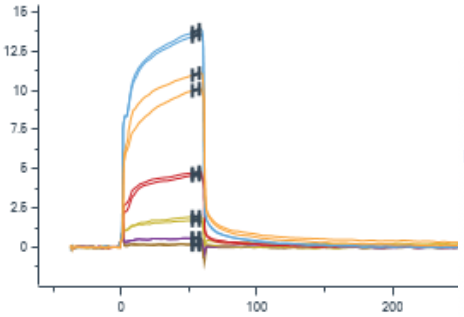
CACHE_ID CACHE2-HO_1439_31
Parent CACHE_1439_43
distance_to_pai 0.5967

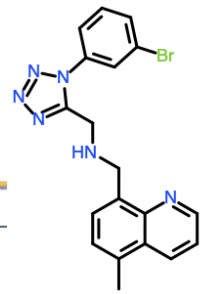


CACHE_ID CACHE2-HO_1439_32
Parent CACHE_1439_43
distance_to_pai 0.6216

PARENT MOLECULE



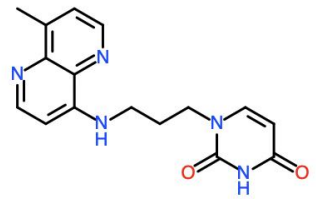




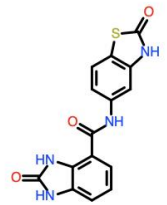
CACHE_1439_43

K_D = 12 µM (poor fit) – 49% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 11

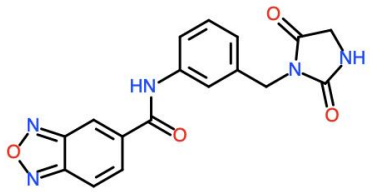
Tested follow-ups



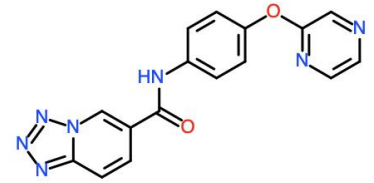
CACHE_ID CACHE2-HO_1439_33
Parent CACHE_1439_43
distance_to_pai 0.6391



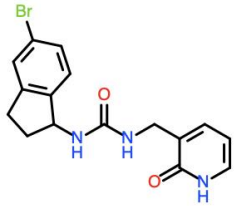
CACHE_ID CACHE2-HO_1439_34
Parent CACHE_1439_43
distance_to_pai 0.6448



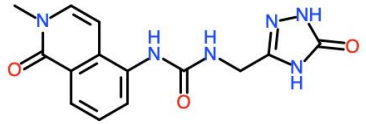
CACHE_ID CACHE2-HO_1439_35
Parent CACHE_1439_43
distance_to_pai 0.6545



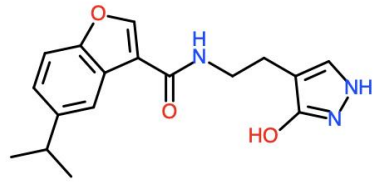
CACHE_ID CACHE2-HO_1439_36
Parent CACHE_1439_43
distance_to_pai 0.6553



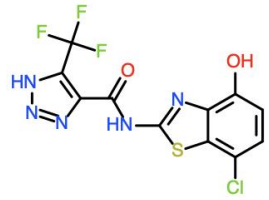
CACHE_ID CACHE2-HO_1439_37
Parent CACHE_1439_43
distance_to_pai 0.6615



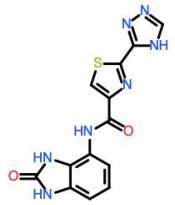
CACHE_ID CACHE2-HO_1439_38
Parent CACHE_1439_43
distance_to_pai 0.6667



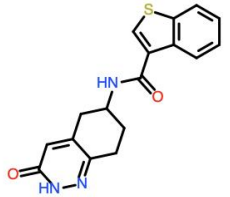
CACHE_ID CACHE2-HO_1439_39
Parent CACHE_1439_43
distance_to_pai 0.6831



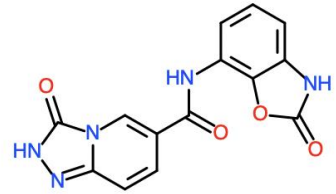
CACHE_ID CACHE2-HO_1439_40
Parent CACHE_1439_43
distance_to_pai 0.6898



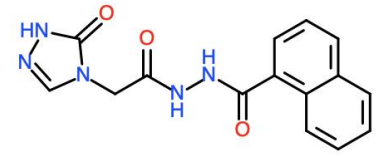
CACHE_ID CACHE2-HO_1439_41
Parent CACHE_1439_43
distance_to_pai 0.6951



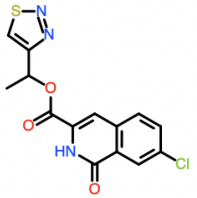
CACHE_ID CACHE2-HO_1439_42
Parent CACHE_1439_43
distance_to_pai 0.6968



CACHE_ID CACHE2-HO_1439_43
Parent CACHE_1439_43
distance_to_pai 0.6988

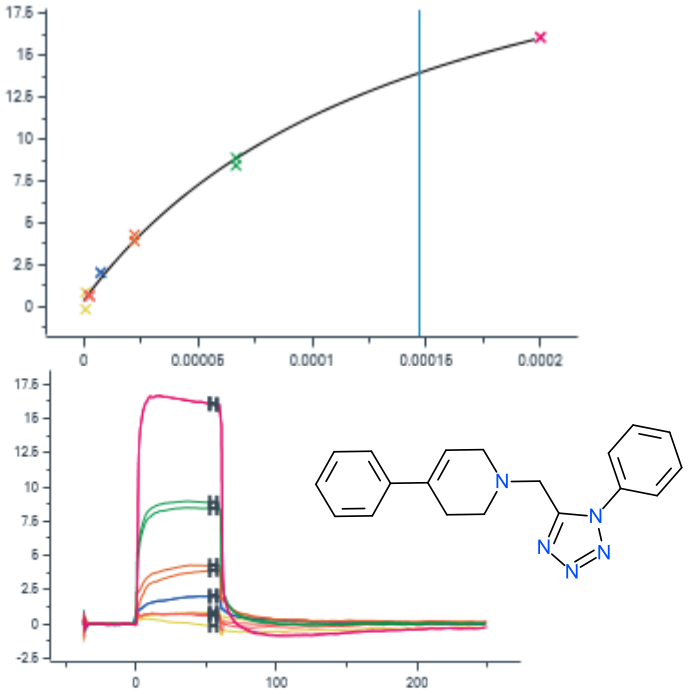


CACHE_ID CACHE2-HO_1439_44
Parent CACHE_1439_43
distance_to_pai 0.7068



CACHE_ID CACHE2-HO_1439_45
Parent CACHE_1439_43
distance_to_pai 0.7084

PARENT MOLECULE

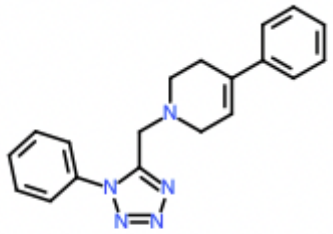


CACHE_1439_26

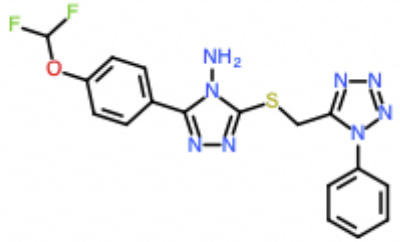
K_D = 147 µM – 127% binding

%inhibition@50 µM_ATPase = no binding

Tested follow-ups

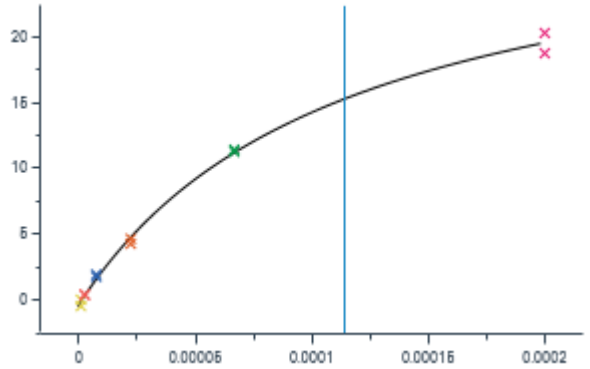


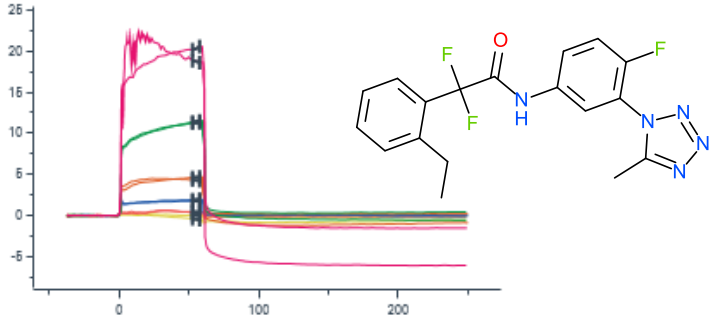
CACHE_ID	CACHE2-HO_1439_1
Parent	CACHE_1439_26
distance_to_pai	0



CACHE_ID	CACHE2-HO_1439_2
Parent	CACHE_1439_26
distance_to_pai	0.543

PARENT MOLECULE





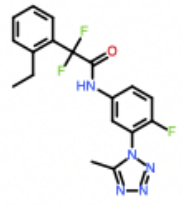
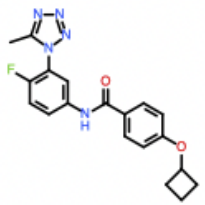
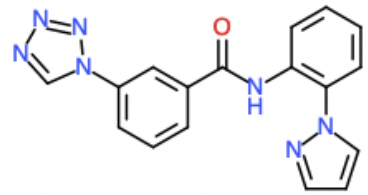
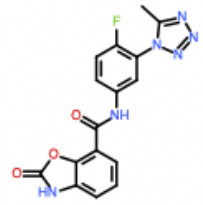
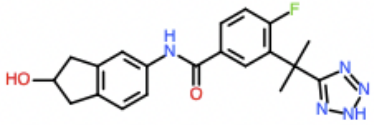
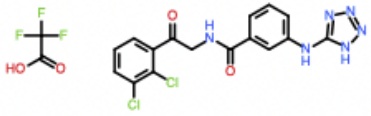
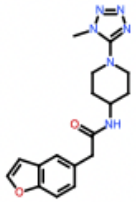
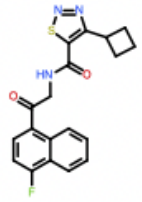
CACHE_1439_38

K_D = 114 µM – 124% binding

DLS (solub@200 µM)

%inhibition@50 µM_ATPase = 11

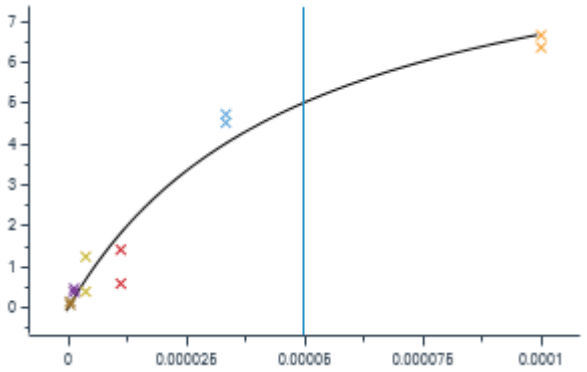
Tested follow-ups

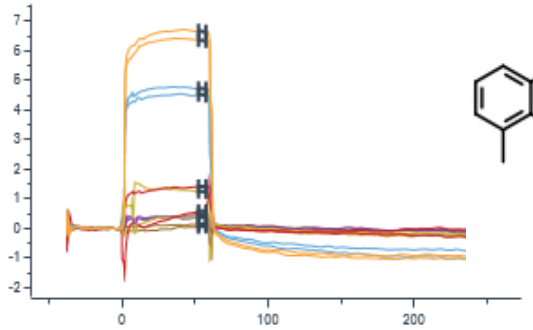
 CACHE_ID CACHE2-HO_1439_4 Parent CACHE_1439_38 distance_to_pai 0	 CACHE_ID CACHE2-HO_1439_5 Parent CACHE_1439_38 distance_to_pai 0.2897	 CACHE_ID CACHE2-HO_1439_6 Parent CACHE_1439_38 distance_to_pai 0.4731	 CACHE_ID CACHE2-HO_1439_7 Parent CACHE_1439_38 distance_to_pai 0.4772
 CACHE_ID CACHE2-HO_1439_8 Parent CACHE_1439_38 distance_to_pai 0.5035	 CACHE_ID CACHE2-HO_1439_9 Parent CACHE_1439_38 distance_to_pai 0.5188	 CACHE_ID CACHE2-HO_1439_10 Parent CACHE_1439_38 distance_to_pai 0.5382	 CACHE_ID CACHE2-HO_1439_11 Parent CACHE_1439_38 distance_to_pai 0.5969

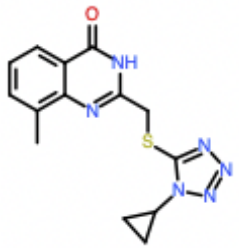
CACHE#2 – NSP13 SARS2

Participant 1442

PARENT MOLECULE







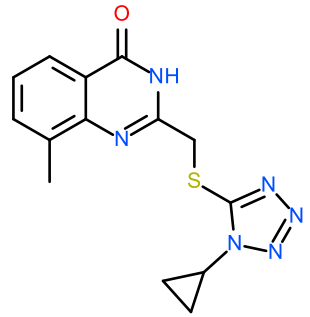
CACHE_1442_89

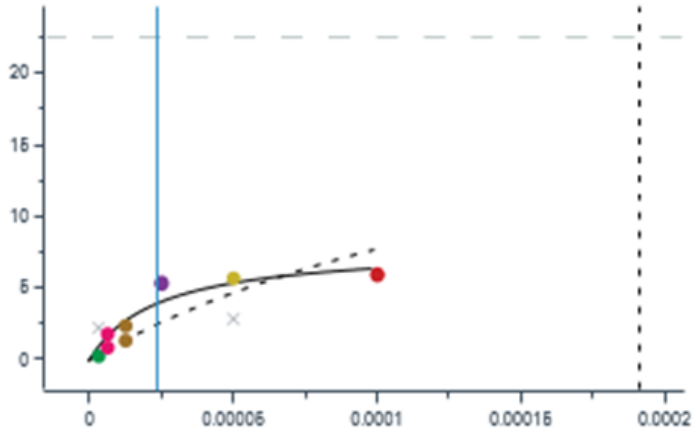
K_D = 50 µM – 41% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
IC_{50}_ATPase > 100 µM

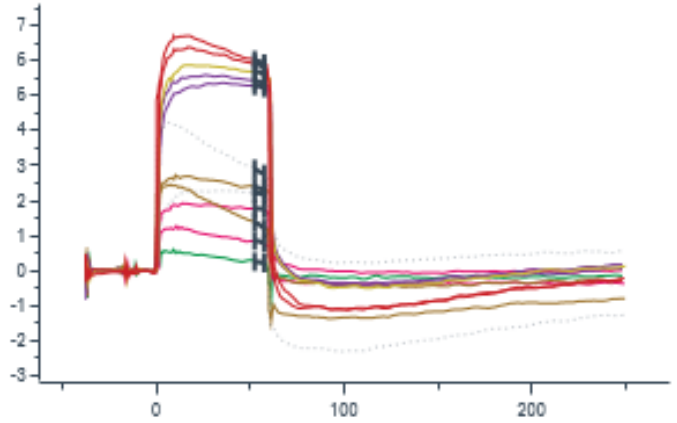
36 analogues of CACHE_1442_89, including re-supplied parent molecule, were submitted for round 2.
Re-supplied hit showed a weak dose dependent binding response.

CACHE2-HO_1442_1

K_D = 24 µM (poor fit) – 35% binding
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 18

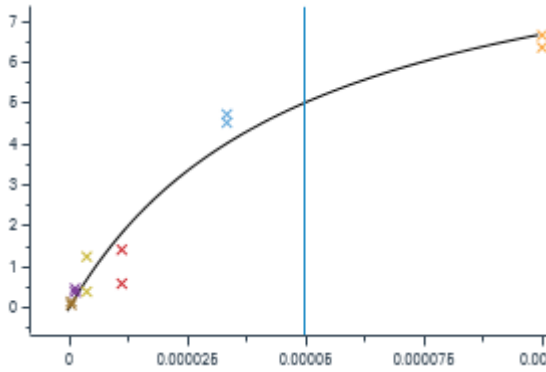


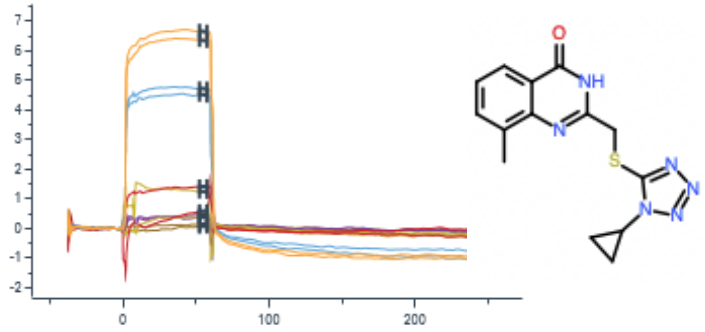




Tested follow-ups

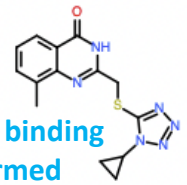
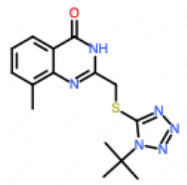
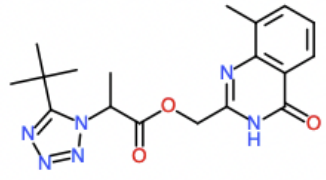
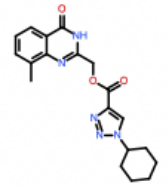
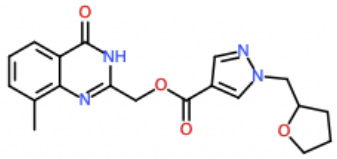
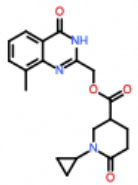
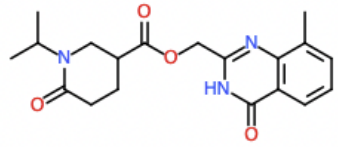
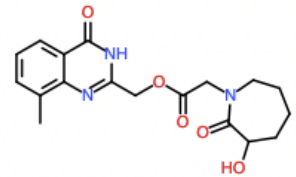
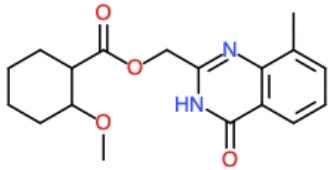
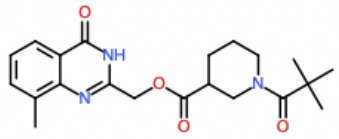
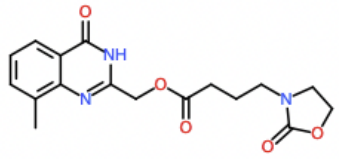
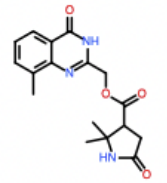
Round 1 HIT MOLECULE





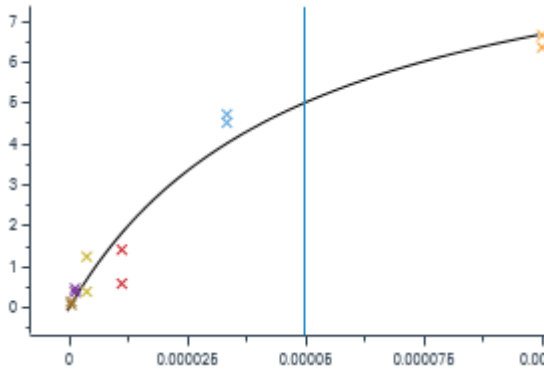
CACHE_1442_89

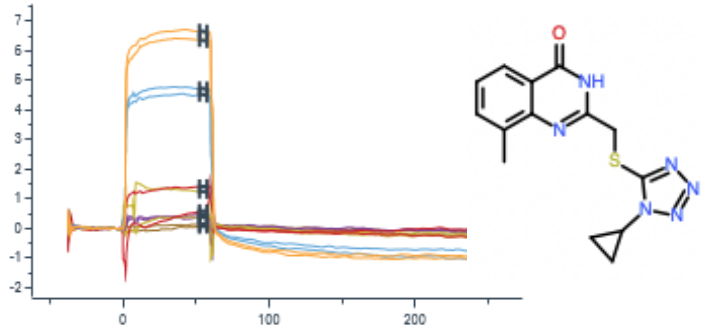
K_D = 50 µM – 41% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
IC_{50}_ATPase > 100 µM

 Weak binding Confirmed CACHE_ID CACHE2-HO_1442_1 Parent CACHE_1442_89 distance_to_pai 0	 CACHE_ID CACHE2-HO_1442_2 Parent CACHE_1442_89 distance_to_pai 0.09643	 CACHE_ID CACHE2-HO_1442_3 Parent CACHE_1442_89 distance_to_pai 0.3245	 CACHE_ID CACHE2-HO_1442_4 Parent CACHE_1442_89 distance_to_pai 0.3536
 CACHE_ID CACHE2-HO_1442_5 Parent CACHE_1442_89 distance_to_pai 0.4033	 CACHE_ID CACHE2-HO_1442_6 Parent CACHE_1442_89 distance_to_pai 0.4088	 CACHE_ID CACHE2-HO_1442_7 Parent CACHE_1442_89 distance_to_pai 0.413	 CACHE_ID CACHE2-HO_1442_8 Parent CACHE_1442_89 distance_to_pai 0.4152
 CACHE_ID CACHE2-HO_1442_9 Parent CACHE_1442_89 distance_to_pai 0.4167	 CACHE_ID CACHE2-HO_1442_10 Parent CACHE_1442_89 distance_to_pai 0.4189	 CACHE_ID CACHE2-HO_1442_11 Parent CACHE_1442_89 distance_to_pai 0.4207	 CACHE_ID CACHE2-HO_1442_12 Parent CACHE_1442_89 distance_to_pai 0.4223

