Virtual Screening

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The holistic integration of virtual screening in drug discovery

Yusuf Tanrikulu[1], Björn Krüger[1] and Ewgenij Proschak[2]

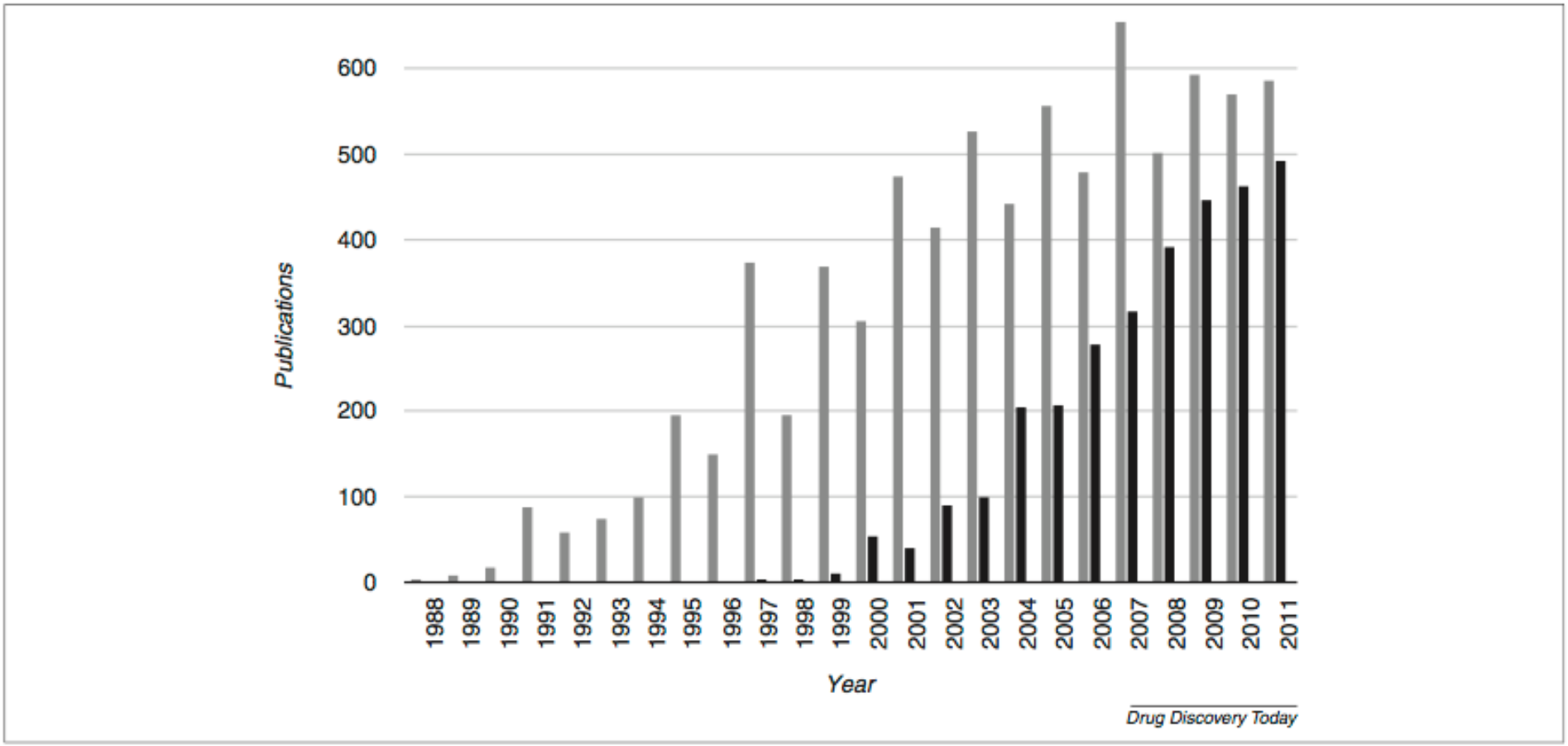

FIGURE 1

Chronological overview of the number of high-throughput screening (HTS; gray bars) and virtual screening (VS; black bars) publications according to ISI Web of Knowledge (Thomson Reuters, http://www.isiknowledge.com).

ZINC − A Free Database of Commercially Available Compounds for Virtual Screening

John J. Irwin and Brian K. Shoichet*

Department of Pharmaceutical Chemistry, University of California San Francisco, Genentech Hall, 600 16th Street, San Francisco, California 94143

