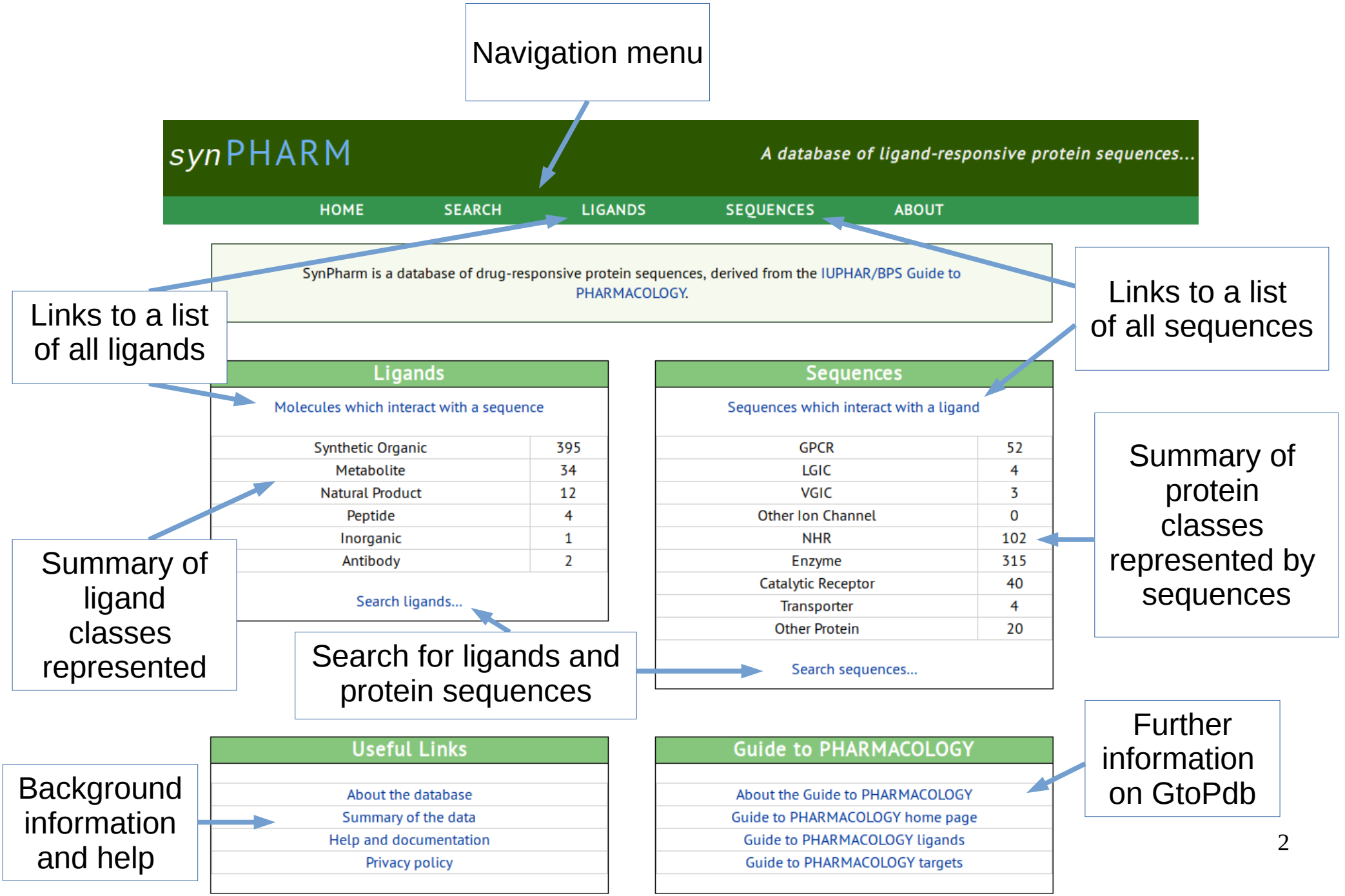
synPHARM tutorial

http://synpharm.guidetopharmacology.org/

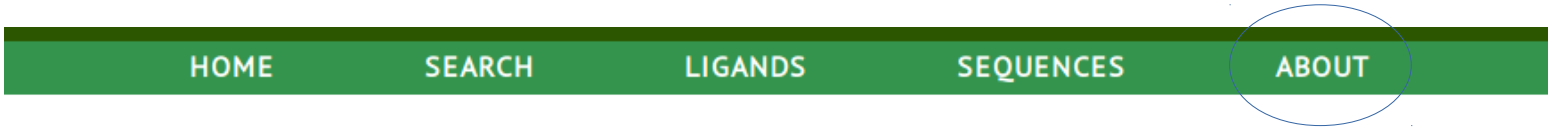
A database of ligand-responsive protein sequences derived from the IUPHAR/BPS Guide to PHARMACOLOGY (GtoPdb) and the Protein Data Bank (PDB)

For further help with using synPHARM please email
enquiries@guidetopharmacology.org

synPHARM home page



Further information and help



About

This Database

SynPharm is a database of drug-responsive protein sequences, derived from the IUPHAR/BPS Guide to PHARMACOLOGY.

The sequences can be used to confer druggability to a synthetic protein, and each sequence contains links back to the Guide to PHARMACOLOGY for more detailed information on the original drug target and the ligand itself.

Read more...

Introduction to synPHARM and the IUPHAR/BPS Guide to PHARMACOLOGY

Help

Documentation for the site, as well as examples of sequence displays. If you require any further assistance, please do get in touch.

Read more...

Full help documentation

Data and Statistics

This section contains various visualisations of the data contained in the SynPharm database, such as breakdowns by type and status for ligands and sequences.

Read more...

Detailed data statistics

About synPHARM

HOME | SEARCH | LIGANDS | SEQUENCES | ABOUT

About the Database

The Guide to PHARMACOLOGY

