

Supplementary information

The iPPI-DB initiative: A community-centered database of Protein-Protein Interaction modulators

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ADD NEW CONTENT

ID	Bibliography	PDB id	Architecture	Composition	PPI	Compounds	Activity Tests
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Let's get started!
Step 1 on 8

Please provide a valid ID for your bibliographic source, either a PubMed ID a patent ID, or a DOI. This ID should correspond to a bibliographic source in its final format. Therefore, PubMed articles in « Just Accepted » format should not be used as a source of data as they are not considered the official version of record.

PubMed ID	Patent	DOI
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Bibliographic ID *

10.1158/0008-5472.CAN-12-2807

Next step

Step 1: Enter the ID of the bibliographic source, such as PubMed ID, patent ID or DOI. The website will automatically fetch the information (title, author...).

ID	Bibliography	PDB id	Architecture	Composition	PPI	Compounds	Activity Tests
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Bibliography informations
Step 2 on 8

According to the ID you provided, we fetched the following data. Please check them and click on the appropriate check boxes.

DOI 10.1158/0008-5472.CAN-12-2807

MDM2 Small-Molecule Antagonist RG7112 Activates p53 Signaling and Regresses Human Tumors in Preclinical Cancer Models

Tovar C., Graves B., Packman K., Filipovic Z., Xia B. H. M., Tardell C., Garrido R., Lee E., Kolinsky K., To K.-H., Linn M., Podlaski F., Wovkulich P., Vu B., Vassilev L. T.
Cancer Research

This publication contains :

- Cytotoxicity data
- In silico study
- In vitro study
- In vivo study
- In cellulo study
- Pharmacokinetic study
- X-Ray data

Next step

Step 2: Select the studies carried out within the publication.

ID	Bibliography	PDB id	Architecture	Composition	PPI	Compounds	Activity Tests
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Your PDB ID please

Step 3 on 8

Please provide a valid PDB code that contains the structure of the full PPI complex and all protein partners.
For example, in the case of a heterodimer the PDB should contain partner A and partner B.

PDB ID *

IYCR

Next step

Step 3: Enter the PDB ID containing the structure of the protein-protein interaction.

ID	Bibliography	PDB id	Architecture	Composition	PPI	Compounds	Activity Tests
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Which architecture fits your PPI?

Step 4 on 8

Now you need to select an architecture for the PPI complex among the proposed schematics below.
If your PPI complex is not among them, please select « Custom »

PPI Complex Type:
Inhibited

Inhibited

<p>Hetero2-merAB</p>	<p>Homo2-merA2</p>	<p>Custom</p>
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Stabilized

<p>Hetero2-merAB</p>	<p>Homo2-merA2</p>	<p>Hetero2-merA2</p>
<p>Hetero3-merA2</p>	<p>Hetero3-merA2 dimer</p>	<p>Hetero4-merA2</p>
<p>Ring Like3-merA2</p>	<p>Ring Like5-merA2</p>	<p>Custom</p>

Next step

Step 4: Select the mode of action of the compounds acting on the interaction between "Inhibited" or "Stabilized" and the type of structural architecture of the target

Protein complex assignment

Step 5 on 8

For the PDB code: **1YCR**You have selected an **Hetero2merAB** that is **inhibited** by the binding of PPI modulator.

Please select the protein that is bound by the modulator and also the protein partner if applicable. You also need to specify the PFAM protein domain(s).

Complex type *	Protein *	Domain
Partner complex	P04637 (Cellular tumor ant	Unknown
Complex type *	Protein *	Domain
Bound complex	Q00987 (E3 ubiquitin-prot	Unknown

Next step

Step 5: Choose the protein that is bound by the compound (bound) and the protein that is displaced by the compound (partner)

PPI target family and associated disease

Step 6 on 8

You have selected an **Hetero2merAB** that is **inhibited** by the binding of PPI modulator.

Please select a PPI target family name for the PPI you are describing. If not already present in the given list, please suggest one.

Also, please select a known disease associate with the PPI you are describing as listed in the MONDO database.

PDB ID	1YCR
PPI Family *	MDM2-Like / P53
Associated diseases	cancer x
Search for associated diseases	cancer

Next step

	Associate to
cancer	MONDO MONDO:0004992
cancerophobia	MONDO MONDO:0003736
cancer of long bone of upper limb	MONDO MONDO:0100085

Step 6: Select/Create the PPI family in the dropdown list, then the known associated diseases. The associated diseases list is built from the Mondo Disease Ontology.

List the compounds of the publication

Step 7 on 8

Please fill the fields below and provide naming and structure information about all the compounds present in the publication.

Name your compound

Name in publication *

RG7112

Common Name

RG7112

PDB Ligand ID

1F0

Draw it



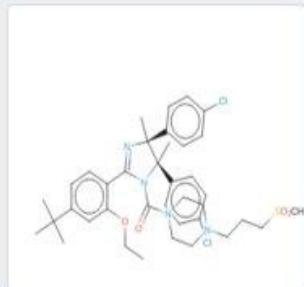
Paste SMILE code



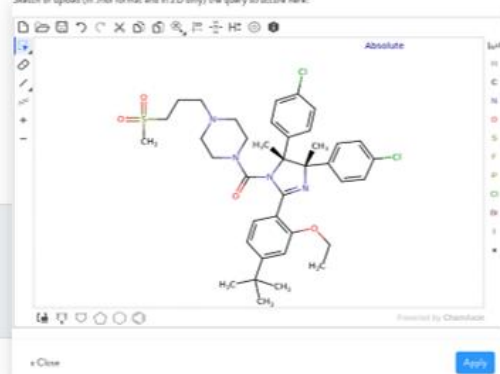
Sketch your compound

Molecule composition as SMILES

```
CCOc1cc(ccc1C2=N[C@@](C)(c3ccc(Cl)cc3)[C@](C)(N2C(=O)N4CCN(CCC[S]
(C)(=O)=O)CC4)c5ccc(Cl)cc5)C(C)(C)C
```



Sketch or upload (in .mol format and in 2D only) the query structure here:



Add complementary informations

 Does this compound contain one or more macrocycles?