Received September 22, 2004

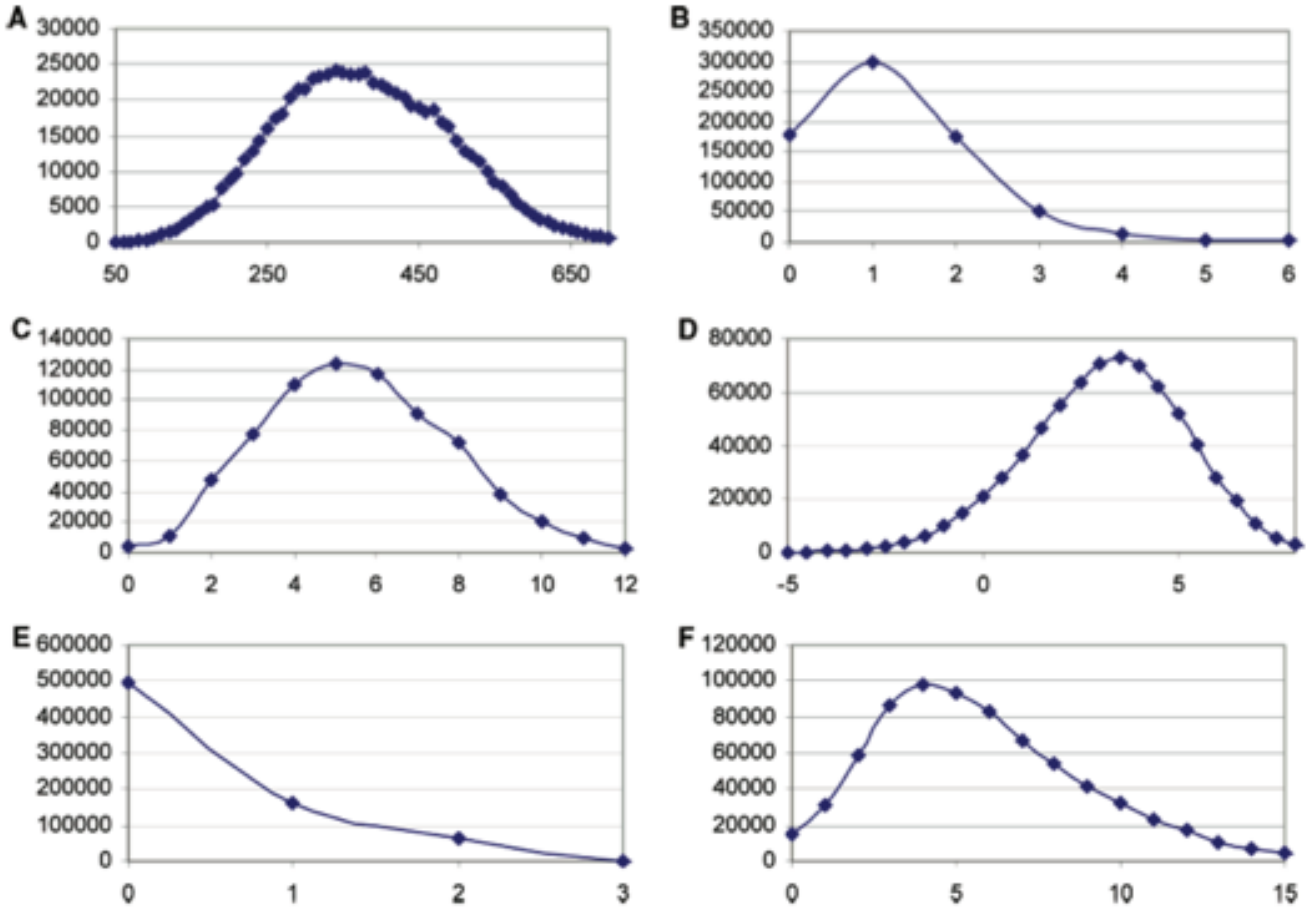

Figure 1. Molecular properties of compounds in ZINC. A. molecular weight, B. hydrogen-bond donors, C. hydrogen-bond acceptors, D. calculated LogP, E. violations of Lipinski's rule-of-fives, and F. rotatable bonds.

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ZINCPharmer: pharmacophore search of the ZINC database