Tested follow-ups

Round 1 HIT MOLECULE





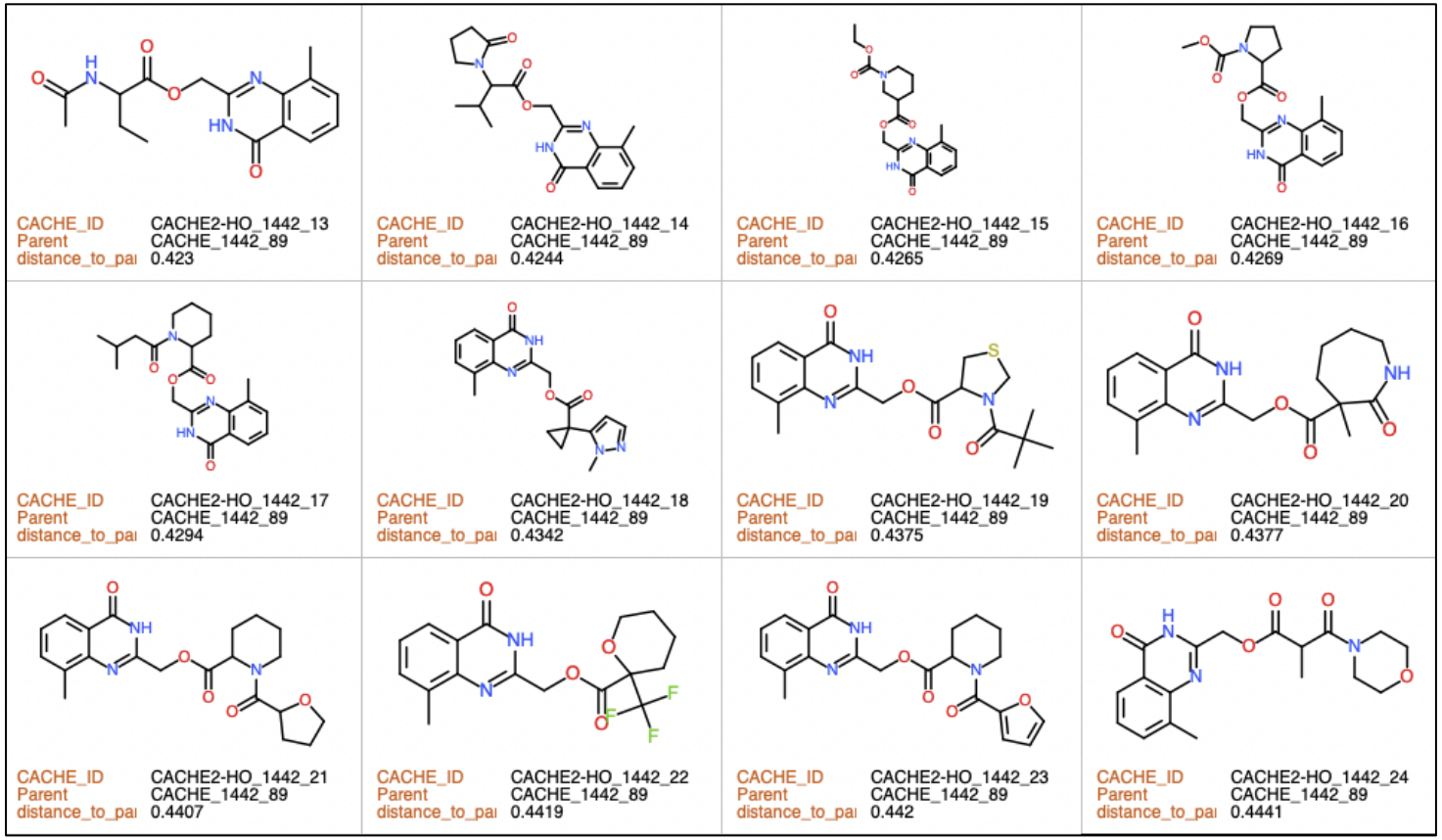
CACHE_1442_89

K_D = 50 µM – 41% binding

Selectivity (unrelated WDR5 protein) – Yes

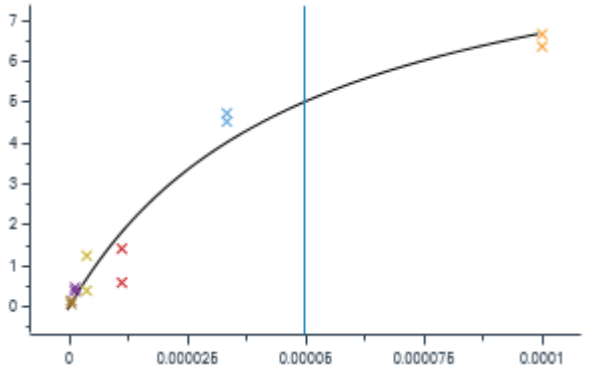
DLS (solub@100 µM)

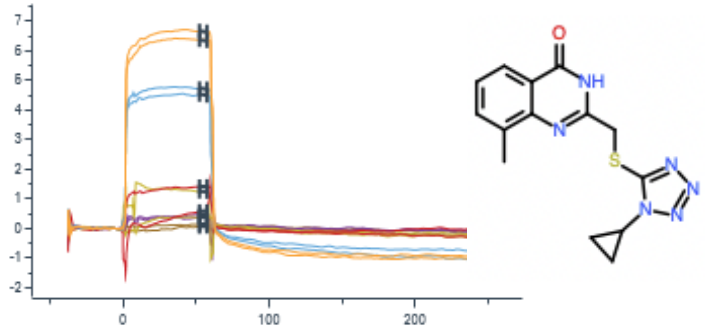
IC_{50}_ATPase > 100 µM



Tested follow-ups

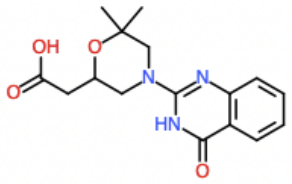
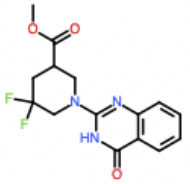
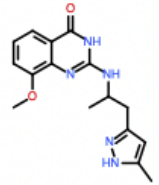
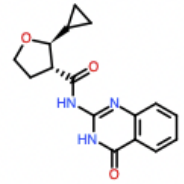
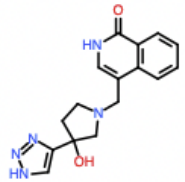
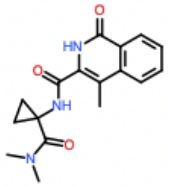
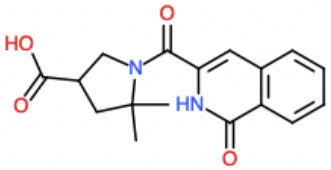
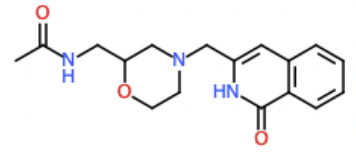
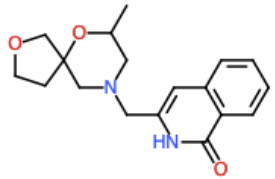
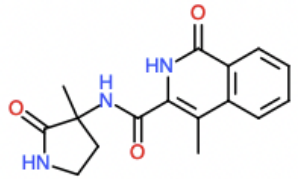
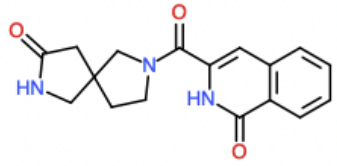
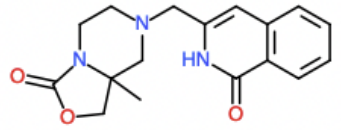
Round 1 HIT MOLECULE





CACHE_1442_89

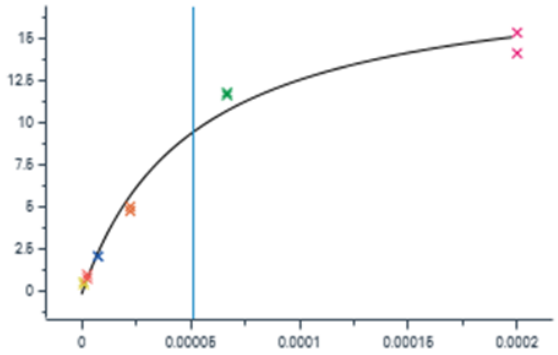
K_D = 50 µM – 41% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
IC_{50}_ATPase > 100 µM

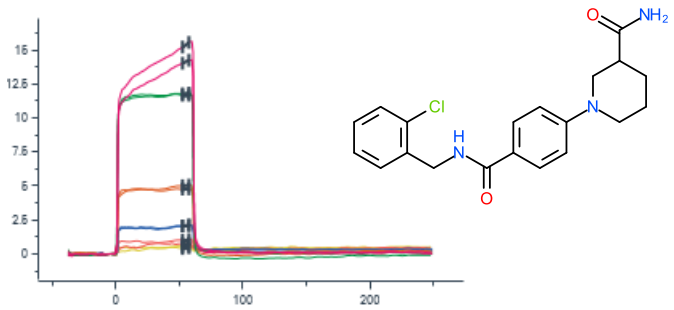
 CACHE_ID CACHE2-HO_1442_29 Parent CACHE_1442_89 distance_to_pai 0.5499	 CACHE_ID CACHE2-HO_1442_30 Parent CACHE_1442_89 distance_to_pai 0.5546	 CACHE_ID CACHE2-HO_1442_31 Parent CACHE_1442_89 distance_to_pai 0.5571	 CACHE_ID CACHE2-HO_1442_32 Parent CACHE_1442_89 distance_to_pai 0.5632
 CACHE_ID CACHE2-HO_1442_33 Parent CACHE_1442_89 distance_to_pai 0.5698	 CACHE_ID CACHE2-HO_1442_34 Parent CACHE_1442_89 distance_to_pai 0.6236	 CACHE_ID CACHE2-HO_1442_35 Parent CACHE_1442_89 distance_to_pai 0.6278	 CACHE_ID CACHE2-HO_1442_36 Parent CACHE_1442_89 distance_to_pai 0.6335
 CACHE_ID CACHE2-HO_1442_37 Parent CACHE_1442_89 distance_to_pai 0.6369	 CACHE_ID CACHE2-HO_1442_38 Parent CACHE_1442_89 distance_to_pai 0.6403	 CACHE_ID CACHE2-HO_1442_39 Parent CACHE_1442_89 distance_to_pai 0.6475	 CACHE_ID CACHE2-HO_1442_40 Parent CACHE_1442_89 distance_to_pai 0.6692

CACHE#2 – NSP13 SARS2

Participant 1448

PARENT MOLECULE

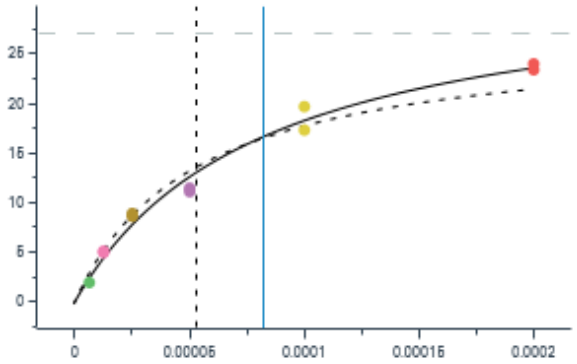


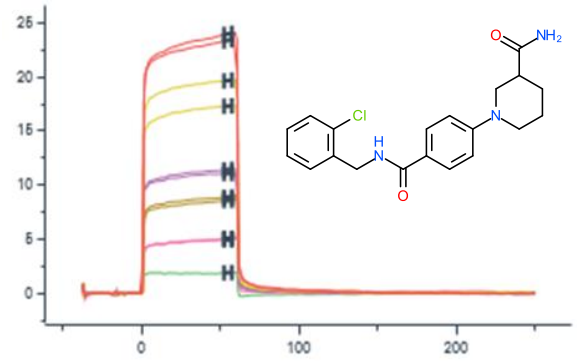


CACHE_1448_70

KD = 51 µM – 76% binding
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 1

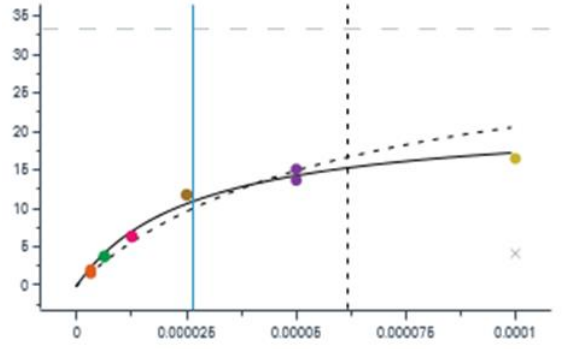
44 analogs of CACHE_1448_70 were submitted for round 2.
3 compounds (including re-supplied parent molecule) showed a dose dependent binding response by SPR.

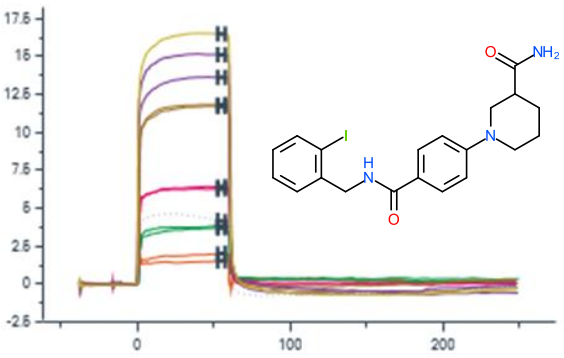




CACHE2-HO_1448_1

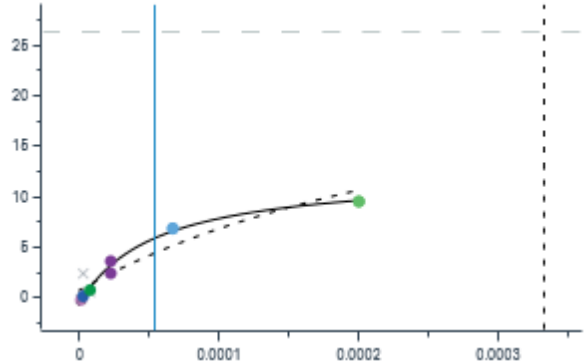
K_D (3% DMSO) = 82 µM – 123% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 9

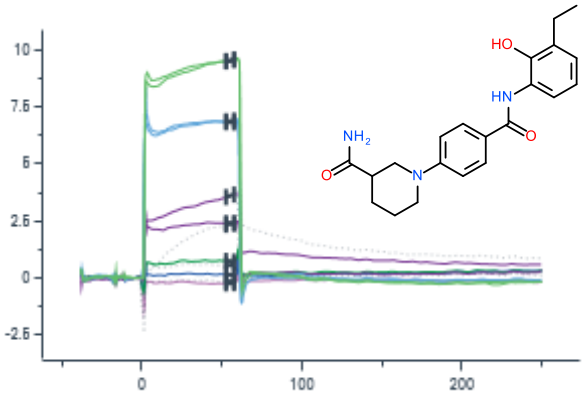




CACHE2-HO_1448_8

K_D = 26 µM – 66% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 6

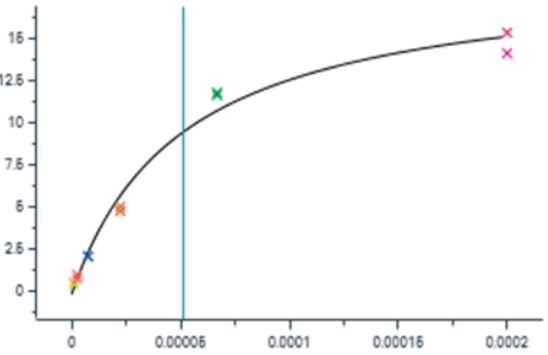


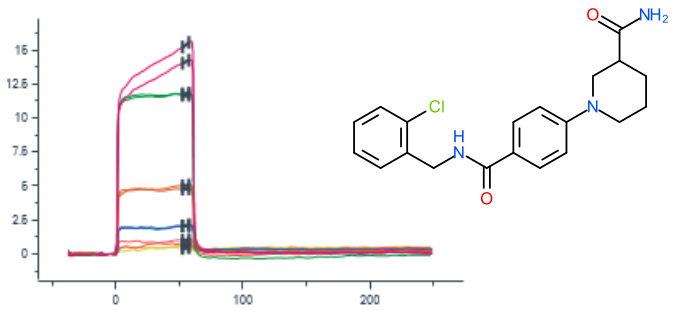


CACHE2-HO_1448_29

K_D = 54 µM – 49% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 6

PARENT MOLECULE





CACHE_1448_70

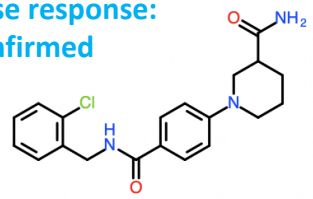
KD = 51 µM – 76% binding

Selectivity (unrelated WDR5 protein) – Yes

%inhibition@50 µM_ATPase = 1

Tested analogs

Dose response: Confirmed



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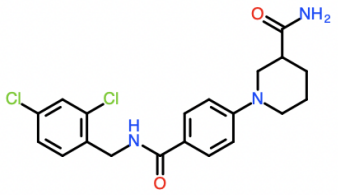
Parent CACHE_1448_70
distance_to_pai 0



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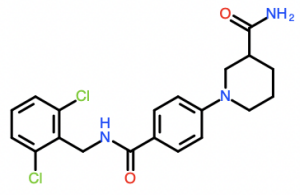
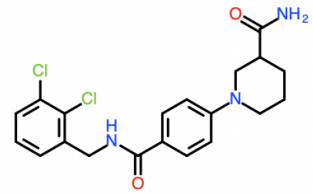


CACHE_ID CACHE2-HO_1448_3
Parent CACHE_1448_70
distance_to_pai 0.01258



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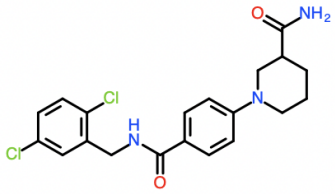
Parent CACHE_1448_70
distance_to_pai 0.03086



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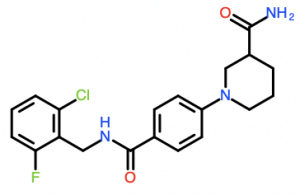
Parent CACHE_1448_70
distance_to_pai 0.03681



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Parent CACHE_1448_70
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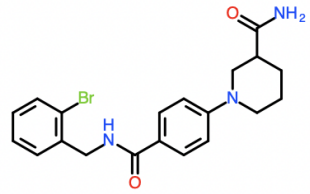
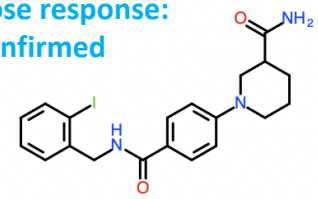


CACHE_ID CACHE2-HO_1448_7
Parent CACHE_1448_70
distance_to_pai 0.07927

Dose response: Confirmed



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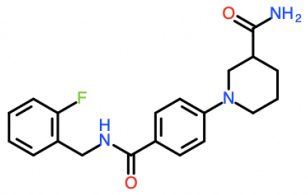
distance_to_pai 0.07927



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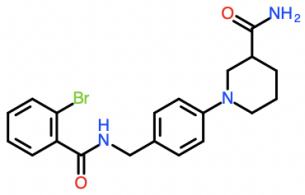
distance_to_pai 0.08485



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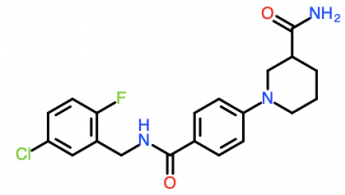
distance_to_pai 0.09036



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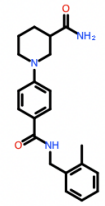
distance_to_pai 0.09357



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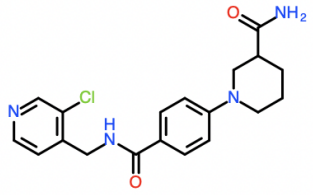
distance_to_pai 0.09434



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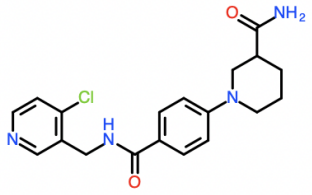

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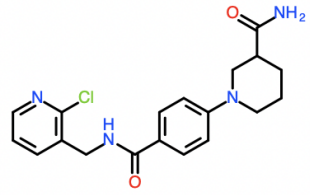
distance_to_pai 0.1105



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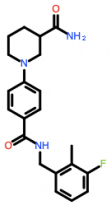

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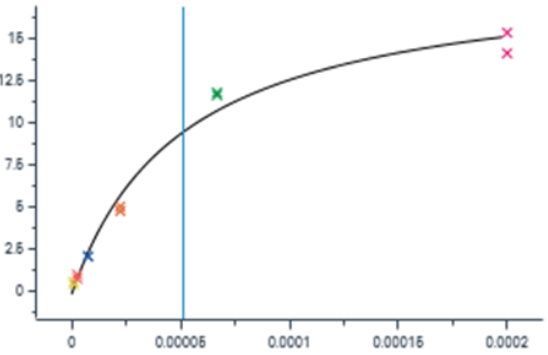
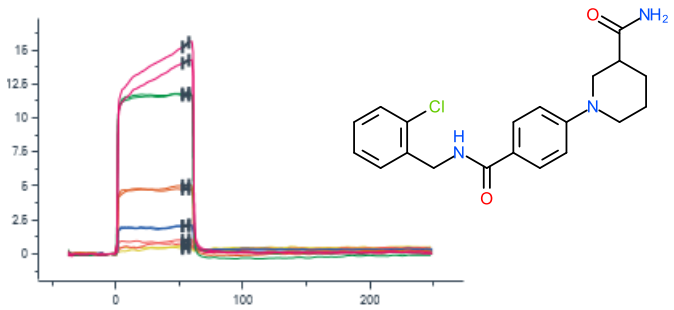
Parent CACHE_1448_70
distance_to_pai 0.1395

PARENT MOLECULE





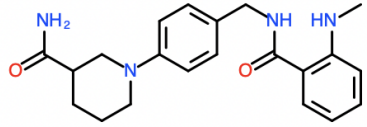
CACHE_1448_70

KD = 51 µM – 76% binding

Selectivity (unrelated WDR5 protein) – Yes

%inhibition@50 µM_ATPase = 1

Tested analogs



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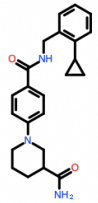
distance_to_pai 0.142



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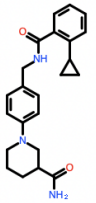

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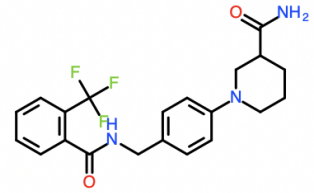
distance_to_pai 0.1676



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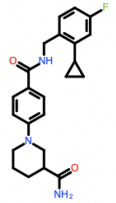

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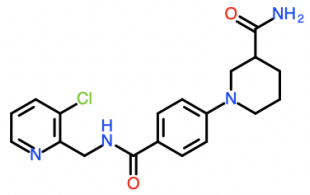

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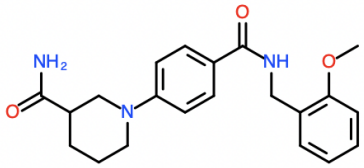

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Parent CACHE_1448_70
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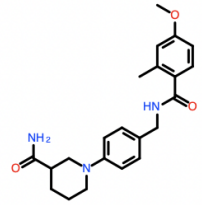

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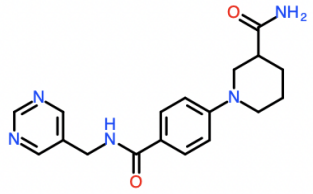
distance_to_pai 0.191