The Guide to PHARMACOLOGY (GtoPdb) is a searchable database with quantitative information on drug targets and the prescription medicines and experimental drugs that act on them. It was originally created in a collaboration between The British Pharmacological Society (BPS) and the International Union of Basic and Clinical Pharmacology (IUPHAR) and is now developed jointly with funding from the Wellcome Trust. It is intended to become a 'one-stop shop' portal to pharmacological information.

This database is an annexe to the Guide to PHARMACOLOGY. All ligands contained here have a corresponding entry in GtoPdb, and all sequences are ultimately derived from an interaction between a GtoPdb ligand and a GtoPdb target.

Find out more about GtoPdb here

SynPharm

SynPharm is a database of ligand-responsive protein sequences, derived from interactions from the Guide to PHARMACOLOGY and using data from the Protein Data Bank.

The sequences here are obtained by identifying the protein chain that interacts with a ligand for a given Guide to PHARMACOLOGY interaction, determining the binding residues, and producing a continuous 'bind sequence' that can be used to confer drugability to another protein.

Each bind sequence also contains metrics such as atomic contact ratio and proportional length, and visualisations such as the residue distance matrix, to allow you to better judge whether a sequence is likely to be able to fold independently.

The rationale for such a project was to enable the development of orthogonal molecular switches - switches which only respond to an exogenous molecular trigger, which itself will not interfere with endogenous receptors.