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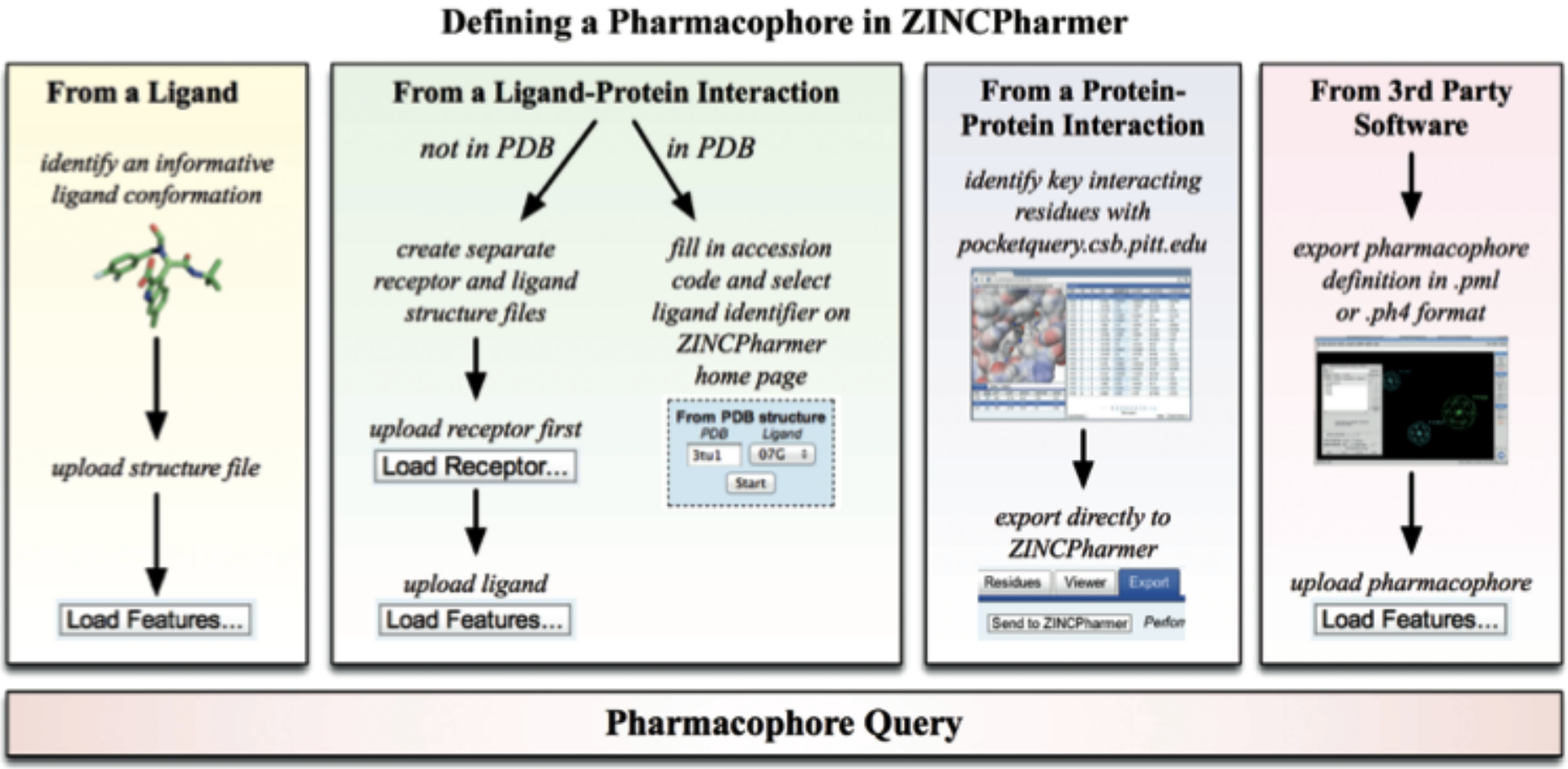
Received January 16, 2012; Revised April 4, 2012; Accepted April 12, 2012



http://zincpharmer.csb.pitt.edu

ZINCPharmer

ZINCPharmer is free pharmacophore search software for screening the purchasable subset of the ZINC database (updates occur monthly). ZINCPharmer can import **LigandScout** and **MOE** pharmacophore definitions, as well as **identify pharmacophore features** directly from structure.

Search ZINC

Java Problems? Try HTML5

From PDB structure

PDB *Ligand*

N/A

Start

User Guide and Forum

Video Tutorials: Defining Pharmacophores Searching and Filtering

Targeting a protein-protein interaction? Design a pharmacophore from the PPI with PocketQuery.

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Interactive Examples

Teach-Discover-Treat: DHODH (PDB)

As part of the Teach-Discover-Treat competition, this pharmacophore for the anti-

ZINCPharmer Entries:

1. Ligand_23.mol2 2. Receptor_T3twiOO.pdb

Blocker	TASK-3 IC_{50} (μM)
THPP (23)	0,035
THPP (12f)	0,074
A1899	0,35
THPP (17e)	0.57
Doxapram	23,1
Mibefradil	24.6
L-703,606	45.5
GW2974	50.1
Loratadine	63.4
Dihydro-Beta-erythroidine	73.8
Mevastatin	159