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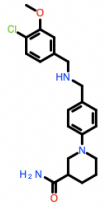
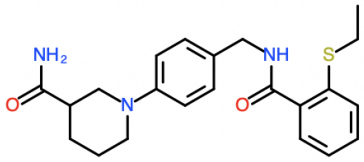
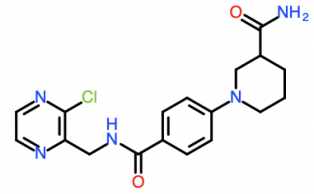


CACHE_ID CACHE2-HO_1448_26
Parent CACHE_1448_70
distance_to_pai 0.2222

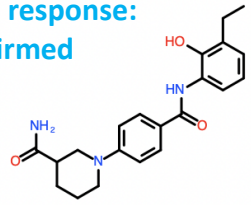


CACHE_ID CACHE2-HO_1448_27
Parent CACHE_1448_70
distance_to_pai 0.2258

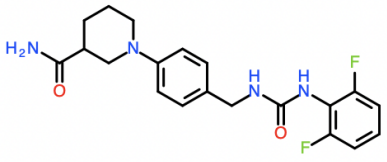


CACHE_ID CACHE2-HO_1448_28
Parent CACHE_1448_70
distance_to_pai 0.228

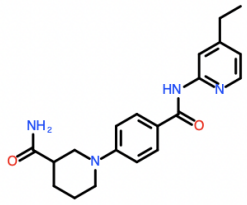
Dose response: Confirmed



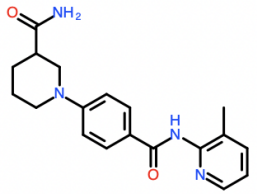
CACHE_ID CACHE2-HO_1448_29
Parent CACHE_1448_70
distance_to_pai 0.2553



CACHE_ID CACHE2-HO_1448_30
Parent CACHE_1448_70
distance_to_pai 0.2593

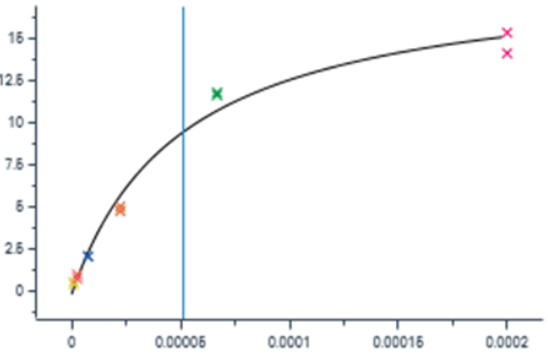


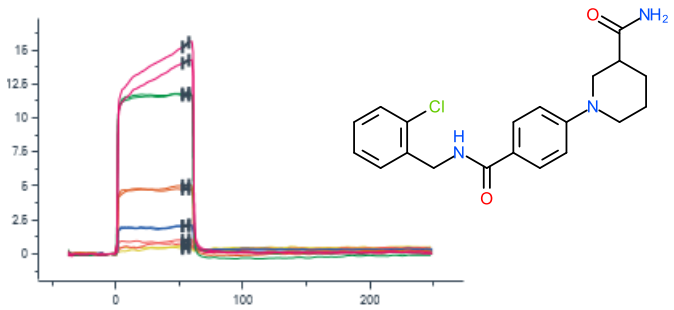
CACHE_ID CACHE2-HO_1448_31
Parent CACHE_1448_70
distance_to_pai 0.2843



CACHE_ID CACHE2-HO_1448_32
Parent CACHE_1448_70
distance_to_pai 0.2929

PARENT MOLECULE





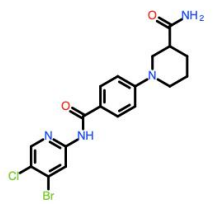
CACHE_1448_70

KD = 51 µM – 76% binding

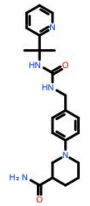
Selectivity (unrelated WDR5 protein) – Yes

%inhibition@50 µM_ATPase = 1

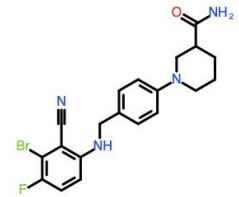
Tested analogs



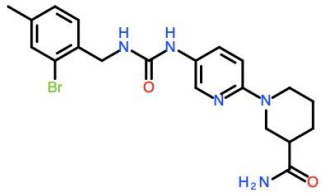
CACHE_ID CACHE2-HO_1448_33
Parent CACHE_1448_70
distance_to_pai 0.3095



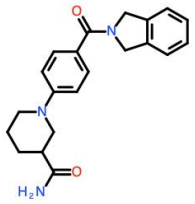
CACHE_ID CACHE2-HO_1448_34
Parent CACHE_1448_70
distance_to_pai 0.3202



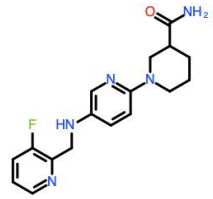
CACHE_ID CACHE2-HO_1448_35
Parent CACHE_1448_70
distance_to_pai 0.3218



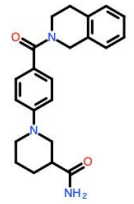
CACHE_ID CACHE2-HO_1448_36
Parent CACHE_1448_70
distance_to_pai 0.3239



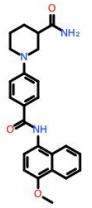
CACHE_ID CACHE2-HO_1448_37
Parent CACHE_1448_70
distance_to_pai 0.3417



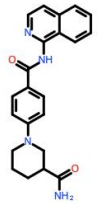
CACHE_ID CACHE2-HO_1448_38
Parent CACHE_1448_70
distance_to_pai 0.3807



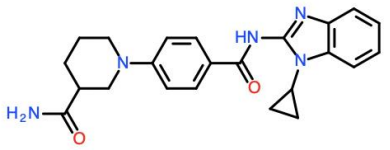
CACHE_ID CACHE2-HO_1448_39
Parent CACHE_1448_70
distance_to_pai 0.3832



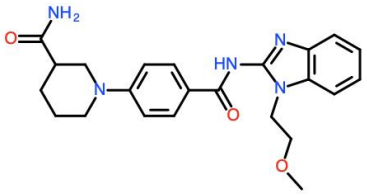
CACHE_ID CACHE2-HO_1448_40
Parent CACHE_1448_70
distance_to_pai 0.3856



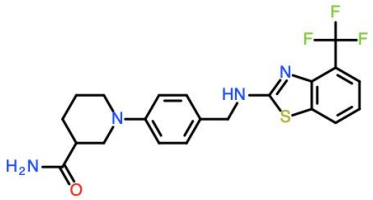
CACHE_ID CACHE2-HO_1448_41
Parent CACHE_1448_70
distance_to_pai 0.3991



CACHE_ID CACHE2-HO_1448_42
Parent CACHE_1448_70
distance_to_pai 0.4828



CACHE_ID CACHE2-HO_1448_43
Parent CACHE_1448_70
distance_to_pai 0.4887

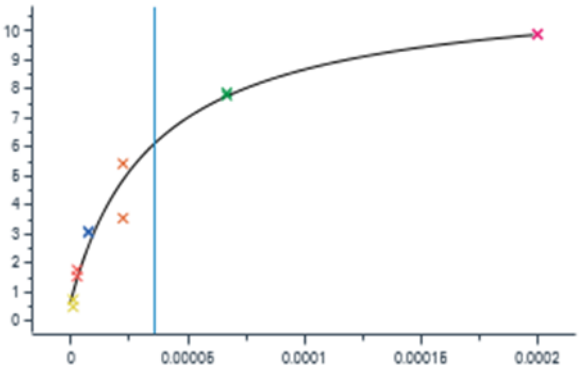


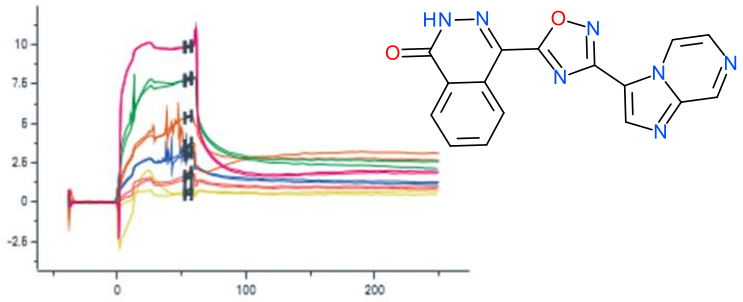
CACHE_ID CACHE2-HO_1448_44
Parent CACHE_1448_70
distance_to_pai 0.5292

CACHE#2 – NSP13 SARS2

Participant 1451

PARENT MOLECULE





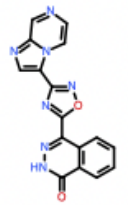
CACHE_1451_96

K_D = 36 µM – 42% binding

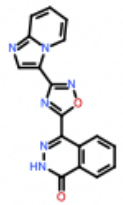
DLS (solub@200 µM)

IC_{50}_ATPase = 24 µM

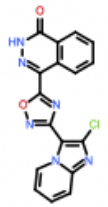
Tested analogs



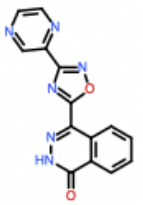
CACHE_ID CACHE2-HO_1451_1
Parent CACHE_1451_96
distance_to_pai 0



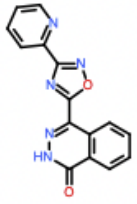
CACHE_ID CACHE2-HO_1451_2
Parent CACHE_1451_96
distance_to_pai 0.08766



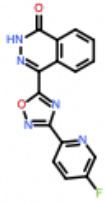
CACHE_ID CACHE2-HO_1451_3
Parent CACHE_1451_96
distance_to_pai 0.1455



CACHE_ID CACHE2-HO_1451_4
Parent CACHE_1451_96
distance_to_pai 0.1627

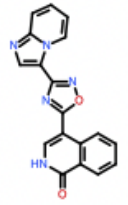


CACHE_ID CACHE2-HO_1451_5
Parent CACHE_1451_96
distance_to_pai 0.2303

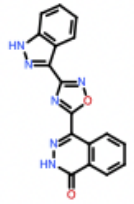


CACHE_ID CACHE2-HO_1451_6
Parent CACHE_1451_96
distance_to_pai 0.2555

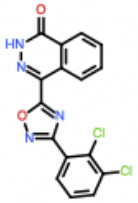
CACHE_ID CACHE2-HO_1451_7
Parent CACHE_1451_96
distance_to_pai 0.2761



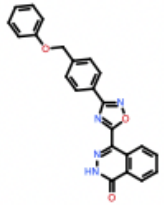
CACHE_ID CACHE2-HO_1451_8
Parent CACHE_1451_96
distance_to_pai 0.2831



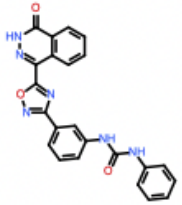
CACHE_ID CACHE2-HO_1451_9
Parent CACHE_1451_96
distance_to_pai 0.2835



CACHE_ID CACHE2-HO_1451_10
Parent CACHE_1451_96
distance_to_pai 0.2884

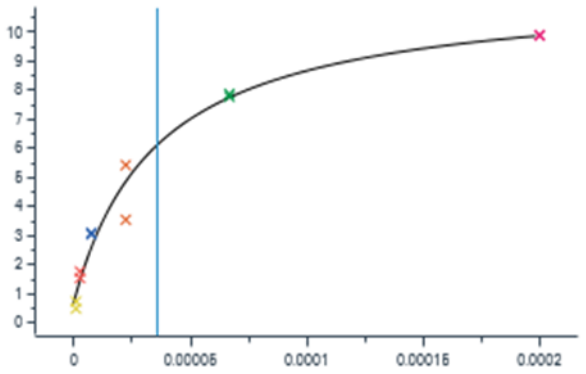


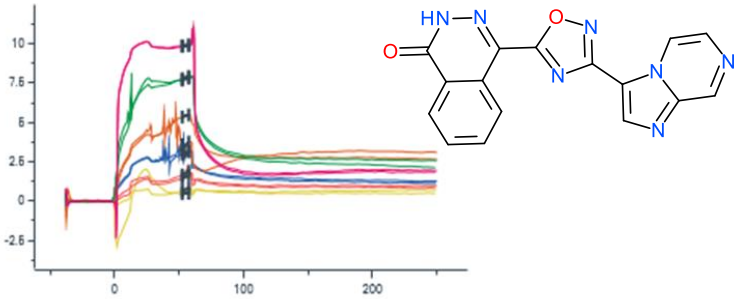
CACHE_ID CACHE2-HO_1451_11
Parent CACHE_1451_96
distance_to_pai 0.3079



CACHE_ID CACHE2-HO_1451_12
Parent CACHE_1451_96
distance_to_pai 0.3079

PARENT MOLECULE

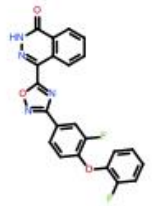
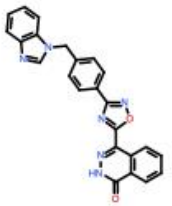
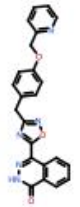
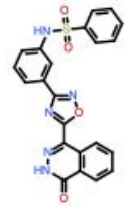
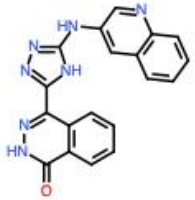




CACHE_1451_96

K_D = 36 µM – 42% binding
DLS (solub@200 µM)
IC_{50}_ATPase = 24 µM

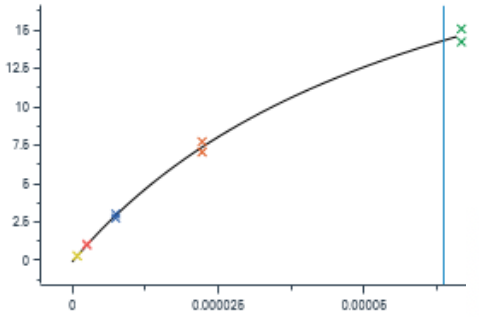
Tested analogs

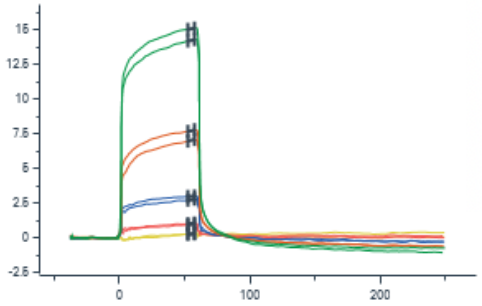
 CACHE_ID CACHE2-HO_1451_13 Parent CACHE_1451_96 distance_to_pai 0.3163	 CACHE_ID CACHE2-HO_1451_14 Parent CACHE_1451_96 distance_to_pai 0.3173	 CACHE_ID CACHE2-HO_1451_15 Parent CACHE_1451_96 distance_to_pai 0.3362	 CACHE_ID CACHE2-HO_1451_16 Parent CACHE_1451_96 distance_to_pai 0.3514
 CACHE_ID CACHE2-HO_1451_17 Parent CACHE_1451_96 distance_to_pai 0.4942	 CACHE_ID CACHE2-HO_1451_18 Parent CACHE_1451_96 distance_to_pai 0.5351		

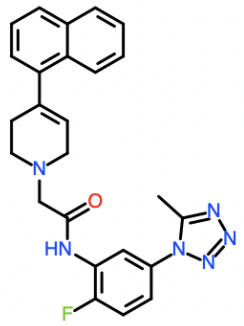
CACHE#2 – NSP13 SARS2

Participant 1454

PARENT MOLECULE



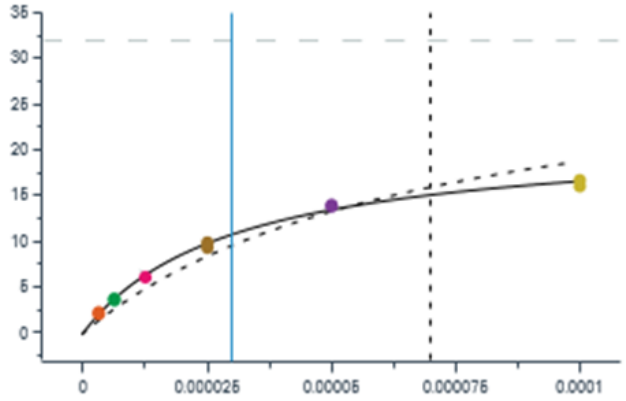


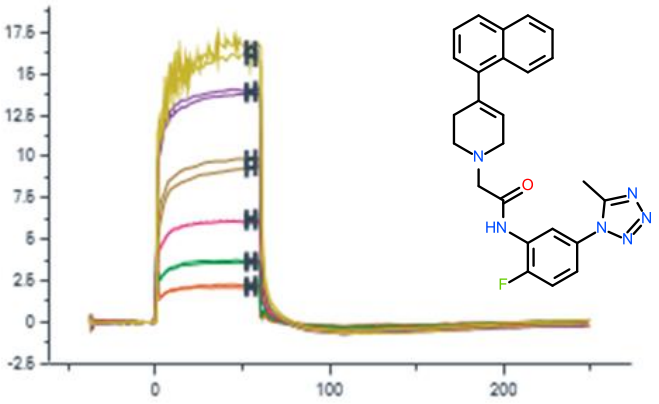


CACHE_1454_20

K_D = 64 µM (does not reach saturation) – 85% binding
Selectivity (unrelated WDR5 protein) – Yes
IC_{50}_ATPase >160 µM

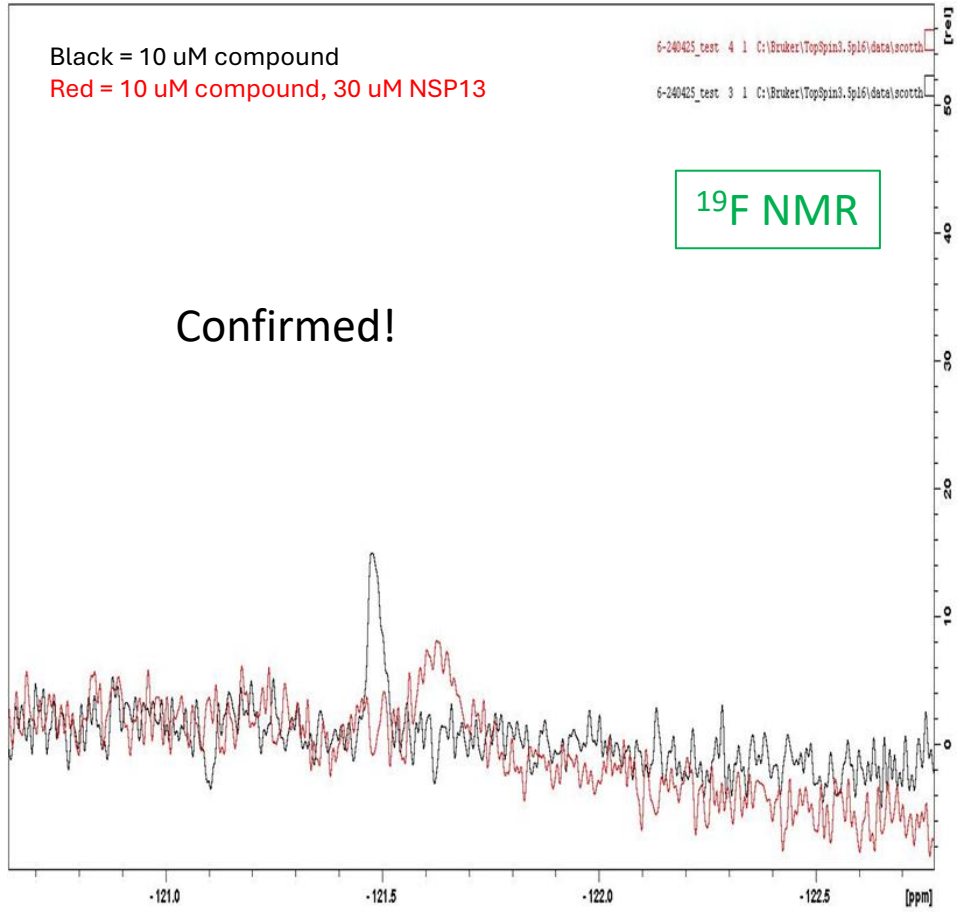
8 analogs of CACHE_1454_20 were submitted for round 2. The re-supplied parent molecule confirmed a selective binding response by SPR and by ^{19}F NMR.