[+ Add an other compound](#)

Step 7: Fill the form describing the compounds according to their name in the publication, their common name, their 3-character PDB ID if any. The compound can be directly built from the SMILES code, drawn using MarvinSketch from ChemAxon, or by pasting a IUPAC code into the MarvinSketch window.

Activity tests

Step 8 on 8

Describe all your activity tests and their results.

Test description

Test type *

Biochemical assay

Test name *

HTRF

Test modulation type *

Inhibition

Total number of active compounds *

1

Test results

Compound name *

RG7112

Modulation type *

Inhibition

Activity type *

IC50 (half maximal inhibitory con

Activity *

18

Activity unit

nmol

Only required if 'activity type' is not Kd ratio.

Test description



Test type *

Cellular assay

Test name *

MTT-assay

Test modulation type *

Inhibition

Total number of active compounds *

1

Cell line

SJSA-1

Test results



Compound name *

RG7112

Modulation type *

Inhibition

Activity type *

EC50 (half maximal effective con

Activity *

0.4

Activity unit

μmol

Only required if 'activity type' is not Kd ratio.

Step 8: Describe activity tests and their results. First, choose the test type: "Biochemical assay" or "Cellular assay". Select the test name, the modulation type (Inhibition, Binding or Stabilization), the number of active compounds and the cell line for the "Cellular assay". Second, fill the activity for each compound (IC50, EC50, Kd, Ki, Kd ratio), which can be declined in different unit (M, mM, μM, nM, pM).

Describe pharmacokinetic test

Step 9 on 9

Describe all your pharmacokinetic tests and their results.

Test description

Test name *	Organism *	Administration mode *	Concentration in mg/l
Mouse PK PO	Mus musculus	ADMINISTRATION_MODES_PC	
Dose in mg/kg *	Dose interval, in hours		
10			

Test results

Tolerated	Oral Bioavailability (%F)	T _{1/2} (mn)	Tmax (mn)
True	46	152	
<input checked="" type="checkbox"/> Area under curve available	<input checked="" type="checkbox"/> Clearance available	<input type="checkbox"/> Maximal concentration available	<input checked="" type="checkbox"/> Volume distribution (Vd) available
Compound name *			
1			

[+ Add result](#)

Step 9: In the case you choose "Pharmacokinetic study" at step 2, a supplementary step appears to fill the data related to these studies. The same is true for cytotoxic assays.

Contribution almost complete!

Your contribution is not saved in the data base yet! Before saving it, you can take a moment to review. You can go back to any step to see what you provided, and then click next for the followings steps up to this final step. Once satisfied, please agree with the following terms and save your contribution.

I understand that the data provided will be, once validated, published publicly on the website. *

[Save in Database](#)

Final step (a): Validation of your contribution to save in database. Compounds added are available in the query mode in orange tagged as "not validated".

2200 not validated



Common name : RG7112

PPI Family : None

Molecular weight: None g/mol

[Read more](#)

Bibliography

MDM2 Small-Molecule Antagonist RG7112 Activates p53 Signaling and Regresses Human Tumors in Preclinical Cancer Models

Tovar C., Graves B., Packman K., Filipovic Z., Xia B. H. M., Tardell C., Garrido R., Lee E., Kolinsky K., To K.-H., Linn M., Podlaski F., Wovkulich P., Vu B., Vassilev L. T. *Cancer Research* (2013) DOI - 10.1158/0008-5472.CAN-12-2807

Contains : X-Ray Data, In Vitro Study, In Cellulo Study, In Vivo Study

PPI Architecture

PDB code of the PPI: [1YCR](#)

PPI family: MDM2-Like / P53

Total number of pockets in the complex: 1

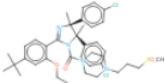
PPI name: MDM2 / P53

PPI symmetry: AS (asymmetric)

Diseases: cancer (MONDO:0004992)

Complex type	Protein	Domain
Partner	P04637	unknown
Bound	Q00987	unknown

Compounds

Compound Name In The Publication	Chemical structure	Iupac Name	Pdb Ligand Id	iPPI-DB ID
RG7112			1FO	2200

Tests

Test Activity Description - MTT-assay

Protein Domain Bound Complex: MDM2 Q00987-unknown (1)

Test Type: Cellular assay

Total Number Of Active Compounds: 1

Is Primary: False

Test Modulation Type: Inhibition

Cell Line: SJSA-1

Compound	Modulation type	Activity type	Activity
RG7112	Inhibition	pEC50	6.40

Test Activity Description - HTRF

Protein Domain Bound Complex: MDM2 Q00987-unknown (1)

Test Type: Biochemical assay

Total Number Of Active Compounds: 1

Is Primary: False

Test Modulation Type: Inhibition

Cell Line: None

Compound	Modulation type	Activity type	Activity
RG7112	Inhibition	pIC50	7.74

Final step (b): The final page summarizing all information about your contribution.