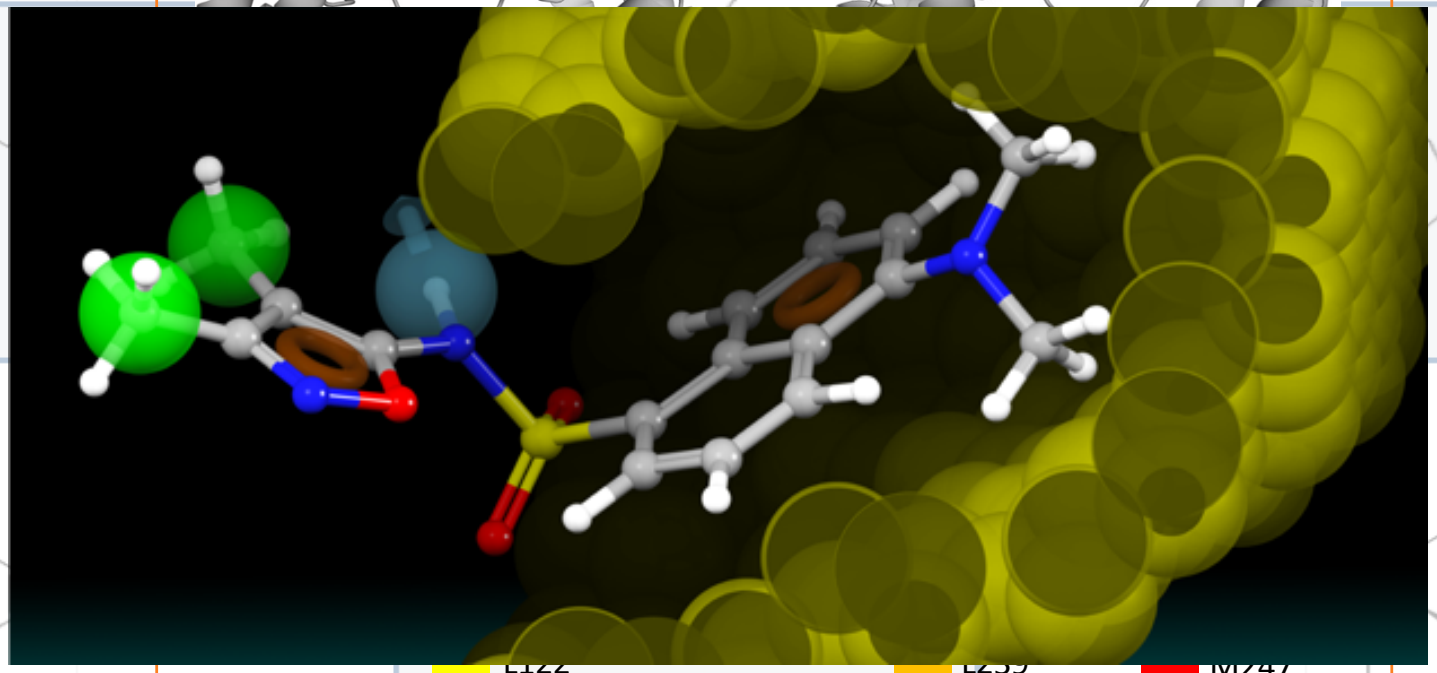
What molecular characteristics are necessary for molecular recognition of a blocker for TASK-3 channels?

Hypothesis 1:

The selected blockers interacts with TASK-3 similar to the intracellular blocker A1899 because they share common molecular characteristics

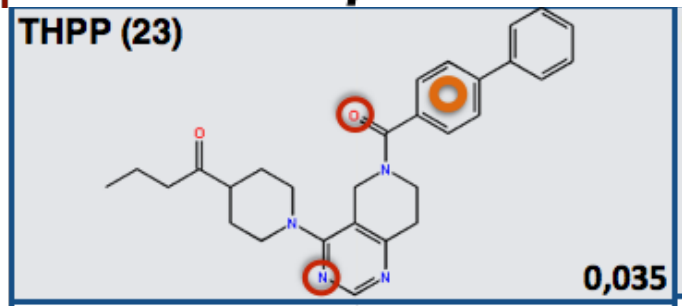
A1899

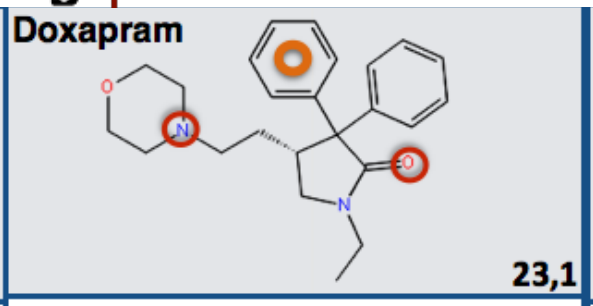
e-Pharmacophore modeling (Phase)