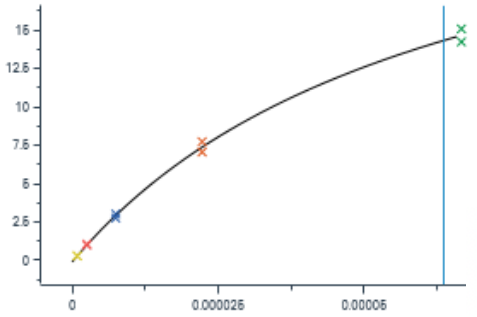


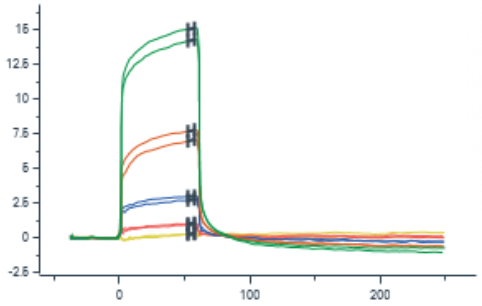
CACHE2-HO_1454_15

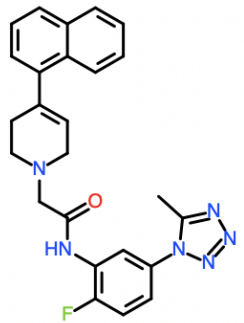
K_D _1 = 31 µM – 53% binding
K_D _2 = 30 µM – 68 %binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 21



PARENT MOLECULE





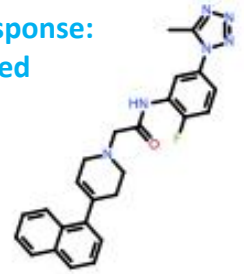


CACHE_1454_20

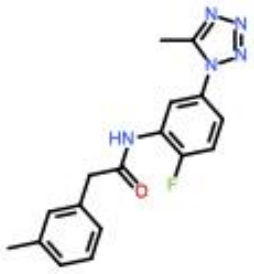
K_D = 64 µM (does not reach saturation) – 85% binding
Selectivity (unrelated WDR5 protein) – Yes
IC_{50}_ATPase >160 µM

Tested analogs

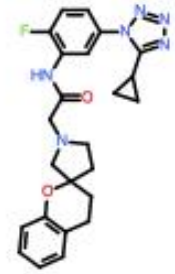
Dose response: Confirmed



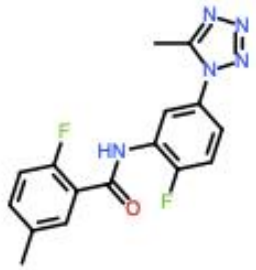
CACHE_ID CACHE2-HO_1454_15
Parent CACHE_1454_20
distance_to_pai 0



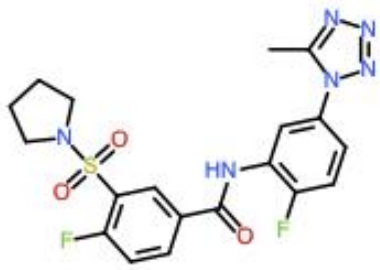
CACHE_ID CACHE2-HO_1454_16
Parent CACHE_1454_20
distance_to_pai 0.3321



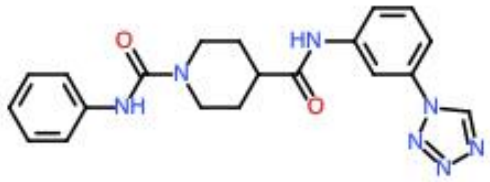
CACHE_ID CACHE2-HO_1454_17
Parent CACHE_1454_20
distance_to_pai 0.344



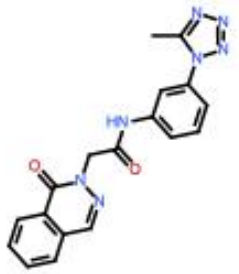
CACHE_ID CACHE2-HO_1454_18
Parent CACHE_1454_20
distance_to_pai 0.369



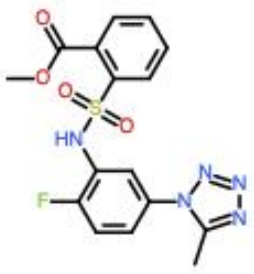
CACHE_ID CACHE2-HO_1454_19
Parent CACHE_1454_20
distance_to_pai 0.3918



CACHE_ID CACHE2-HO_1454_20
Parent CACHE_1454_20
distance_to_pai 0.4152

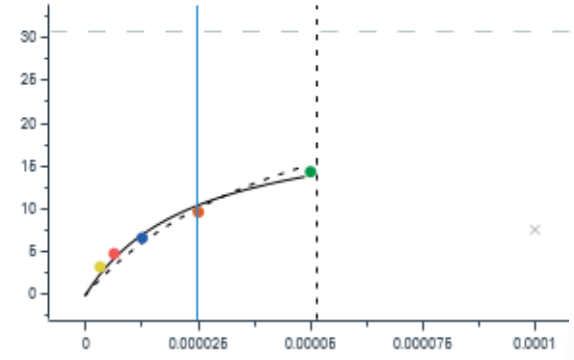


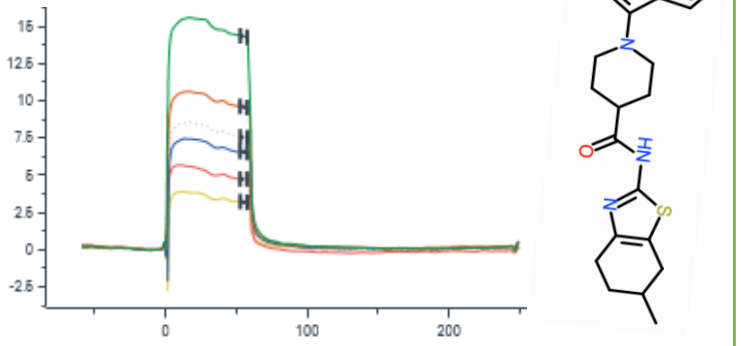
CACHE_ID CACHE2-HO_1454_21
Parent CACHE_1454_20
distance_to_pai 0.4683



CACHE_ID CACHE2-HO_1454_22
Parent CACHE_1454_20
distance_to_pai 0.5123

PARENT MOLECULE

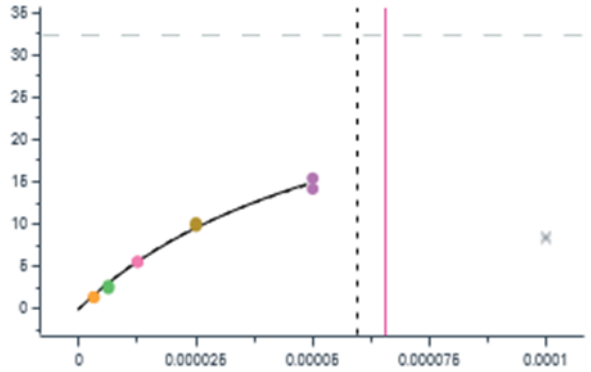


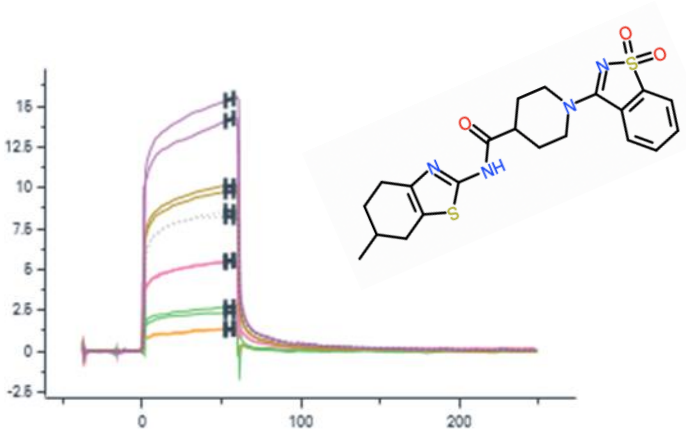


CACHE_1454_98

K_D = 25 µM (solubility issues) – 69% binding
Selectivity (unrelated WDR5 protein) – 26% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 1

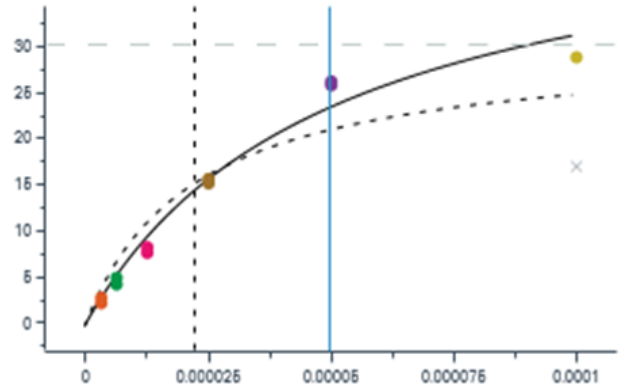
7 analogs of CACHE_1454_98 were submitted for round 2.
2 compound (including re-supplied parent molecule) showed a dose dependent binding response by SPR with a tendency to reach saturation.

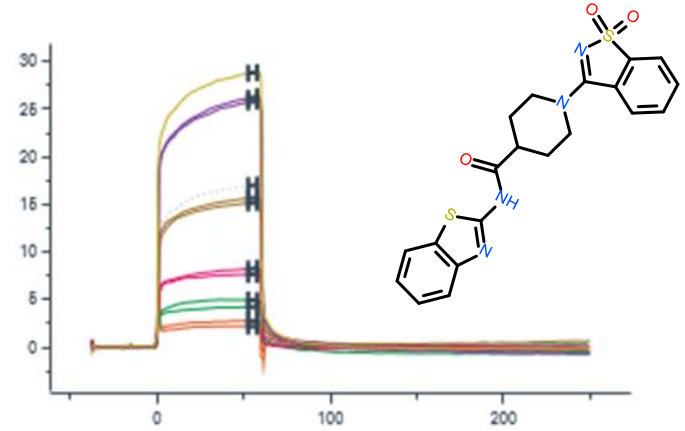




CACHE2-HO_1454_44

K_D = 65 µM (solubility issues) – 107% binding
%inhibition@50 µM_ATPase = 8

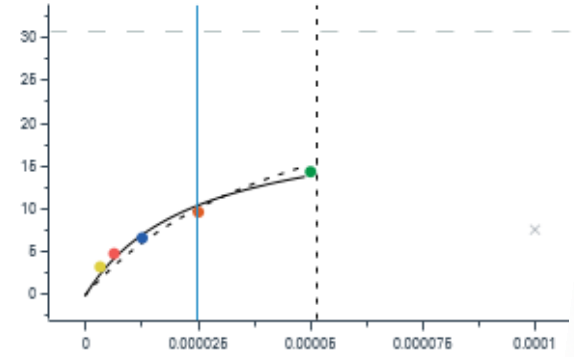


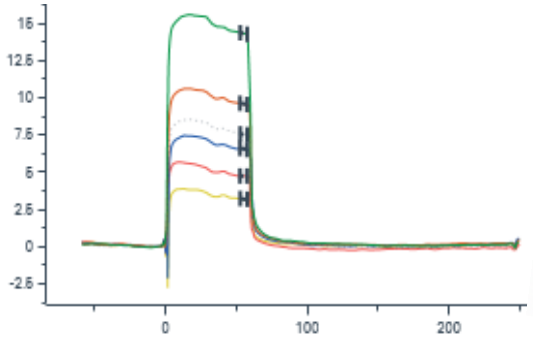


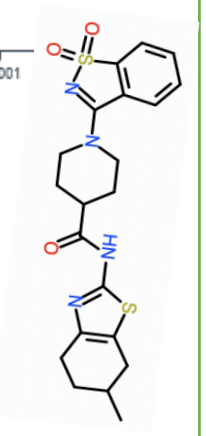
CACHE2-HO_1454_45

K_D _1 = 44 µM – 135% binding
K_D _2 = 50 µM – 155% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 11

PARENT MOLECULE



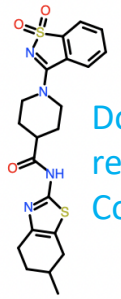




CACHE_1454_98

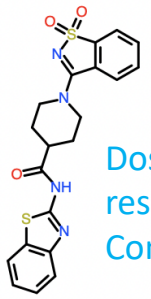
K_D = 25 µM (solubility issues) – 69% binding
Selectivity (unrelated WDR5 protein) – 26% binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 1

Tested analogs



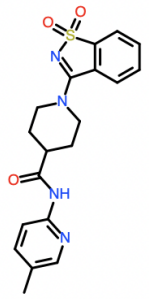
Dose response: Confirmed

CACHE_ID	CACHE2-HO_1454_44
Parent	CACHE_1454_98
distance_to_pare	0

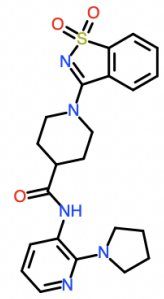


Dose response: Confirmed

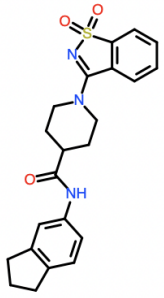
CACHE_ID	CACHE2-HO_1454_45
Parent	CACHE_1454_98
distance_to_pare	0.1552



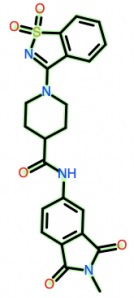
CACHE_ID	CACHE2-HO_1454_46
Parent	CACHE_1454_98
distance_to_pare	0.3182



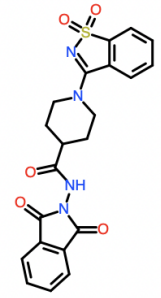
CACHE_ID	CACHE2-HO_1454_47
Parent	CACHE_1454_98
distance_to_pare	0.3406



CACHE_ID	CACHE2-HO_1454_48
Parent	CACHE_1454_98
distance_to_pare	0.3619

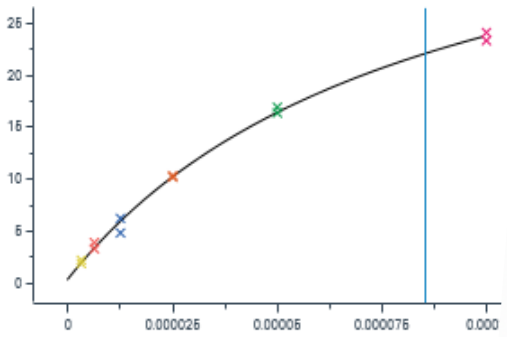


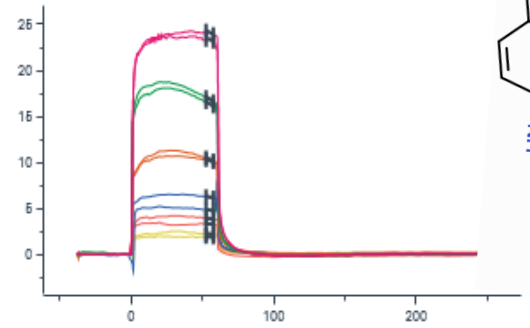
CACHE_ID	CACHE2-HO_1454_49
Parent	CACHE_1454_98
distance_to_pare	0.4027

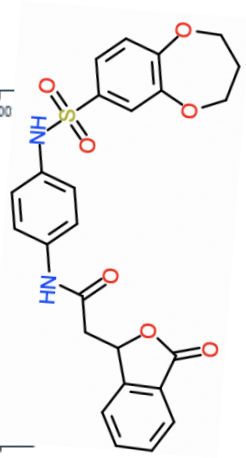


CACHE_ID	CACHE2-HO_1454_50
Parent	CACHE_1454_98
distance_to_pare	0.4096

PARENT MOLECULE







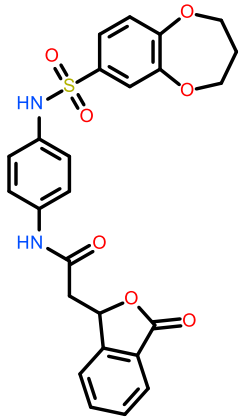
CACHE_1454_13

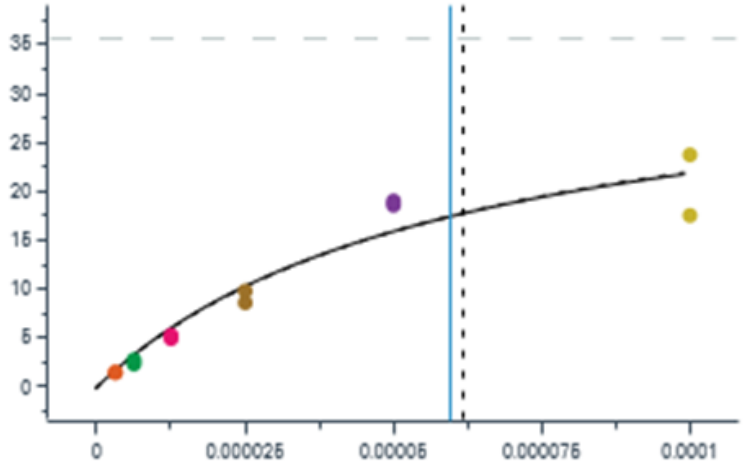
K_D = 86±4 µM – 142±11% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 13

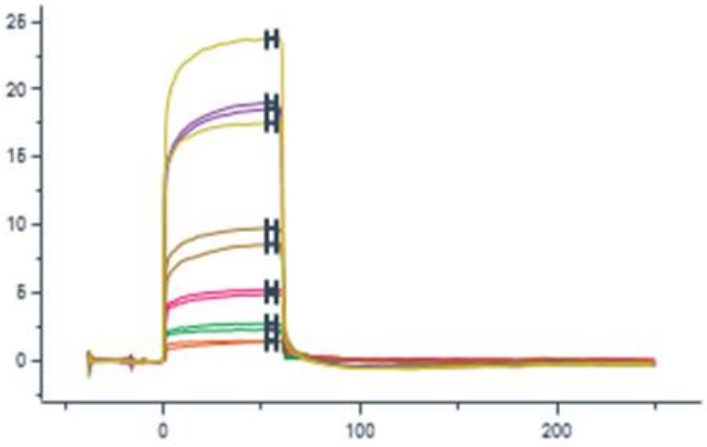
6 analogs of CACHE_1454_13 were submitted for round 2. The re-supplied parent molecule confirmed a selective dose dependent binding response with a tendency to reach saturation.

CACHE2-HO_1454_1

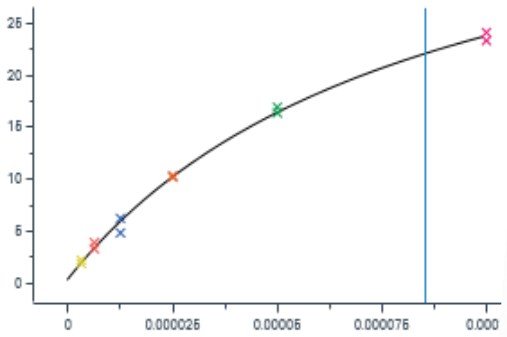
K_D _1 = 92 µM – 111% binding
K_D _2 = 60 µM – 98% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 uM)
%inhibition@50 µM_ATPase = 5

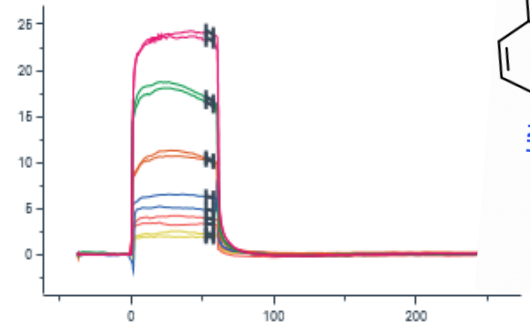


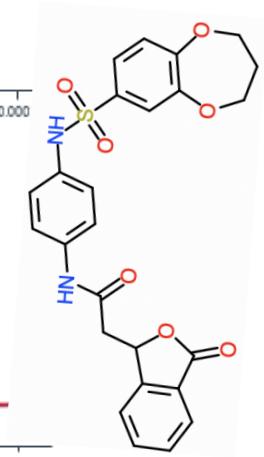




PARENT MOLECULE



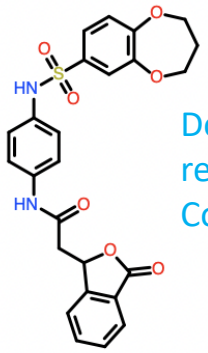




CACHE_1454_13

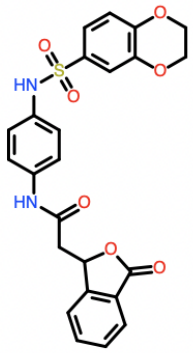
K_D = 86±4 µM – 142±11% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 7

Tested analogs

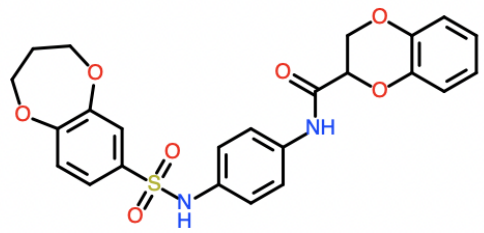


Dose response: Confirmed

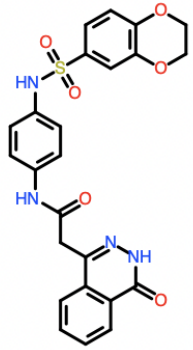
CACHE_ID	CACHE2-HO_1454_1
Parent	CACHE_1454_13
distance_to_par	0



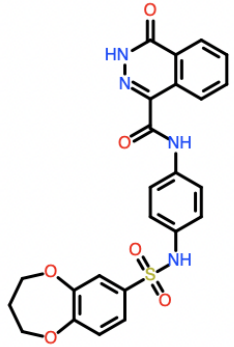
CACHE_ID	CACHE2-HO_1454_2
Parent	CACHE_1454_13
distance_to_par	0.0429



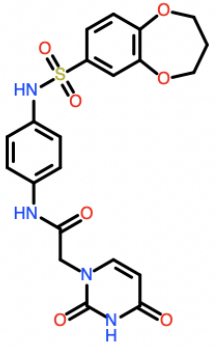
CACHE_ID	CACHE2-HO_1454_3
Parent	CACHE_1454_13
distance_to_par	0.3084



CACHE_ID	CACHE2-HO_1454_4
Parent	CACHE_1454_13
distance_to_par	0.3646

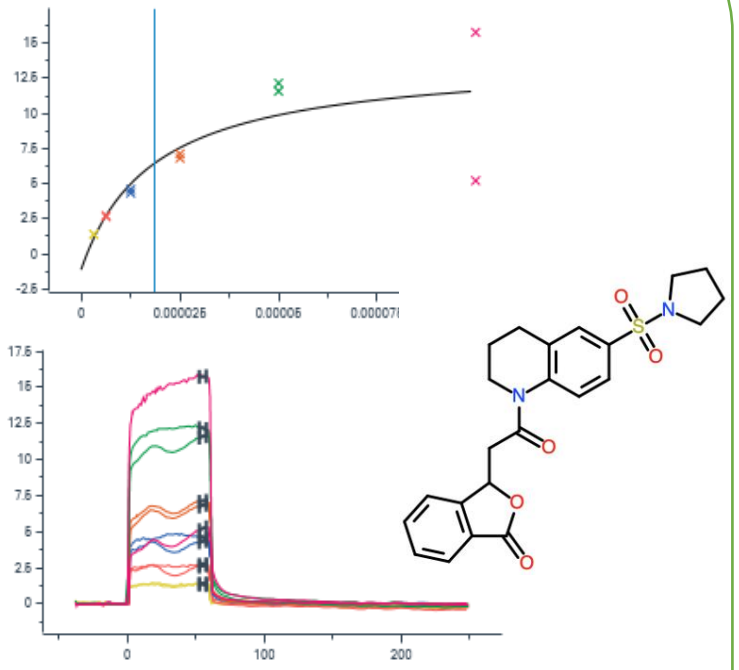


CACHE_ID	CACHE2-HO_1454_5
Parent	CACHE_1454_13
distance_to_par	0.393



CACHE_ID	CACHE2-HO_1454_6
Parent	CACHE_1454_13
distance_to_par	0.4017

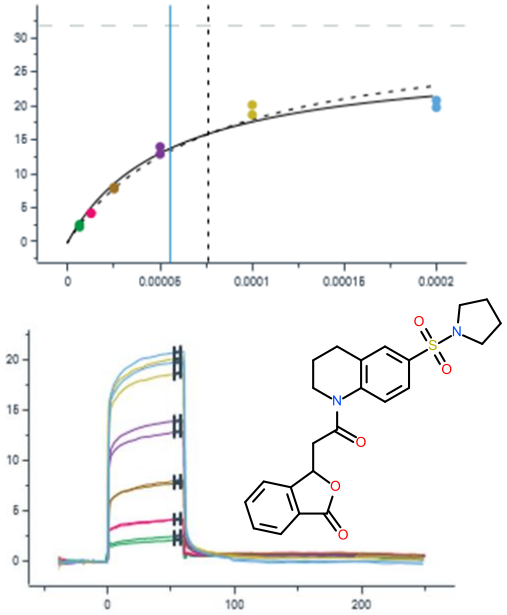
PARENT MOLECULE



CACHE_1454_91

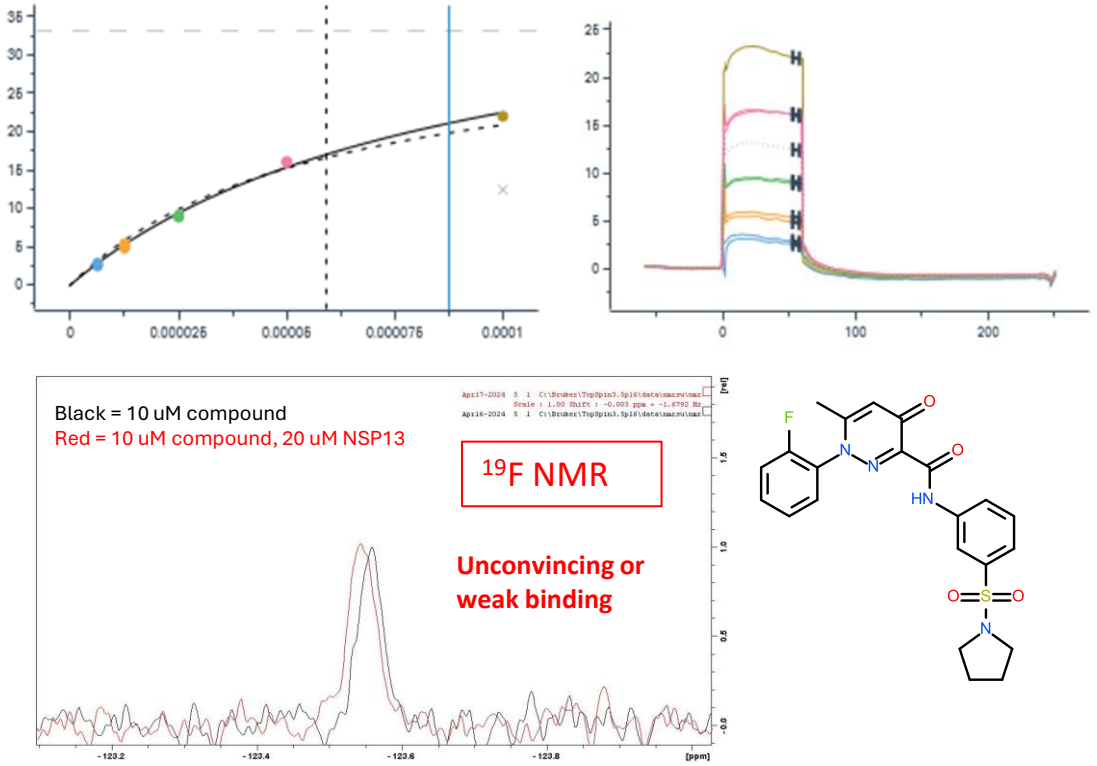
K_D = 35±42 µM – 71±34% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 1

23 analogs of CACHE_1454_91 were submitted for round 2.
2 compound (including re-supplied parent molecule) confirmed a selective dose dependent binding response with a tendency to reach saturation.