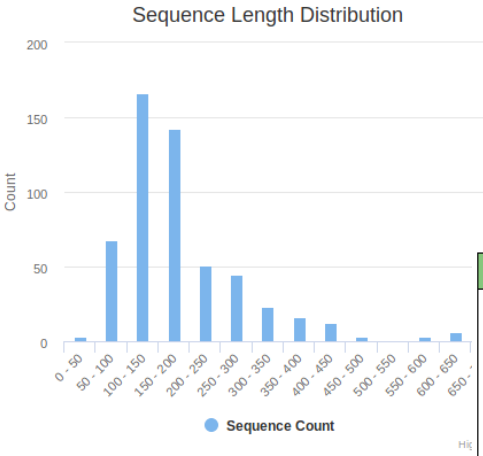
Find out more about the RCSB PDB here

Data content and statistics

Sequences by Length

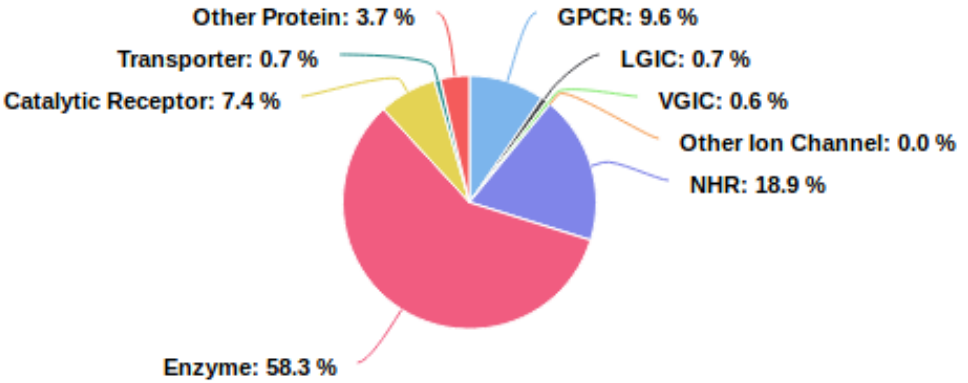
A breakdown of the sequences in the SynPharm database by sequence length.

Sequence Length (residues)	Count
0 - 50	3
50 - 100	68
100 - 150	166
150 - 200	142
200 - 250	51
250 - 300	45
300 - 350	23
350 - 400	16
400 - 450	12
450 - 500	3
500 - 550	1
550 - 600	3
600 - 650	6
650 - 700	0
700 - 750	1



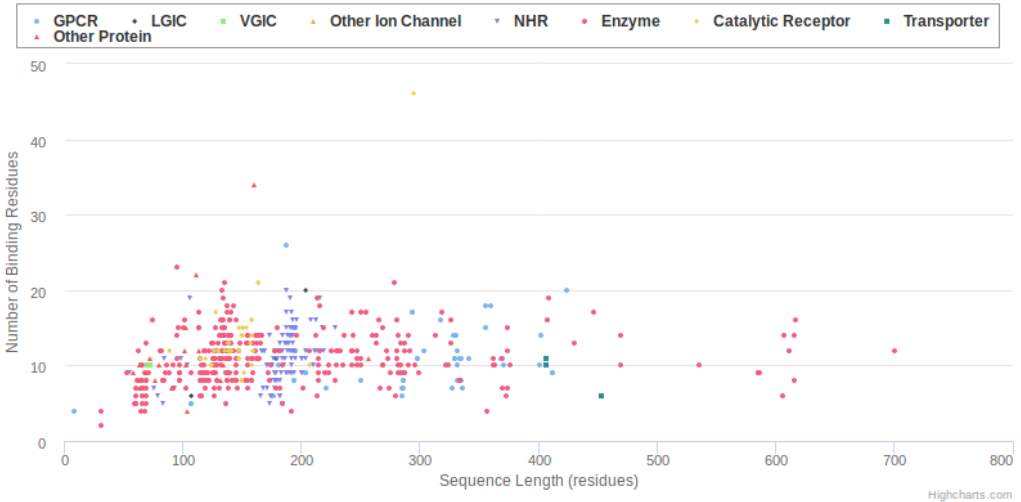
Examples of charts and statistics available on the Data and Statistics page