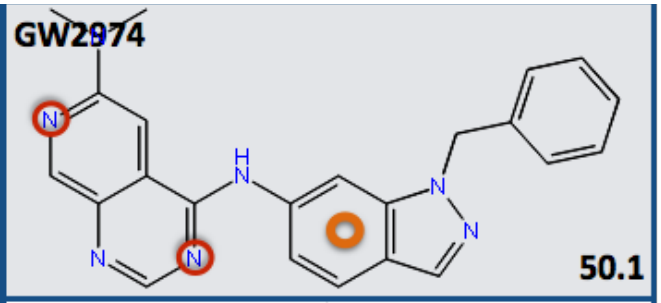


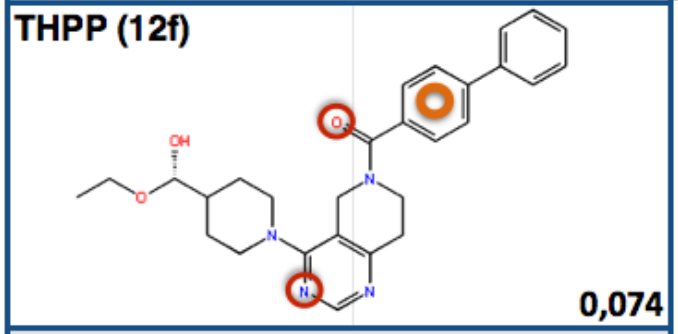
e-Pharmacophore modeling

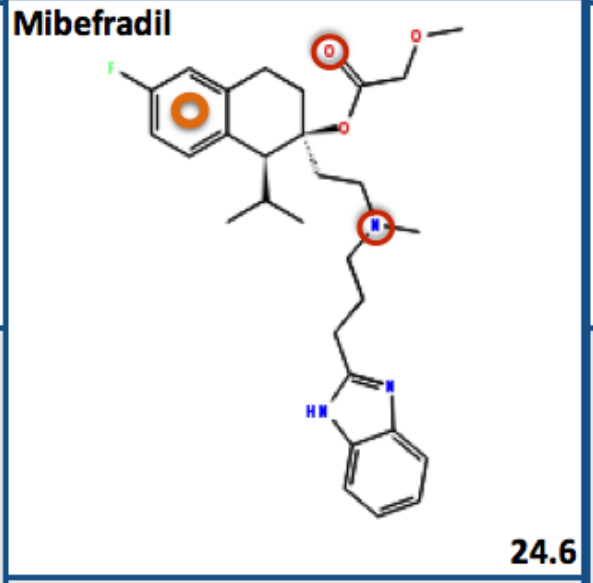
(Hydrogen bond acceptor); (Aromatic ring)