CACHE2-HO_1454_38

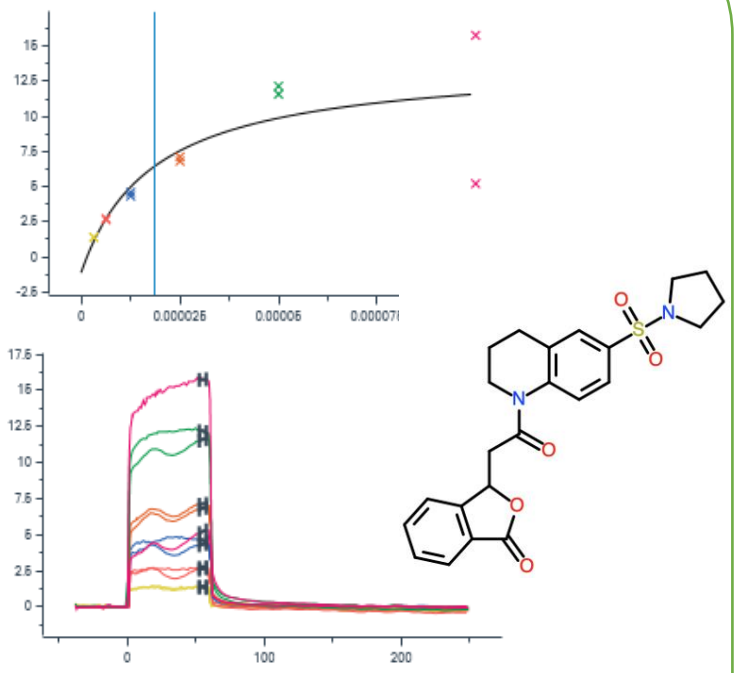
K_D = 55 µM – 86% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 9



CACHE2-HO_1454_36

K_D (3% DMSO) = 88 µM - 127% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 10

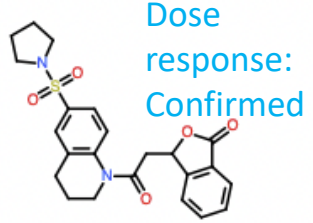
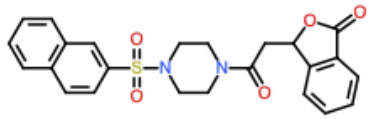
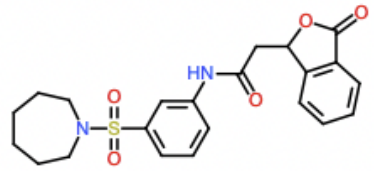
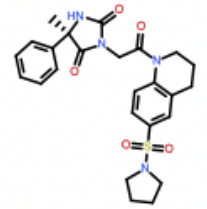
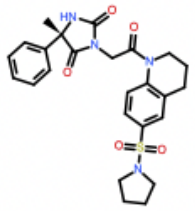
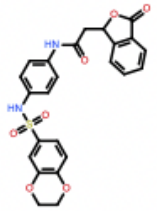
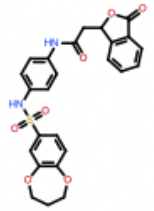
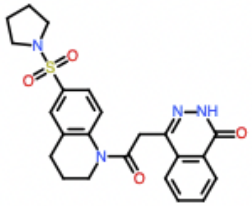
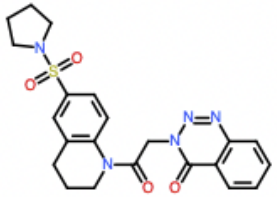
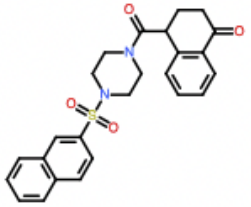
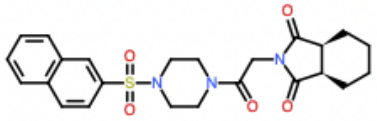
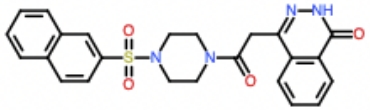
PARENT MOLECULE



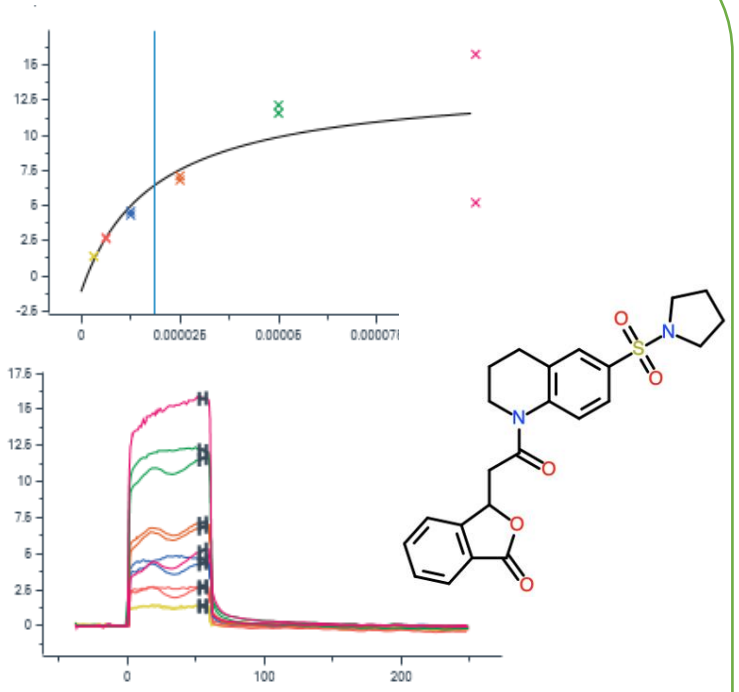
CACHE_1454_91

K_D = 35±42 µM – 71±34% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 1

Tested analogs

Dose response: Confirmed  CACHE_ID CACHE2-HO_1454_38 Parent CACHE_1454_91 distance_to_pa 0.006757	 CACHE_ID CACHE2-HO_1454_23 Parent CACHE_1454_91 distance_to_pa 0.2293	 CACHE_ID CACHE2-HO_1454_39 Parent CACHE_1454_91 distance_to_pa 0.2685	 CACHE_ID CACHE2-HO_1454_40 Parent CACHE_1454_91 distance_to_pa 0.3153
 CACHE_ID CACHE2-HO_1454_41 Parent CACHE_1454_91 distance_to_pa 0.3153	 CACHE_ID CACHE2-HO_1454_2 Parent CACHE_1454_91 distance_to_pa 0.3333	 CACHE_ID CACHE2-HO_1454_1 Parent CACHE_1454_91 distance_to_pa 0.3389	 CACHE_ID CACHE2-HO_1454_42 Parent CACHE_1454_91 distance_to_pa 0.3398
 CACHE_ID CACHE2-HO_1454_43 Parent CACHE_1454_91 distance_to_pa 0.3653	 CACHE_ID CACHE2-HO_1454_24 Parent CACHE_1454_91 distance_to_pa 0.4209	 CACHE_ID CACHE2-HO_1454_25 Parent CACHE_1454_91 distance_to_pa 0.4765	 CACHE_ID CACHE2-HO_1454_26 Parent CACHE_1454_91 distance_to_pa 0.5174

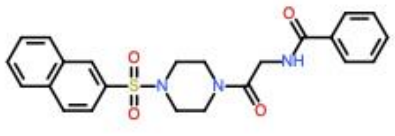
PARENT MOLECULE



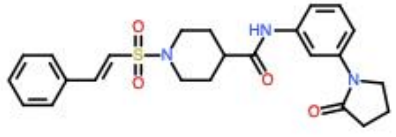
CACHE_1454_91

K_D = 35±42 µM – 71±34% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 1

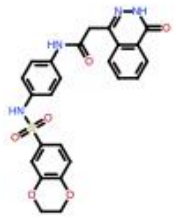
Tested analogs



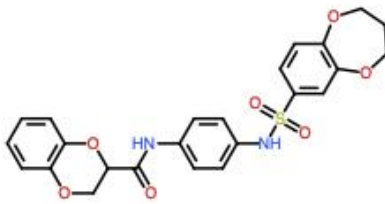
CACHE_ID CACHE2-HO_1454_27
Parent CACHE_1454_91
distance_to_pa 0.5221



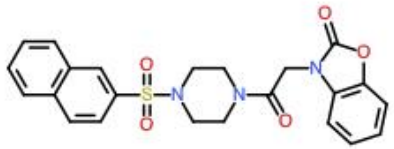
CACHE_ID CACHE2-HO_1454_13
Parent CACHE_1454_91
distance_to_pa 0.549



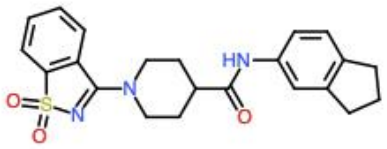
CACHE_ID CACHE2-HO_1454_4
Parent CACHE_1454_91
distance_to_pa 0.5599



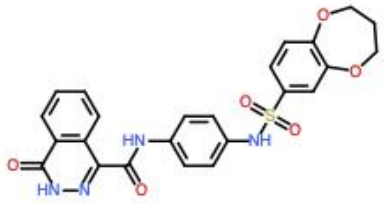
CACHE_ID CACHE2-HO_1454_3
Parent CACHE_1454_91
distance_to_pa 0.5638



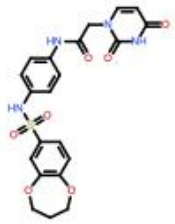
CACHE_ID CACHE2-HO_1454_28
Parent CACHE_1454_91
distance_to_pa 0.5672



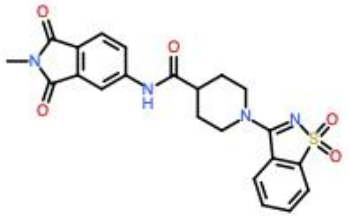
CACHE_ID CACHE2-HO_1454_48
Parent CACHE_1454_91
distance_to_pa 0.5738



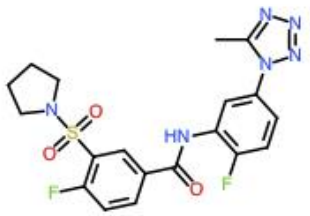
CACHE_ID CACHE2-HO_1454_5
Parent CACHE_1454_91
distance_to_pa 0.5919



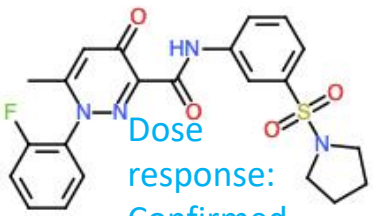
CACHE_ID CACHE2-HO_1454_6
Parent CACHE_1454_91
distance_to_pa 0.5931



CACHE_ID CACHE2-HO_1454_49
Parent CACHE_1454_91
distance_to_pa 0.5977



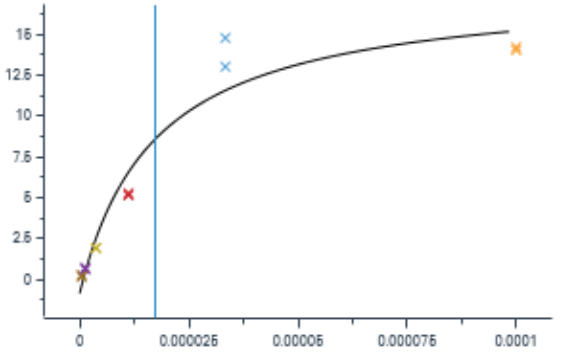
CACHE_ID CACHE2-HO_1454_19
Parent CACHE_1454_91
distance_to_pa 0.5985

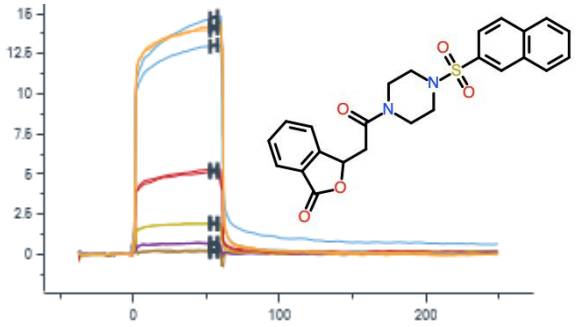


Dose response: Confirmed

CACHE_ID CACHE2-HO_1454_36
Parent CACHE_1454_91
distance_to_pa 0.6

PARENT MOLECULE

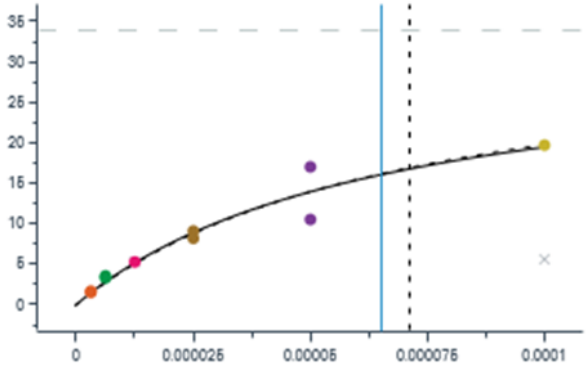


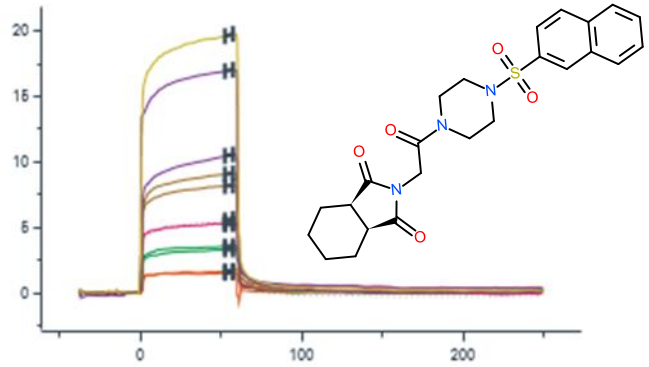


CACHE_1454_46

K_D = 17 µM – 58% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = no inhibition

6 analogs of CACHE_1454_46 were submitted for round 2.
One compounds confirmed a selective dose dependent binding response by SPR.

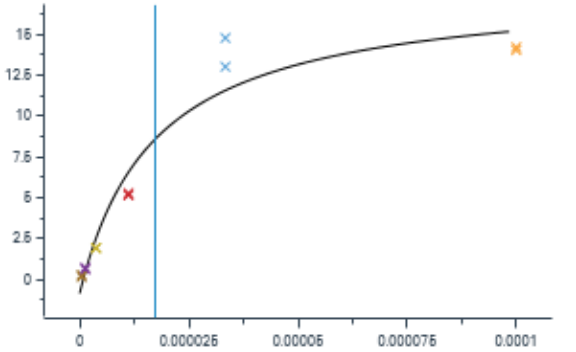


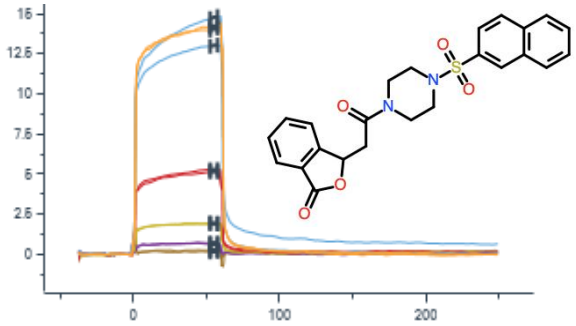


CACHE2-HO_1454_25

K_D _1 = 43 µM – 69% binding
K_D _2 = 65 µM – 95% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 14

PARENT MOLECULE

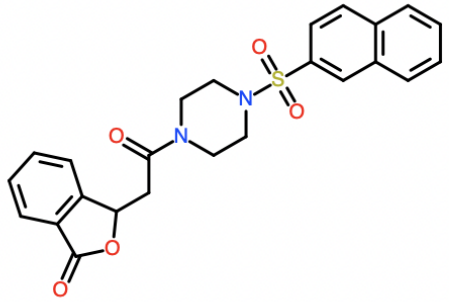




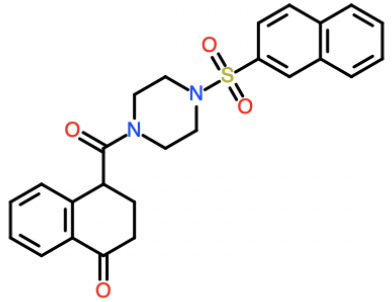
CACHE_1454_46

K_D = 17 µM – 58% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = no inhibition

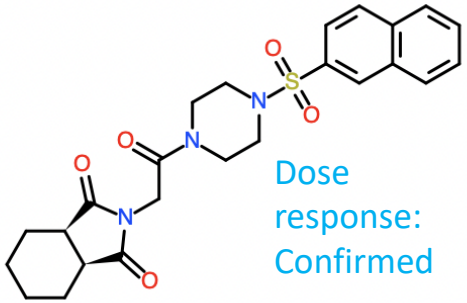
Tested analogs



CACHE_ID CACHE2-HO_1454_23
Parent CACHE_1454_46
distance_to_pare 0

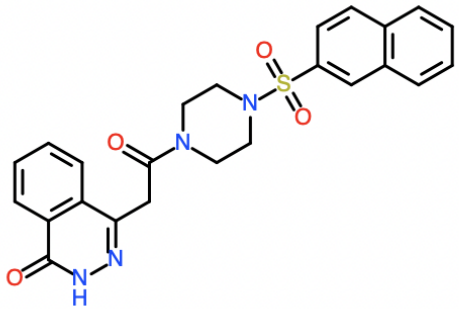


CACHE_ID CACHE2-HO_1454_24
Parent CACHE_1454_46
distance_to_pare 0.2753

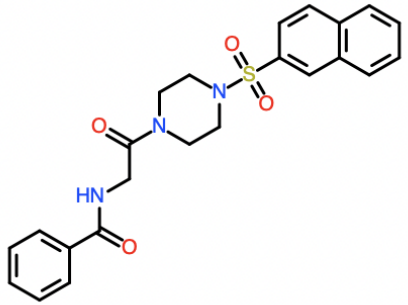


Dose response: Confirmed

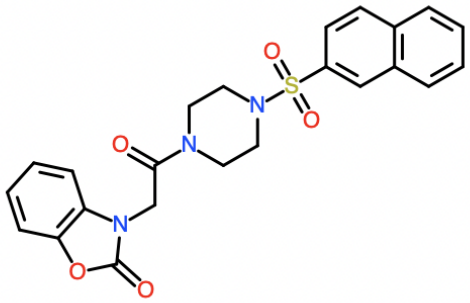
CACHE_ID CACHE2-HO_1454_25
Parent CACHE_1454_46
distance_to_pare 0.392



CACHE_ID CACHE2-HO_1454_26
Parent CACHE_1454_46
distance_to_pare 0.3932

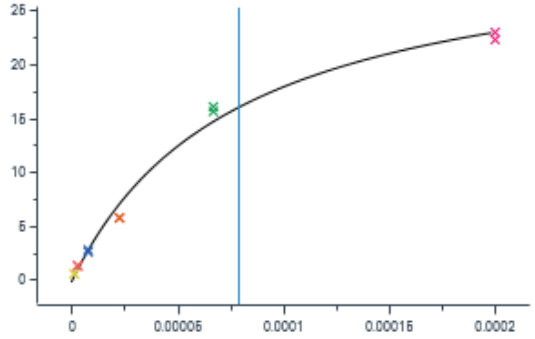


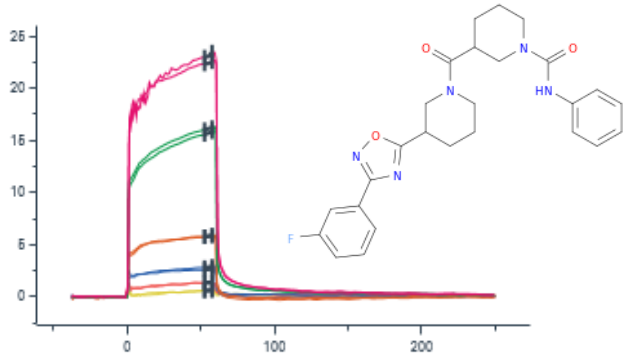
CACHE_ID CACHE2-HO_1454_27
Parent CACHE_1454_46
distance_to_pare 0.3952



CACHE_ID CACHE2-HO_1454_28
Parent CACHE_1454_46
distance_to_pare 0.511

PARENT MOLECULE





CACHE_1454_19

K_D = 79 µM – 100% binding

%inhibition@50 µM_ATPase = no inhibition

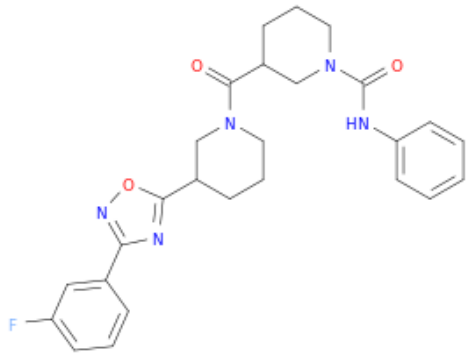
5 analogs of CACHE_1454_19 were submitted for round 2. Re-supplied parent molecule confirmed a selective dose dependent binding response by SPR.