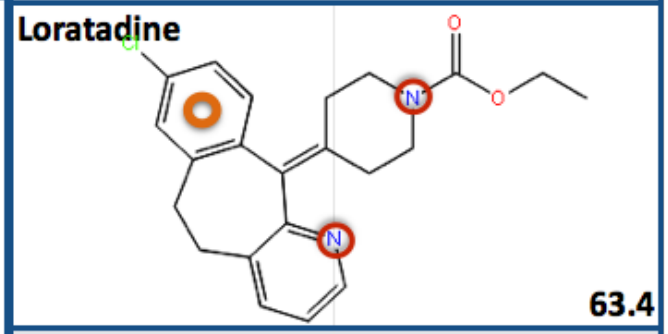


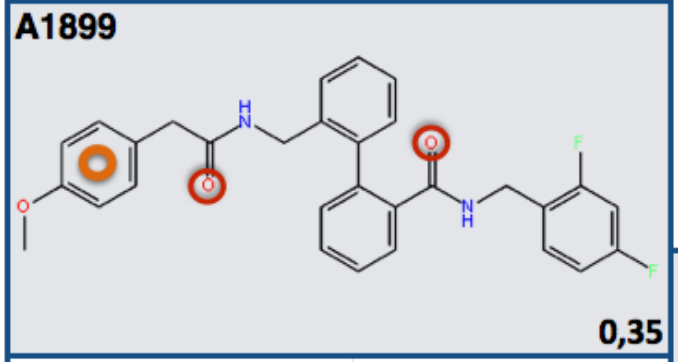


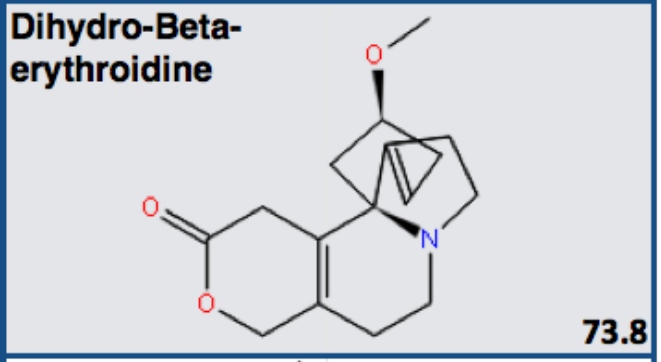


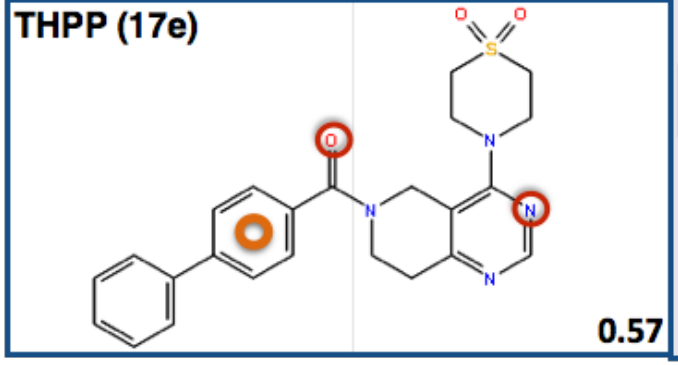


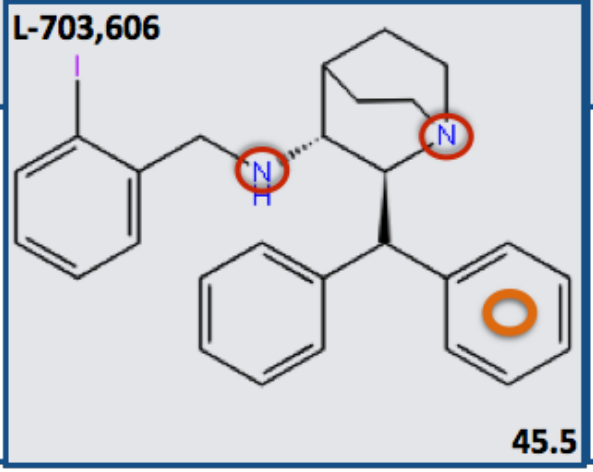


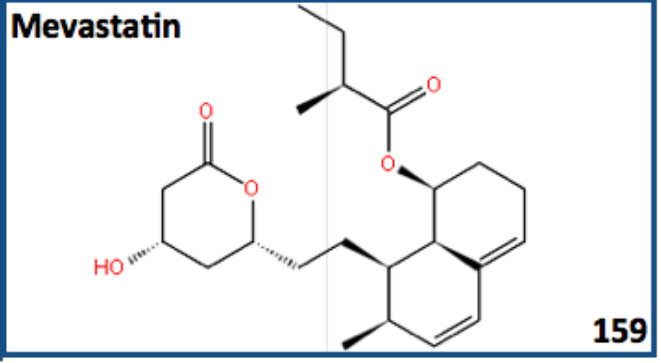




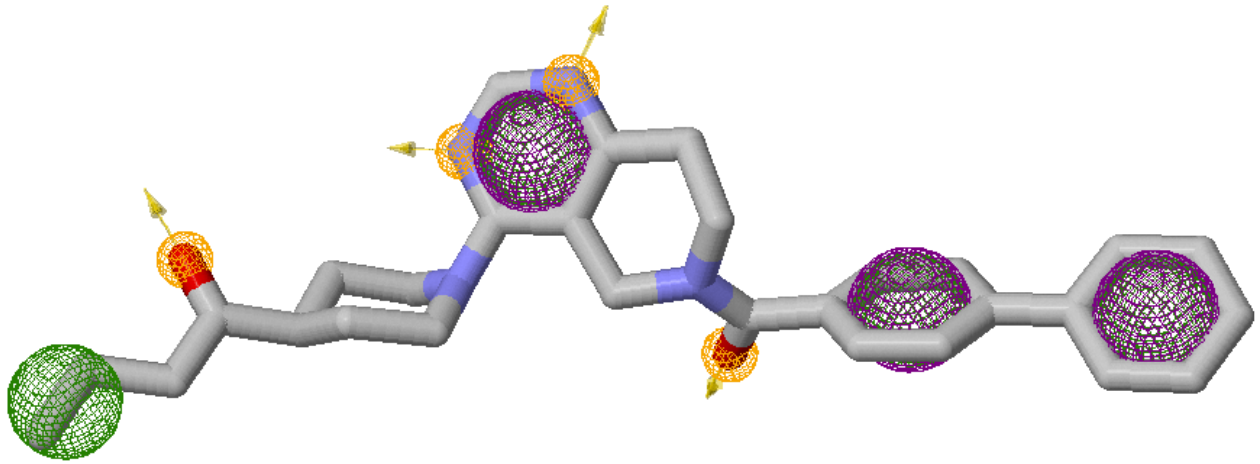








zincpharmer.csb.pitt.edu/pharmer.html



Pharmacophore | Filters | Viewer

Submit Query

	Pharmacophore Class	x	y	z	Radius	Enabled	
>	Aromatic	-11.46	-4.16	12.09	1.10	☑	▾
>	Aromatic	-5.41	-1.23	9.54	1.10	☑	▾
>	Aromatic	-2.09	1.56	9.38	1.10	☑	▾
>	HydrogenAcceptor	-11.51	-3.04	12.90	0.50	☑	▾
>	HydrogenAcceptor	-12.59	-4.94	11.94	0.50	☑	▾
>	HydrogenAcceptor	-7.99	-3.49	8.35	0.50	☑	▾
>	HydrogenAcceptor	-14.77	-9.79	11.87	0.50	☑	▾
>	Hydrophobic	-11.46	-4.16	12.09	1.00	☑	▾
>	Hydrophobic	-5.41	-1.23	9.54	1.00	☑	▾
>	Hydrophobic	-2.09	1.56	9.38	1.00	☑	▾
>	Hydrophobic	-13.88	-13.25	12.00	1.00	☑	▾

Add Feature | Load Features... | Load Receptor... | Clear ▾ | Load Session... | Save Session...

Results

Name	RMSD	Mass	RBnds
No Query Specified			

Save Results...

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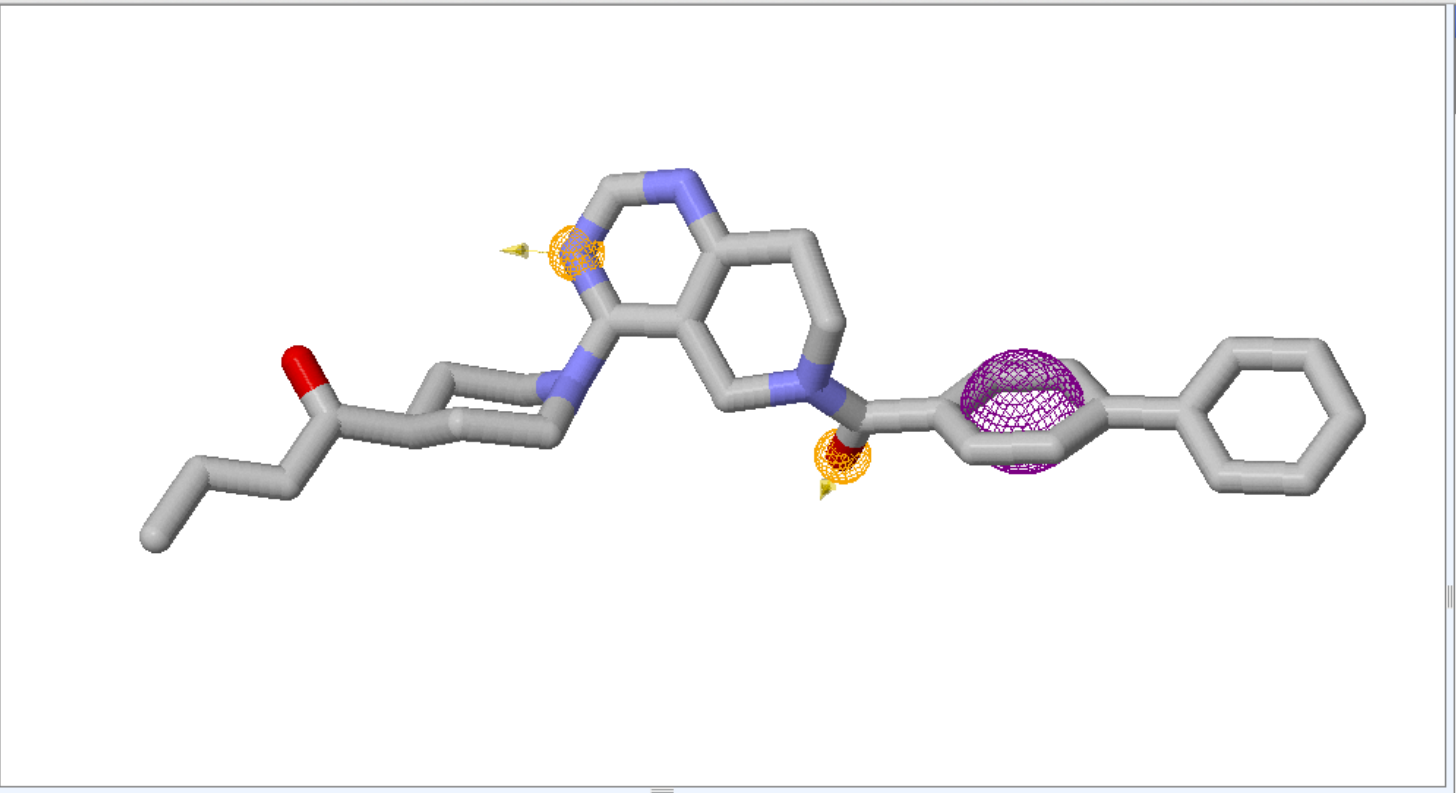

Results

Name	RMSD	Mass	RBnds
No Query Specified			

Pharmacophore | Filters | Viewer — Submit Query

	Pharmacophore Class	x	y	z	Radius	Enabled	
>	Aromatic	-5.41	-1.23	9.54	1.10	☑	▾
>	HydrogenAcceptor	-12.59	-4.94	11.94	0.50	☑	▾
>	HydrogenAcceptor	-7.99	-3.49	8.35	0.50	☑	▾

Add Feature | Load Features... | Load Receptor... | Clear ▾ | Load Session... | Save Session...

Save Results...

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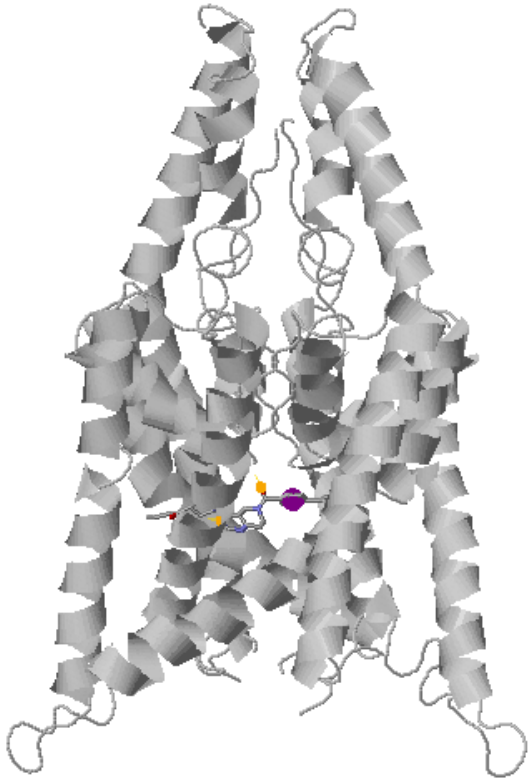

Pharmacophore | Filters | Viewer

Submit Query

Ligand
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Style: Sticks
Color: RasMol CPK