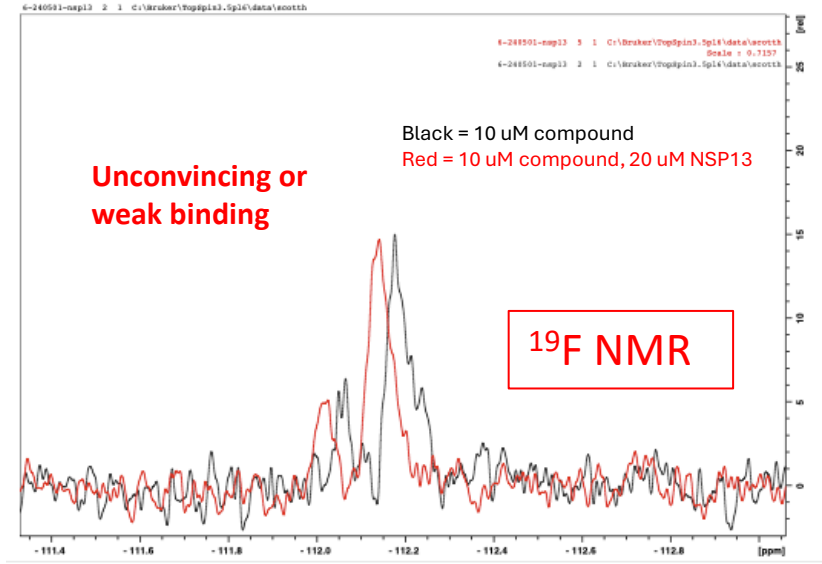
CACHE2-HO_1454_7

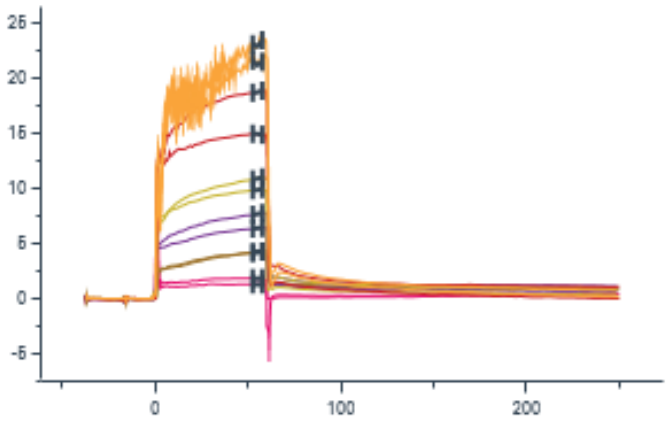
K_D = 102 µM – 98% binding

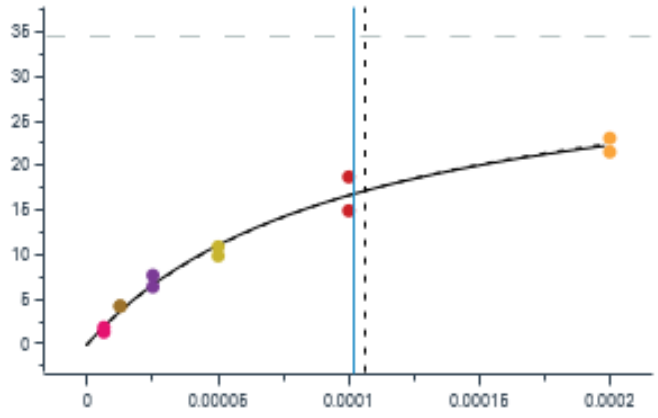
Selectivity (unrelated WDR5 protein) – Yes

%inhibition@50 µM_ATPase = 11

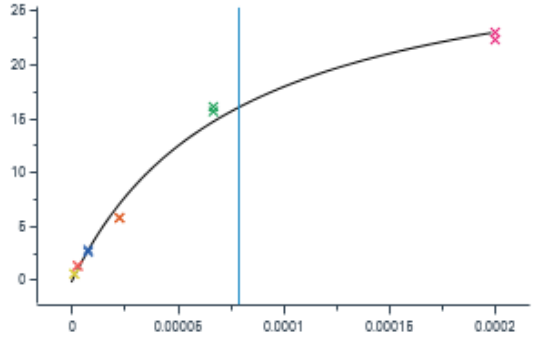


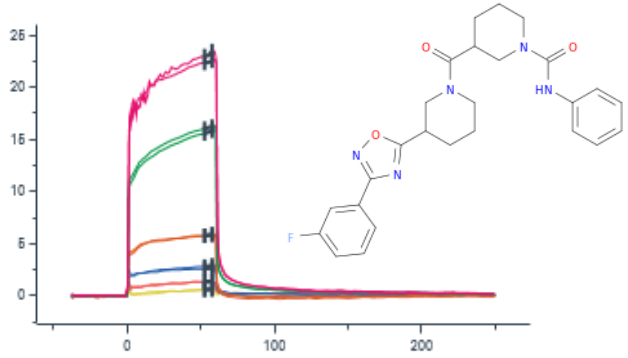






PARENT MOLECULE





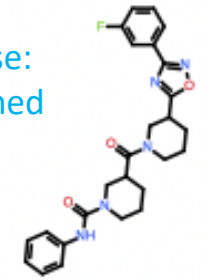
CACHE_1454_19

K_D = 79 µM – 100% binding

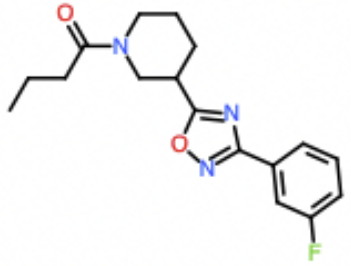
%inhibition@50 µM_ATPase = no inhibition

Tested analogs

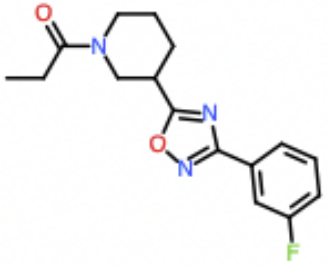
Dose response: Confirmed



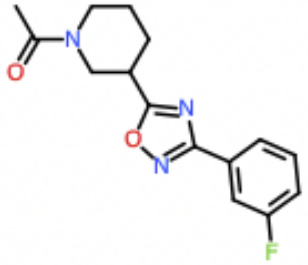
CACHE_ID	CACHE2-HO_1454_7
Parent	CACHE_1454_19
distance_to_pai	0.007968



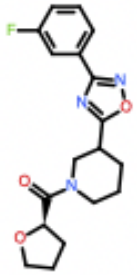
CACHE_ID	CACHE2-HO_1454_8
Parent	CACHE_1454_19
distance_to_pai	0.1772



CACHE_ID	CACHE2-HO_1454_9
Parent	CACHE_1454_19
distance_to_pai	0.1858

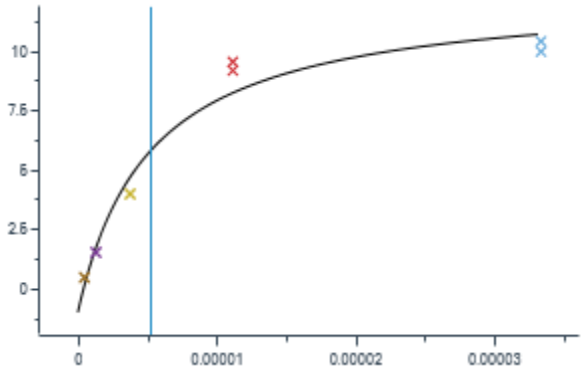


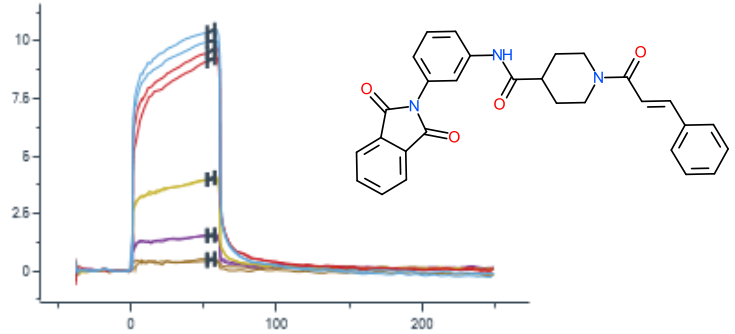
CACHE_ID	CACHE2-HO_1454_10
Parent	CACHE_1454_19
distance_to_pai	0.1944



CACHE_ID	CACHE2-HO_1454_11
Parent	CACHE_1454_19
distance_to_pai	0.2374

PARENT MOLECULE

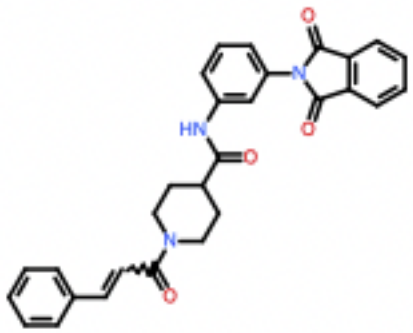




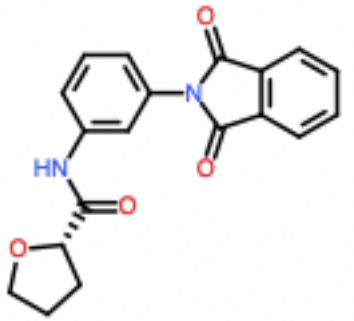
CACHE_1454_61

K_D = 5 µM – 36% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
IC_{50}_ATPase = 29 µM

Tested analogs

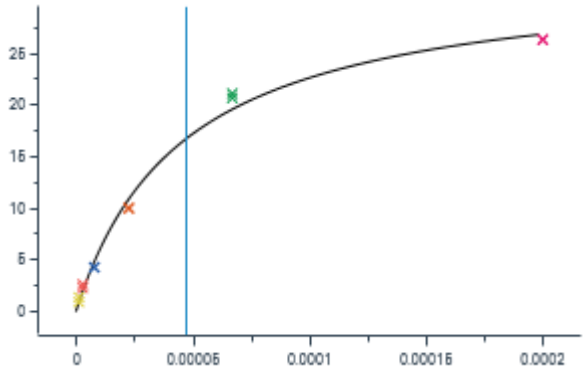


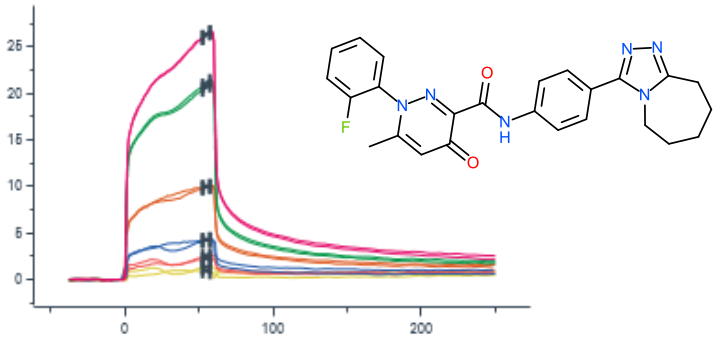
CACHE_ID	CACHE2-HO_1454_29
Parent	CACHE_1454_61
distance_to_pai	0



CACHE_ID	CACHE2-HO_1454_30
Parent	CACHE_1454_61
distance_to_pai	0.2819

PARENT MOLECULE

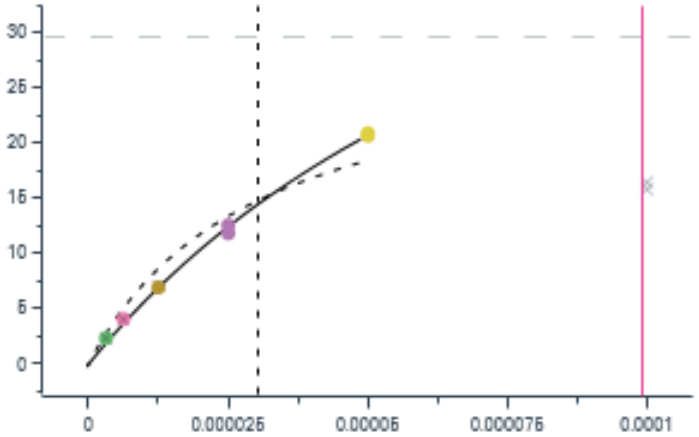


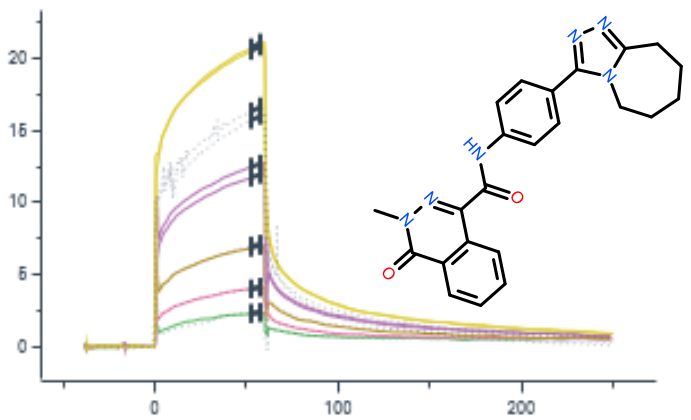


CACHE_1454_75

K_D = 47 µM (slow on/off) – 106% binding
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 1

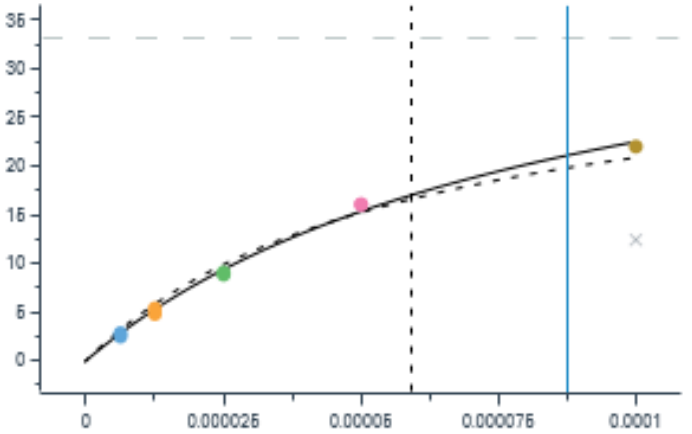
7 analogs of CACHE_1454_75 were submitted for round 2.
1 compounds showed a selective dose dependent binding response by SPR.

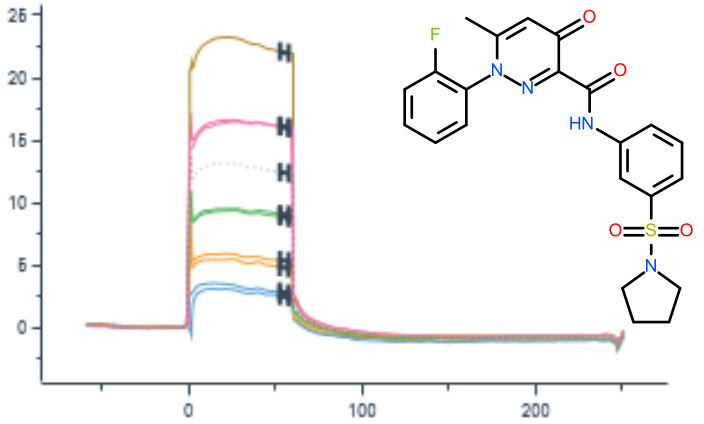




CACHE2-HO_1454_33

K_D (3% DMSO) = 99 µM (does not reach saturation/solubility issue) – 209% binding
DLS(solub@200 µM)
%inhibition@50 µM_ATPase = 14

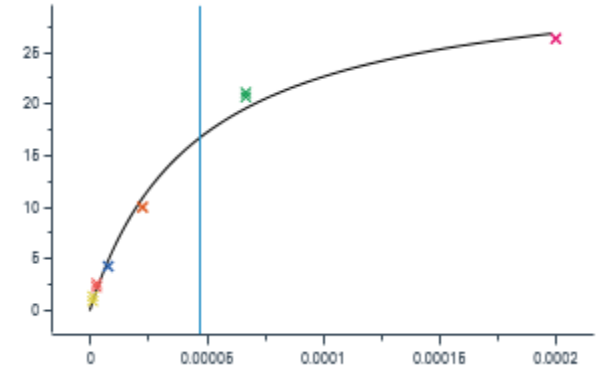


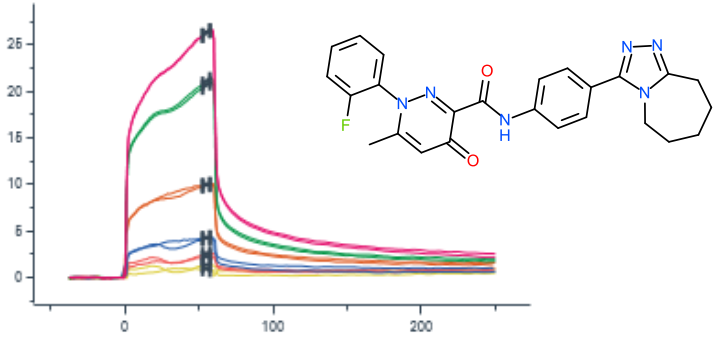


CACHE2-HO_1454_36

K_D (3% DMSO) = 88 µM – 127% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS(solub@200 µM)
%inhibition@50 µM_ATPase = 10

PARENT MOLECULE

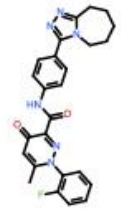
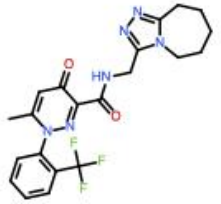
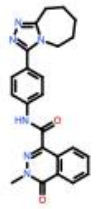
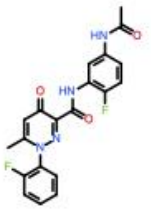
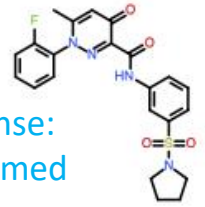
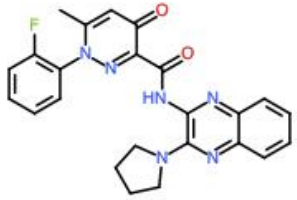




CACHE_1454_75

K_D = 47 µM (slow on/off) – 106% binding
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 1

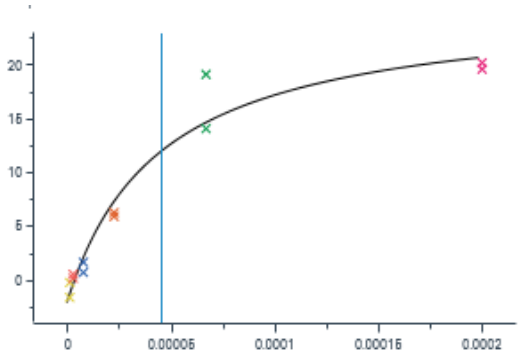
Tested analogs

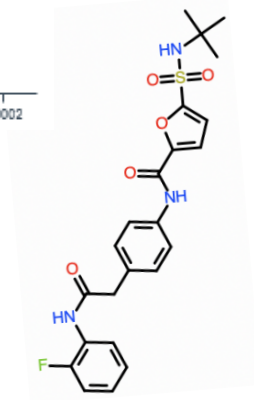
 CACHE_ID CACHE2-HO_1454_31 Parent CACHE_1454_75 distance_to_pai 0	 CACHE_ID CACHE2-HO_1454_32 Parent CACHE_1454_75 distance_to_pai 0.1983	 CACHE_ID CACHE2-HO_1454_33 Parent CACHE_1454_75 distance_to_pai 0.2661	 CACHE_ID CACHE2-HO_1454_34 Parent CACHE_1454_75 distance_to_pai 0.3561
 CACHE_ID CACHE2-HO_1454_35 Parent CACHE_1454_75 distance_to_pai 0.3614	Dose response: Confirmed  CACHE_ID CACHE2-HO_1454_36 Parent CACHE_1454_75 distance_to_pai 0.3806	 CACHE_ID CACHE2-HO_1454_37 Parent CACHE_1454_75 distance_to_pai 0.4385	

CACHE#2 – NSP13 SARS2

Participant 1456

PARENT MOLECULE

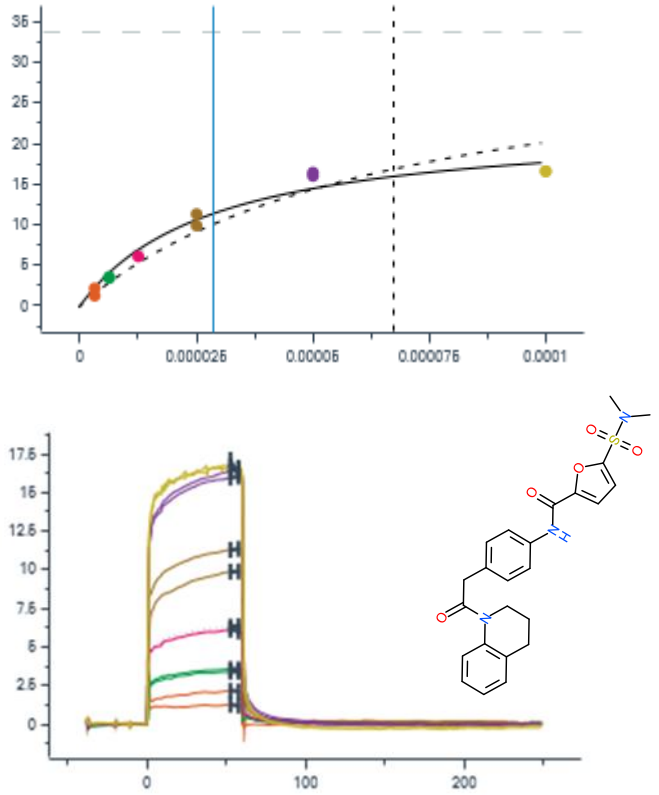




CACHE_1456_73

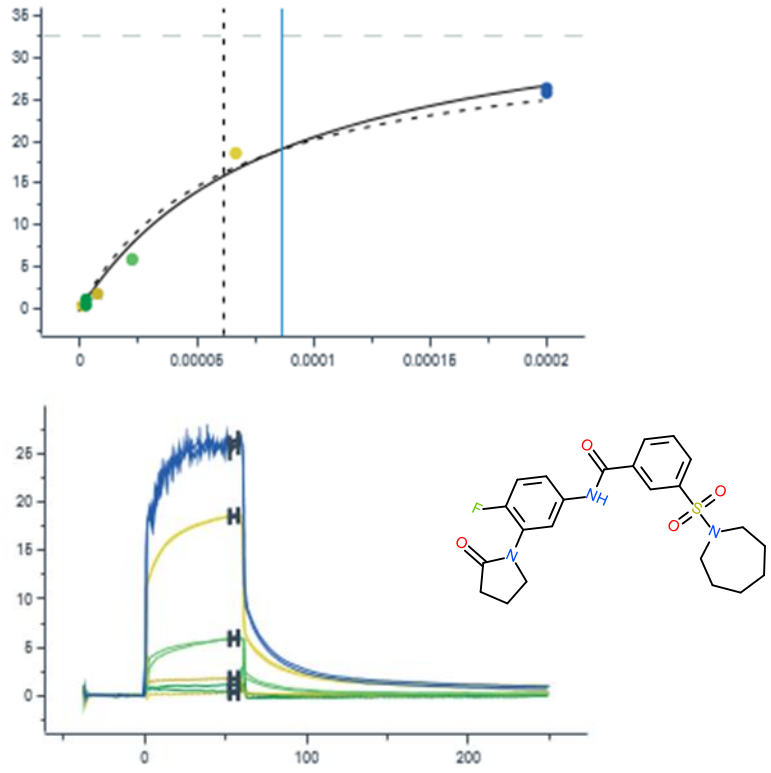
K_D = 45 µM – 88% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = no inhibition

16 analogs of CACHE_1456_73 were submitted for round 2. 2 compound showed a dose dependent binding response by SPR.



CACHE2-HO_1456_42

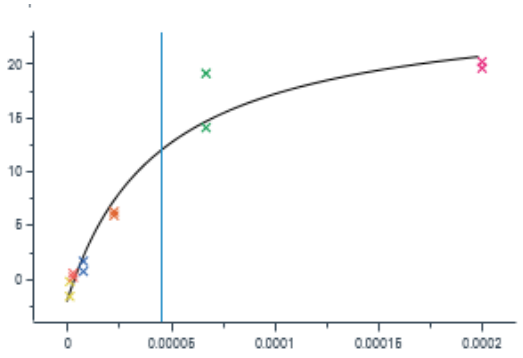
K_D _1 = 36 µM – 65% binding
K_D _2 = 29 µM – 67% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 9

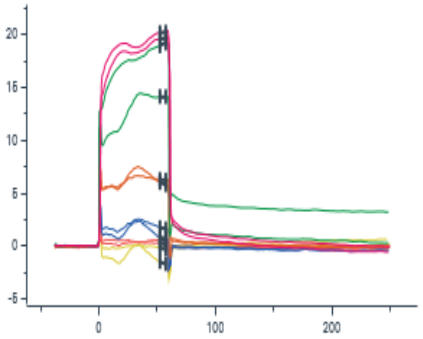


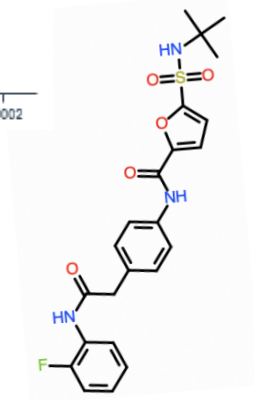
CACHE2-HO_1456_26

K_D = 86 µM – 116% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 19

PARENT MOLECULE







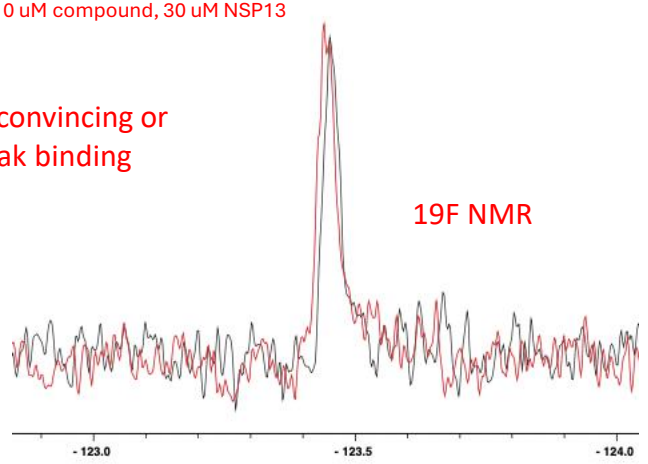
CACHE_1456_73

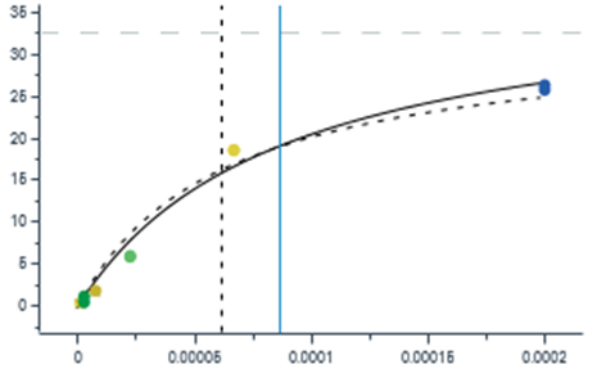
K_D = 45 µM – 88% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = no inhibition

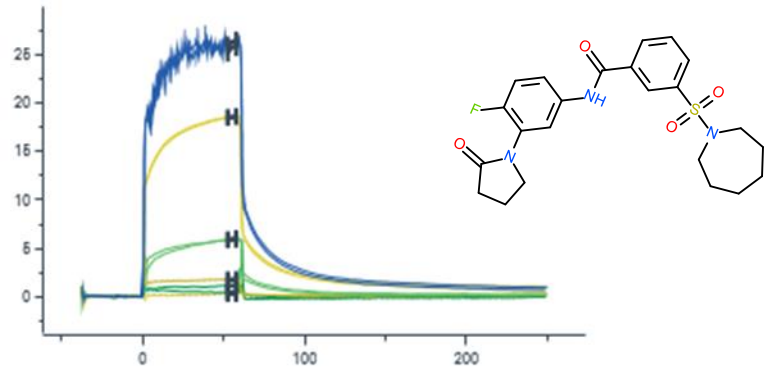
Black = 10 uM compound
Red = 10 uM compound, 30 uM NSP13

Unconvincing or weak binding

19F NMR



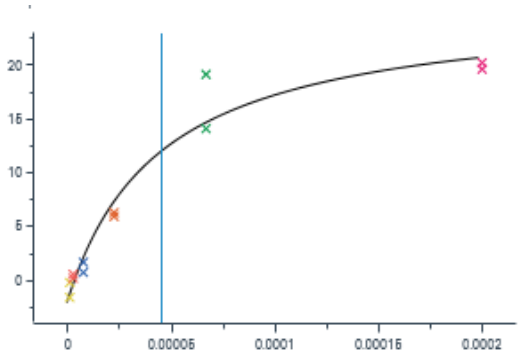


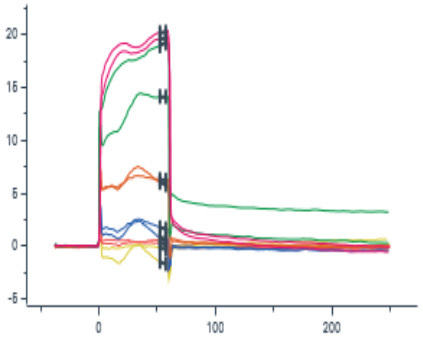


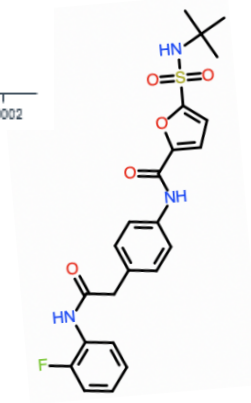
CACHE2-HO_1456_26

K_D = 86 µM – 117% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 19

PARENT MOLECULE



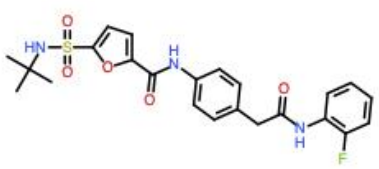
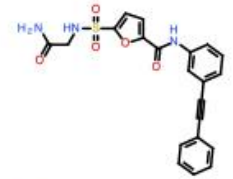
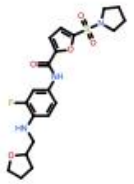
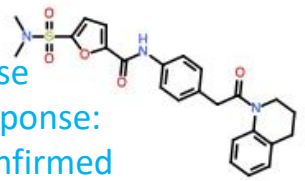
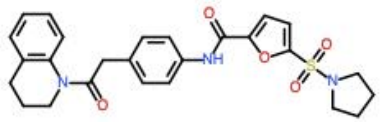
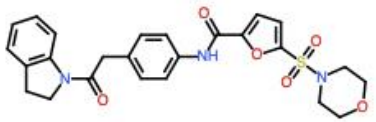
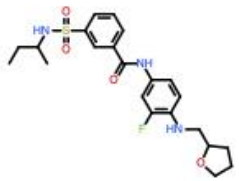
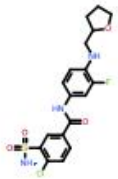
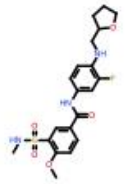
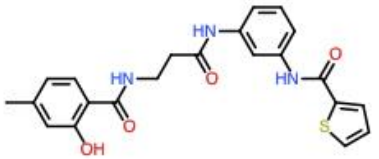
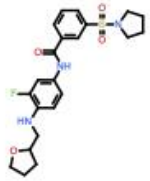
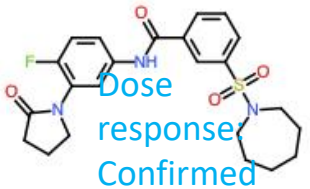
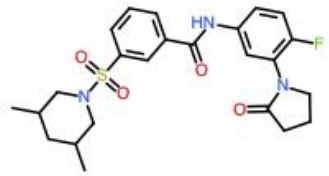




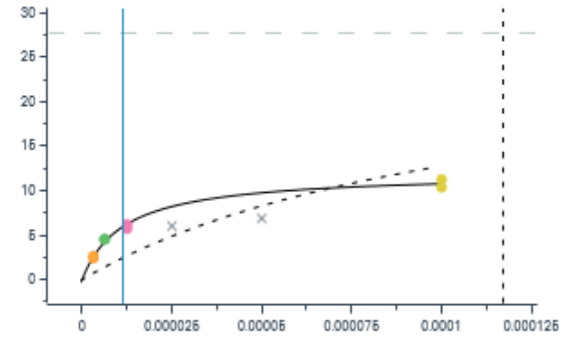
CACHE_1456_73

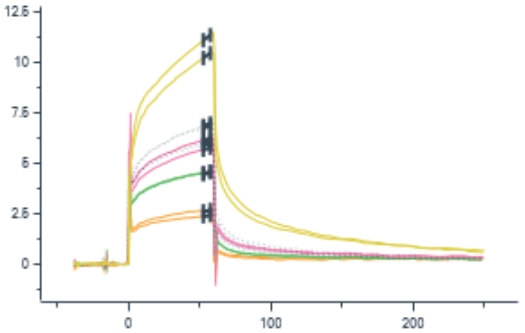
K_D = 45 µM – 88% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = no inhibition

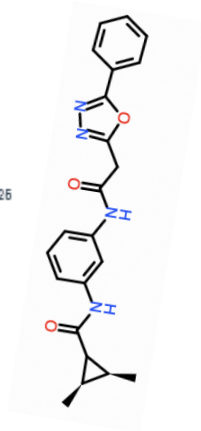
Tested analogs

 CACHE_ID CACHE2-HO_1456_38 Parent CACHE_1456_73 distance_to_pai 0	 CACHE_ID CACHE2-HO_1456_39 Parent CACHE_1456_73 distance_to_pai 0.1868	 CACHE_ID CACHE2-HO_1456_40 Parent CACHE_1456_73 distance_to_pai 0.218	 CACHE_ID CACHE2-HO_1456_41 Parent CACHE_1456_73 distance_to_pai 0.2416
 CACHE_ID CACHE2-HO_1456_23 Parent CACHE_1456_73 distance_to_pai 0.311	Dose response: Confirmed  CACHE_ID CACHE2-HO_1456_42 Parent CACHE_1456_73 distance_to_pai 0.3533	 CACHE_ID CACHE2-HO_1456_43 Parent CACHE_1456_73 distance_to_pai 0.3656	 CACHE_ID CACHE2-HO_1456_44 Parent CACHE_1456_73 distance_to_pai 0.383
 CACHE_ID CACHE2-HO_1456_21 Parent CACHE_1456_73 distance_to_pai 0.4035	 CACHE_ID CACHE2-HO_1456_22 Parent CACHE_1456_73 distance_to_pai 0.4542	 CACHE_ID CACHE2-HO_1456_24 Parent CACHE_1456_73 distance_to_pai 0.4548	 CACHE_ID CACHE2-HO_1456_13 Parent CACHE_1456_73 distance_to_pai 0.4593
 CACHE_ID CACHE2-HO_1456_20 Parent CACHE_1456_73 distance_to_pai 0.4618	 CACHE_ID CACHE2-HO_1456_8 Parent CACHE_1456_73 distance_to_pai 0.4746	Dose response: Confirmed  CACHE_ID CACHE2-HO_1456_26 Parent CACHE_1456_73 distance_to_pai 0.4751	 CACHE_ID CACHE2-HO_1456_25 Parent CACHE_1456_73 distance_to_pai 0.482

PARENT MOLECULE







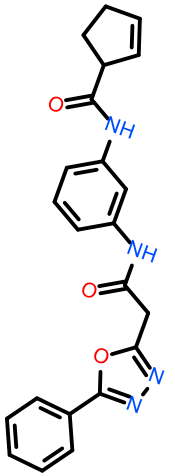
CACHE_1456_57

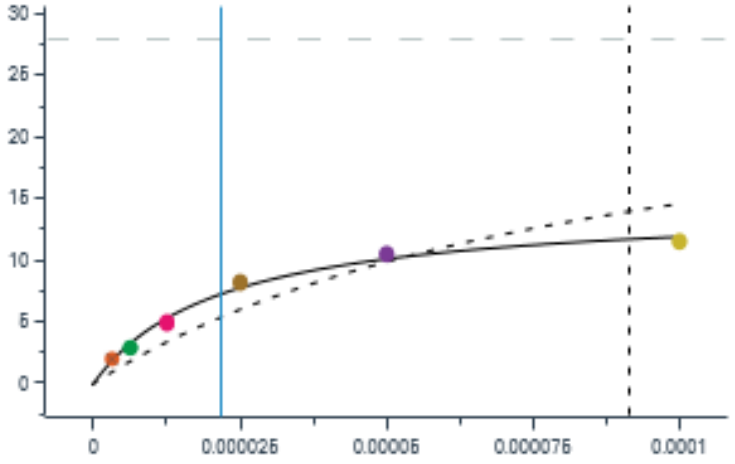
K_D (3% DMSO) = 12 µM – 43% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
%inhibition@50 µM_ATPase = 59%, upon retesting was 31%

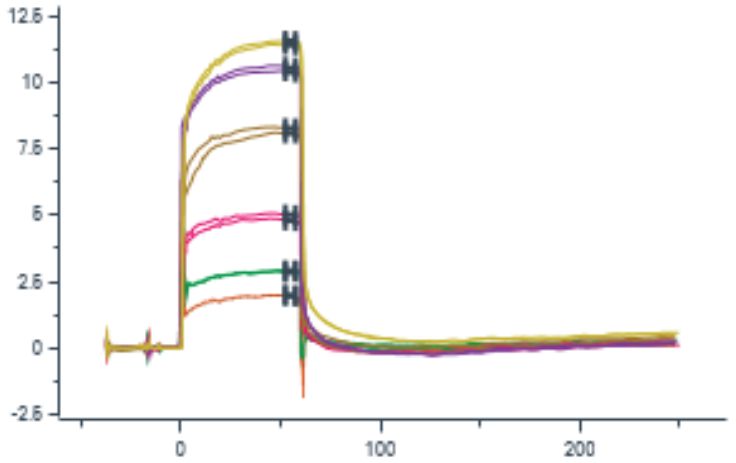
11 analogs of CACHE_1456_57 were submitted for round 2.
1 compound showed a binding response reaching saturation.

CACHE2-HO_1456_32

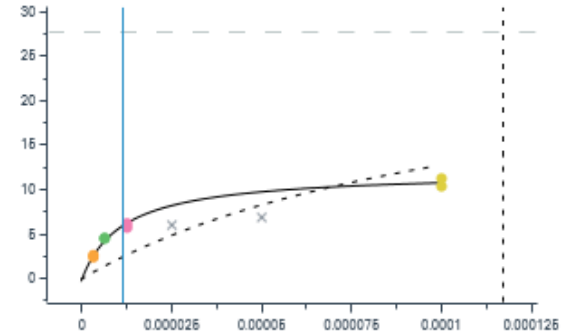
K_D = 22 µM – 52% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 24

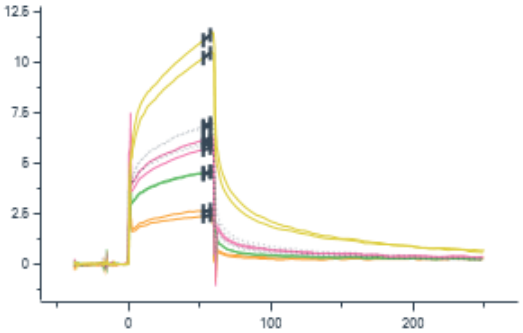


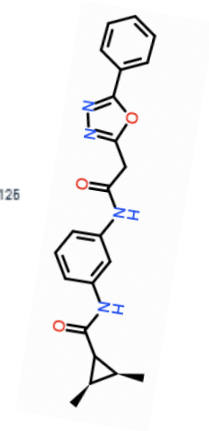




PARENT MOLECULE



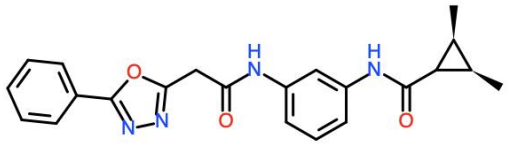




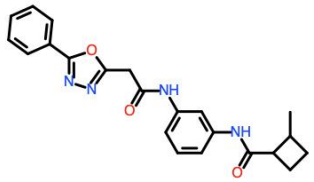
CACHE_1456_57

K_D (3% DMSO) = 12 µM – 43% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@100 µM)
%inhibition@50 µM_ATPase = 59%, upon retesting was 31%

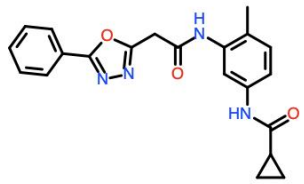
Tested analogs



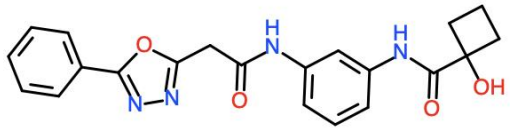
CACHE_ID CACHE2-HO_1456_27
Parent CACHE_1456_57
distance_to_parent 0



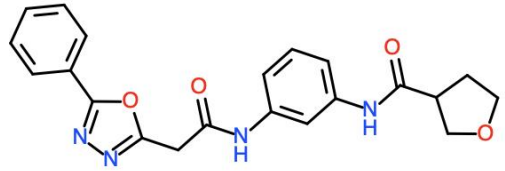
CACHE_ID CACHE2-HO_1456_28
Parent CACHE_1456_57
distance_to_parent 0.0303



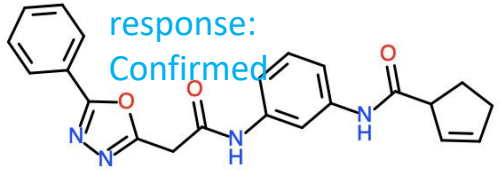
CACHE_ID CACHE2-HO_1456_29
Parent CACHE_1456_57
distance_to_parent 0.07805



CACHE_ID CACHE2-HO_1456_30
Parent CACHE_1456_57
distance_to_parent 0.08696

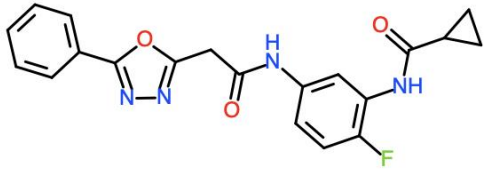


CACHE_ID CACHE2-HO_1456_31
Parent CACHE_1456_57
distance_to_parent 0.1215

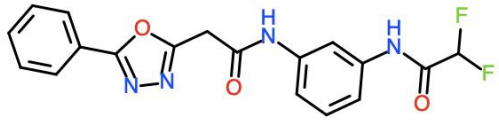


CACHE_ID CACHE2-HO_1456_32
Parent CACHE_1456_57
distance_to_parent 0.1215

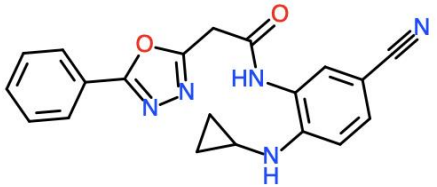
Dose response: Confirmed



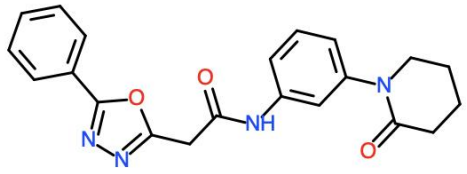
CACHE_ID CACHE2-HO_1456_33
Parent CACHE_1456_57
distance_to_parent 0.125



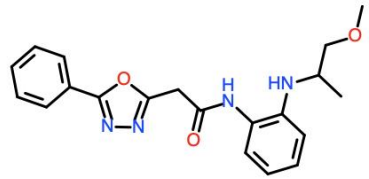
CACHE_ID CACHE2-HO_1456_34
Parent CACHE_1456_57
distance_to_parent 0.1408



CACHE_ID CACHE2-HO_1456_35
Parent CACHE_1456_57
distance_to_parent 0.1449

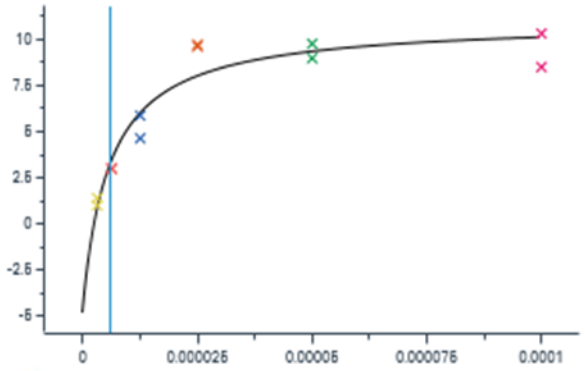


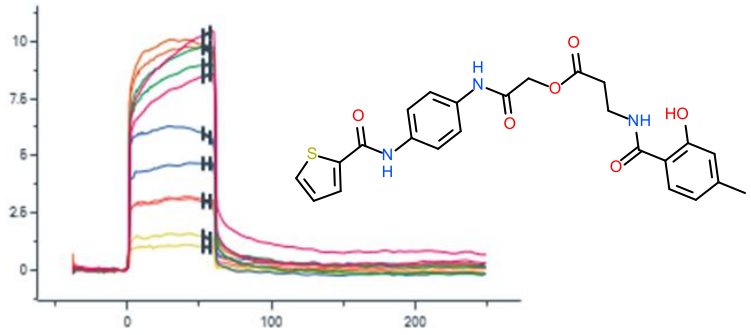
CACHE_ID CACHE2-HO_1456_36
Parent CACHE_1456_57
distance_to_parent 0.1507