Receptor Residues
Visible: ☑
Style: Cartoon
Color: RasMol CPK

Results
Visible: ☐
Style: Sticks
Color: RasMol CPK

Query
Visible: ☑

Receptor Surface
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Color: Map Partial Charge (pdb on
Transparency:

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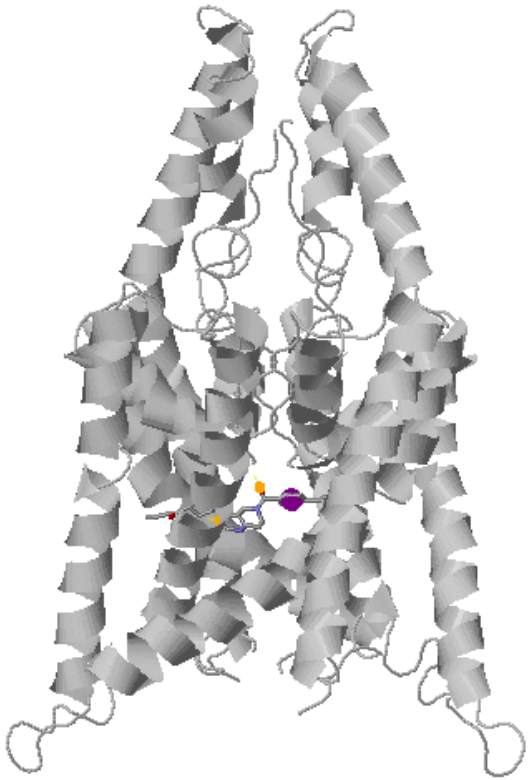

Pharmacophore | Filters | Viewer

Submit Query

Hit Reduction

Max Hits per Conf:	1
Max Hits per Mol:	1
Max Total Hits:	500
Max RMSD:	1

Hit Screening

≤ Molecular Weight ≤

≤ Rotatable Bonds ≤

Subset Selection

ZINC Purchasable: Last Updated 12

Descriptions

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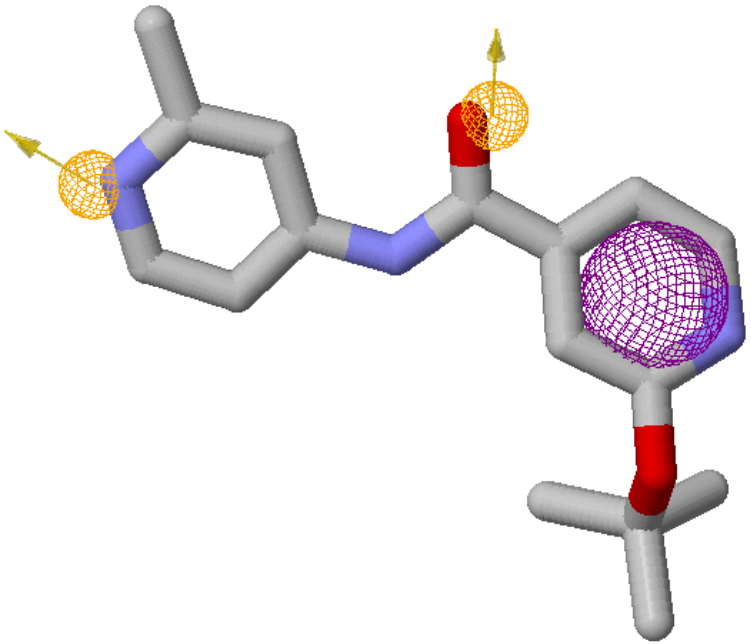

Pharmacophore | Filters | Viewer

Submit Query

Ligand
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Style: Sticks
Color: RasMol CPK

Receptor Residues
Visible: ☐
Style: Cartoon
Color: RasMol CPK

Results
Visible: ☑
Style: Sticks
Color: RasMol CPK

Query
Visible: ☑

Receptor Surface
Style: None
Color: Map Partial Charge (pdb on
Transparency:

Results

Name	RMSD	Mass	RBnds
ZINC94132267	0.343	285	7
ZINC33271594	0.486	451	9
ZINC92257303	0.573	338	8
ZINC68677302	0.473	380	8
ZINC83325093	0.540	428	5
ZINC20228241	0.698	451	11
ZINC37400892	0.497	496	11
ZINC02375871	0.346	449	7
ZINC65536088	0.663	367	4
ZINC61598286	0.514	344	4
ZINC12296390	0.489	455	4
ZINC35487005	0.620	478	15
ZINC32803464	0.592	328	10
ZINC89862032	0.330	320	3
ZINC09514222	0.522	333	6
ZINC38917312	0.527	399	8
ZINC05460836	0.408	358	6
ZINC74185531	0.271	317	4
ZINC90443294	0.405	328	7
ZINC06280919	0.190	413	4
ZINC19766230	0.398	408	7
ZINC65065386	0.339	385	4
ZINC12699660	0.593	506	13
ZINC09183643	0.501	466	10
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500 hits
24.367s

Save Results...