CACHE_ID CACHE2-HO_1456_37
Parent CACHE_1456_57
distance_to_parent 0.1721

PARENT MOLECULE

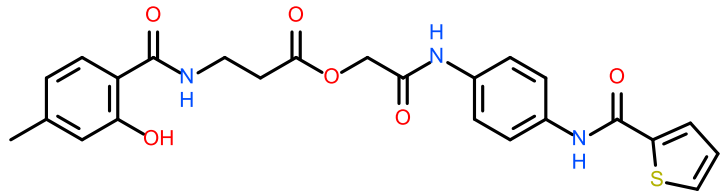




CACHE_1456_38

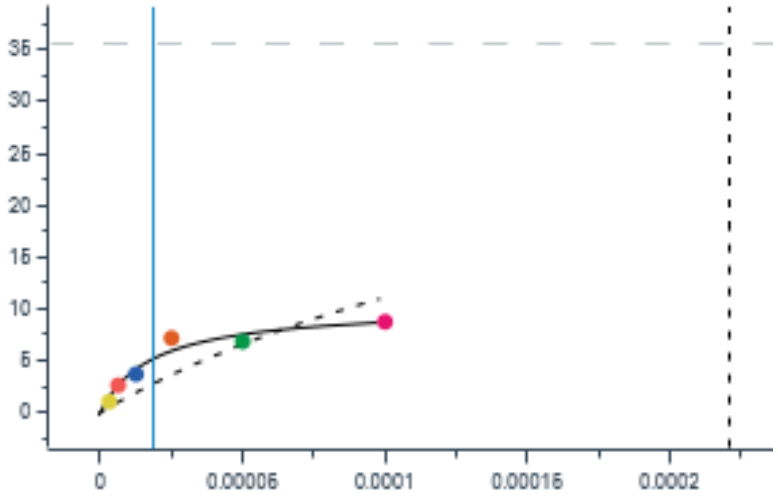
K_D = 6±1 µM – 52±1% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 20

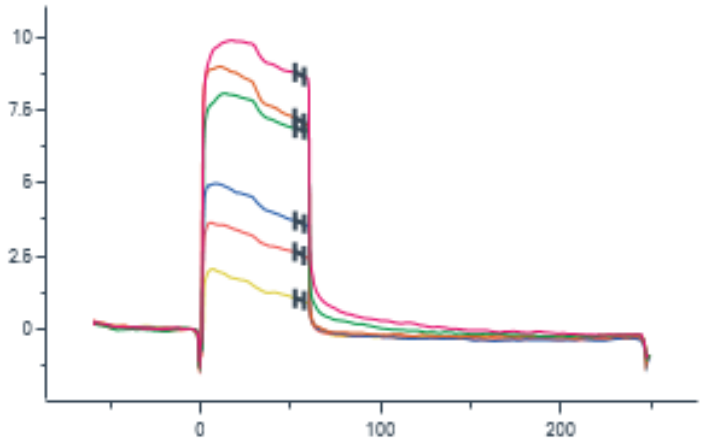
12 analogs of CACHE_1456_38, including the re-supplied hit molecule, were submitted for round 2.
1 compound (re-supplied parent molecule) confirmed weak binding by SPR, reaching saturation.



CACHE2-HO_1456_8

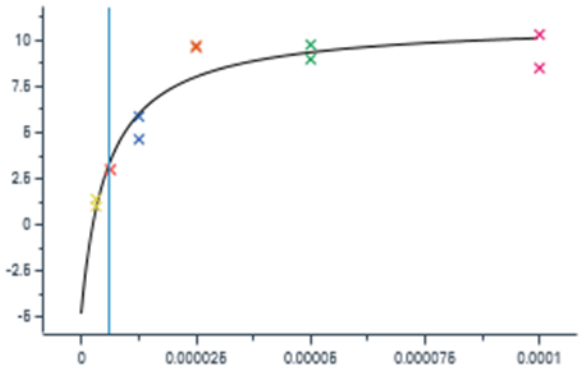
K_D = 19±0.4 µM – 30±1% binding
Selectivity (unrelated WDR5 protein) – 10% binding
IC_{50}_ATPase > 100 µM

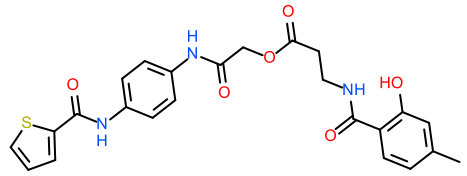




Tested analogs

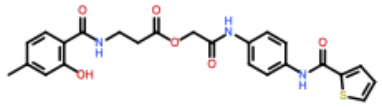
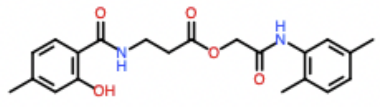
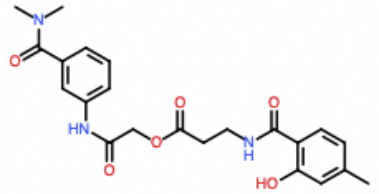
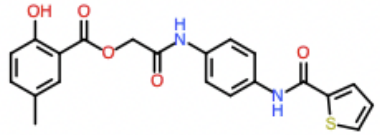
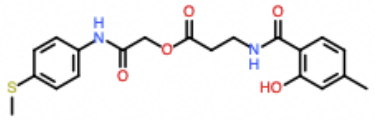
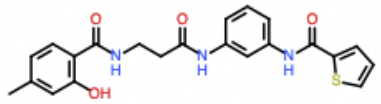
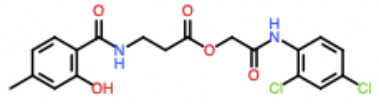
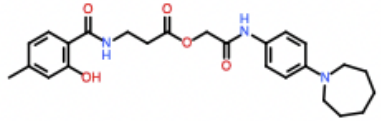
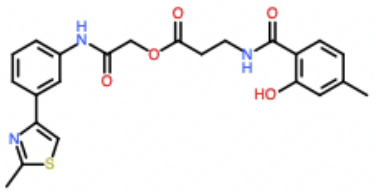
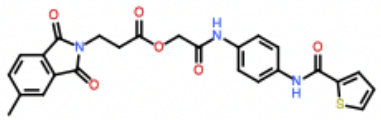
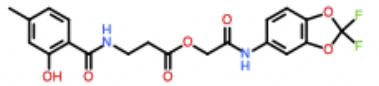
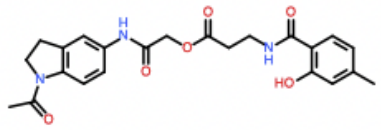
PARENT MOLECULE



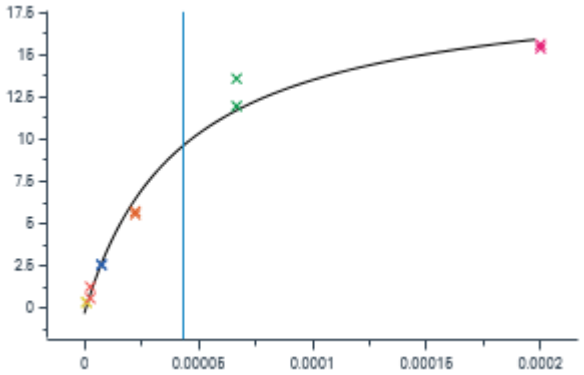


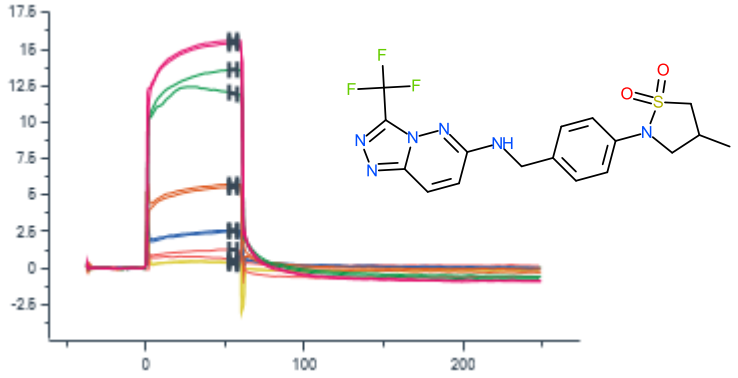
CACHE_1456_38

K_D = 6±1 µM – 52±1% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 20

Weak binding confirmed  CACHE_ID CACHE2-HO_1456_8 Parent CACHE_1456_38 distance_to_pai 0	 CACHE_ID CACHE2-HO_1456_9 Parent CACHE_1456_38 distance_to_pai 0.1759	 CACHE_ID CACHE2-HO_1456_10 Parent CACHE_1456_38 distance_to_pai 0.181	 CACHE_ID CACHE2-HO_1456_11 Parent CACHE_1456_38 distance_to_pai 0.1883
 CACHE_ID CACHE2-HO_1456_12 Parent CACHE_1456_38 distance_to_pai 0.1928	 CACHE_ID CACHE2-HO_1456_13 Parent CACHE_1456_38 distance_to_pai 0.1953	 CACHE_ID CACHE2-HO_1456_14 Parent CACHE_1456_38 distance_to_pai 0.2124	 CACHE_ID CACHE2-HO_1456_15 Parent CACHE_1456_38 distance_to_pai 0.2298
 CACHE_ID CACHE2-HO_1456_16 Parent CACHE_1456_38 distance_to_pai 0.2302	 CACHE_ID CACHE2-HO_1456_17 Parent CACHE_1456_38 distance_to_pai 0.3322	 CACHE_ID CACHE2-HO_1456_18 Parent CACHE_1456_38 distance_to_pai 0.3559	 CACHE_ID CACHE2-HO_1456_19 Parent CACHE_1456_38 distance_to_pai 0.3733

PARENT MOLECULE

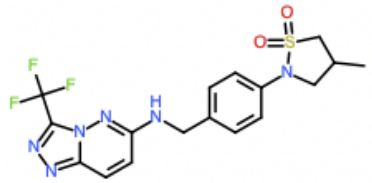




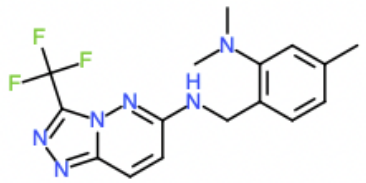
CACHE_1456_37

K_D = 43 µM – 71% binding
Selectivity (unrelated WDR5 protein) – mild binding
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 16

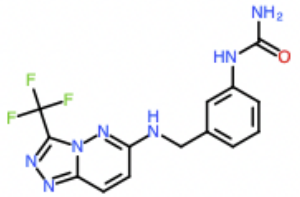
Tested analogs



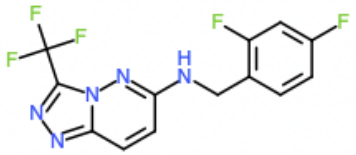
CACHE_ID CACHE2-HO_1456_1
Parent CACHE_1456_37
distance_to_pai 0



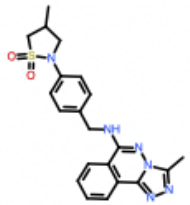
CACHE_ID CACHE2-HO_1456_2
Parent CACHE_1456_37
distance_to_pai 0.2492



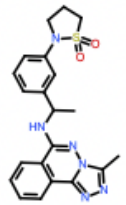
CACHE_ID CACHE2-HO_1456_3
Parent CACHE_1456_37
distance_to_pai 0.2701



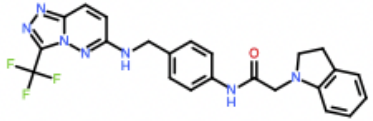
CACHE_ID CACHE2-HO_1456_4
Parent CACHE_1456_37
distance_to_pai 0.2871



CACHE_ID CACHE2-HO_1456_5
Parent CACHE_1456_37
distance_to_pai 0.306

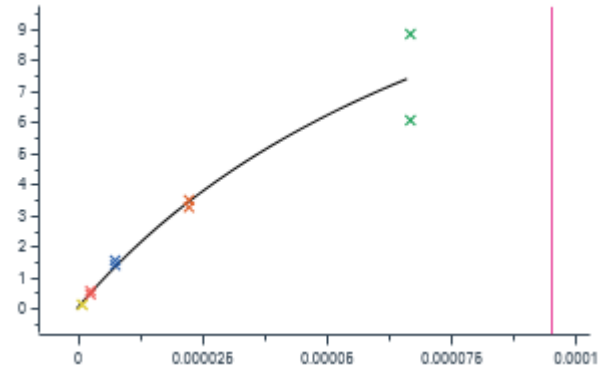


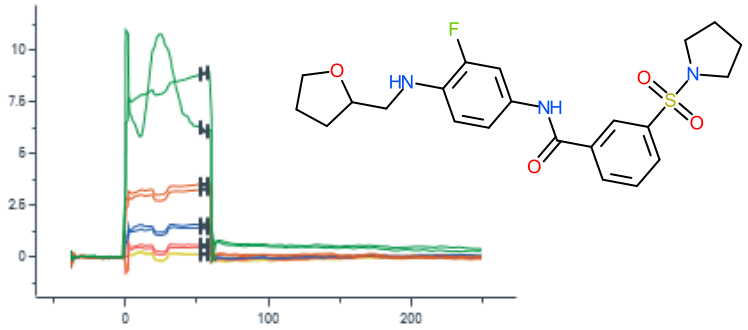
CACHE_ID CACHE2-HO_1456_6
Parent CACHE_1456_37
distance_to_pai 0.3307



CACHE_ID CACHE2-HO_1456_7
Parent CACHE_1456_37
distance_to_pai 0.3431

PARENT MOLECULE

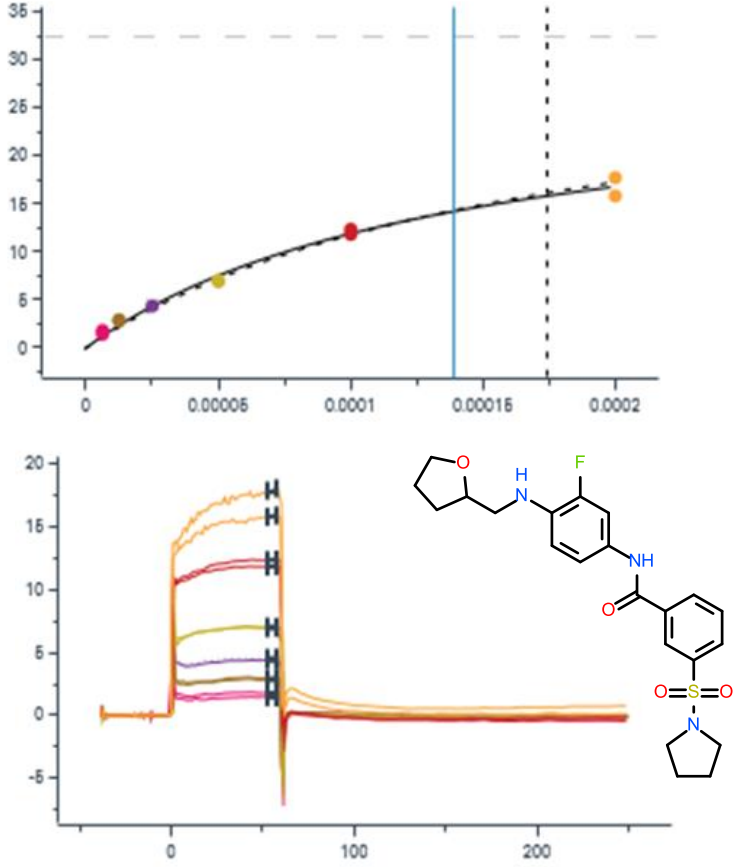




CACHE_1456_42

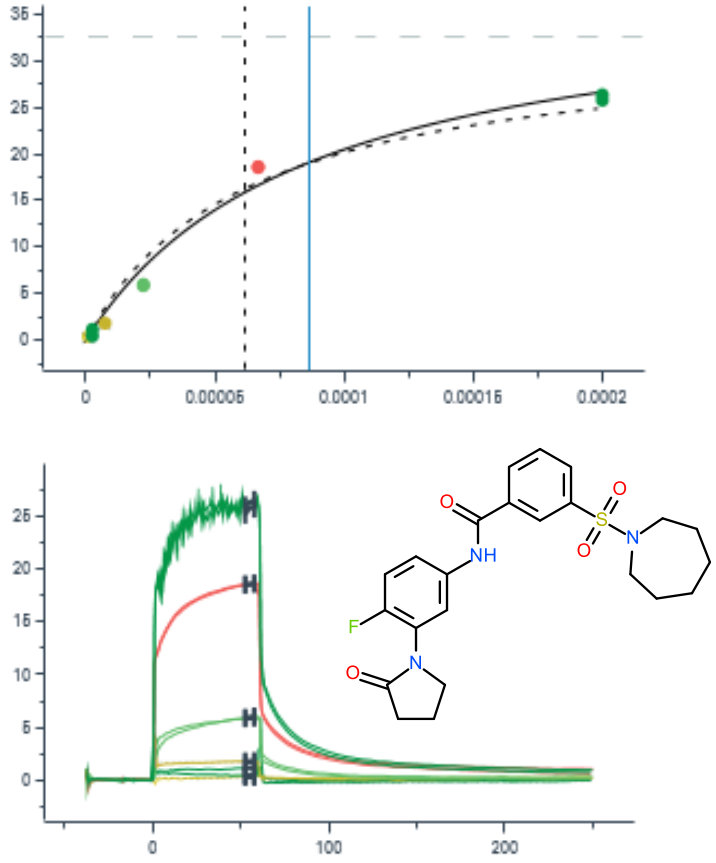
K_D = 95 µM (does not reach saturation) – 59% binding
aggreg@200 µM
%inhibition@50 µM_ATPase = 12

7 analogs of CACHE_1456_42 were submitted for round 2.
2 compounds (including re-supplied parent molecule) showed a dose dependent binding response with a tendency to reach saturation.



CACHE2-HO_1456_20

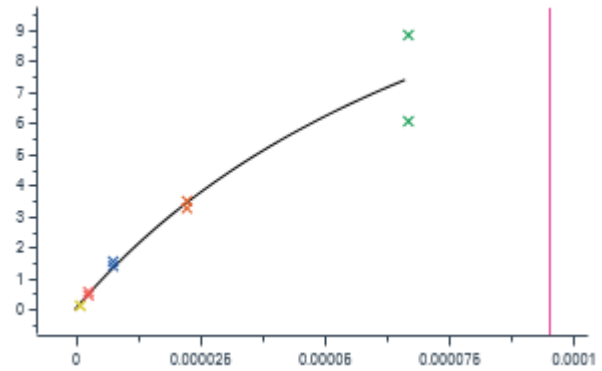
K_D = 139 µM – 88% binding
Selectivity (unrelated WDR5 protein) – Yes
%inhibition@50 µM_ATPase = 13

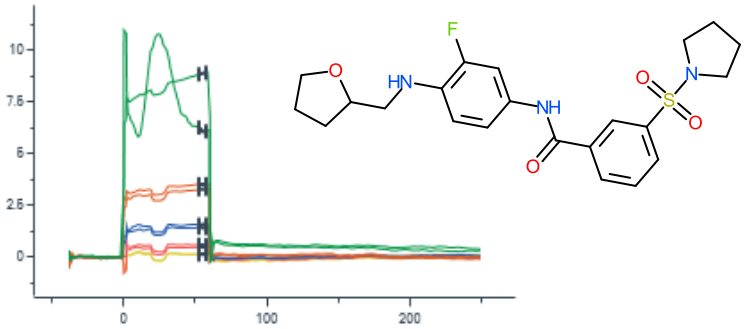


CACHE2-HO_1456_26

K_D = 86 µM – 117% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 19

PARENT MOLECULE





CACHE_1456_42

K_D = 95 µM (does not reach saturation) – 59% binding

aggreg@200 µM

%inhibition@50 µM_ATPase = 12

Tested analogs

Dose response: Confirmed

CACHE_ID	CACHE2-HO_1456_20
Parent	CACHE_1456_42
distance_to_pai	0

CACHE_ID	CACHE2-HO_1456_21
Parent	CACHE_1456_42
distance_to_pai	0.1356

CACHE_ID	CACHE2-HO_1456_22
Parent	CACHE_1456_42
distance_to_pai	0.2034

CACHE_ID	CACHE2-HO_1456_23
Parent	CACHE_1456_42
distance_to_pai	0.2182

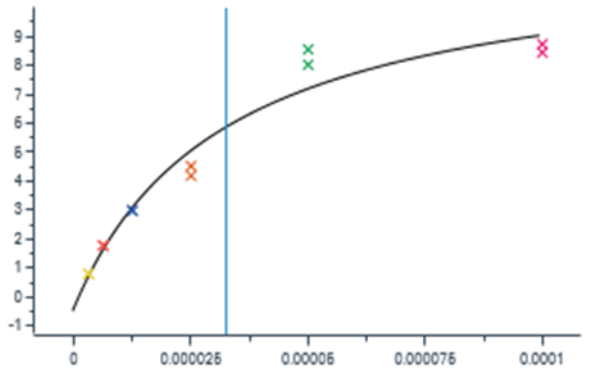
CACHE_ID	CACHE2-HO_1456_24
Parent	CACHE_1456_42
distance_to_pai	0.2191

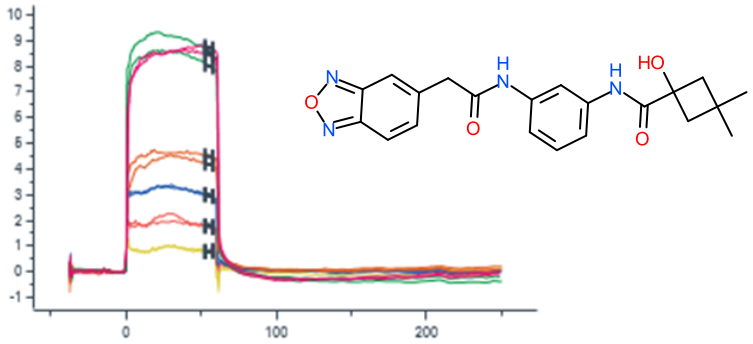
CACHE_ID	CACHE2-HO_1456_25
Parent	CACHE_1456_42
distance_to_pai	0.2431

Dose response: Confirmed

CACHE_ID	CACHE2-HO_1456_26
Parent	CACHE_1456_42
distance_to_pai	0.2451

Round 1 HIT MOLECULE





CACHE_1456_17

K_D = 33±2 µM – 50±13% binding
Selectivity (unrelated WDR5 protein) – Yes
DLS (solub@200 µM)
%inhibition@50 µM_ATPase = 5

No analog in Round 2