Proportion of sequences by target type

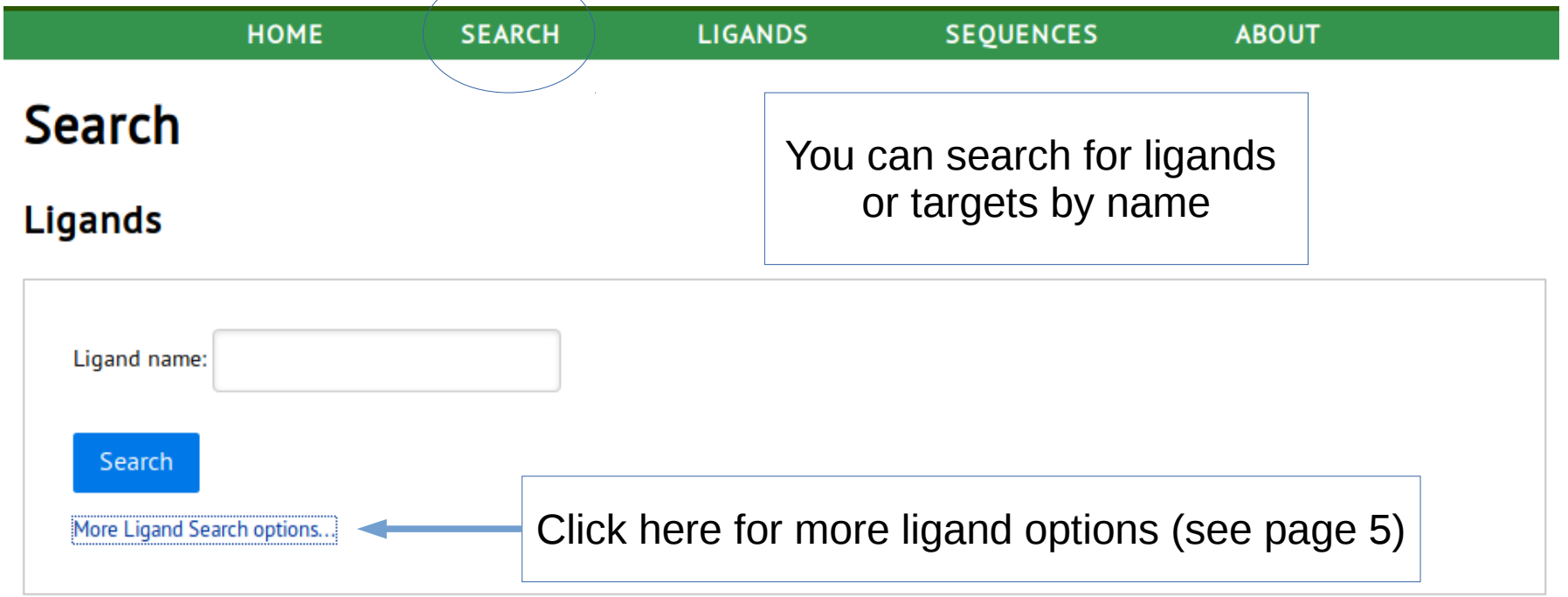


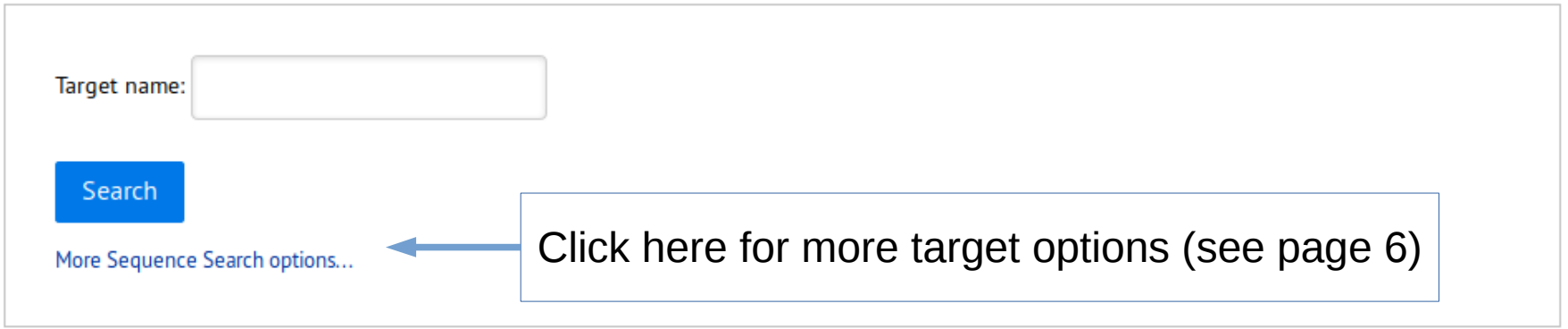
Sequence Contiguity by Target Type

This is a measure of how close together on the sequence the actual binding residues are - sequences with low contiguity will have widely separated residues. Here it is represented as the proportion of binding residues to non-binding residues.



Search synPHARM





Search Ligands

Search by chemical property or ligand class

Ligand name:

Mass greater than:

Mass less than:

H-bond acceptors greater than:

H-bond acceptors less than:

H-bond donors greater than:

H-bond donors less than:

Polar surface area greater than:

Polar surface area less than:

Lipinski rules broken greater than:

Lipinski rules broken less than:

logP greater than:

logP less than:

Ligand type:

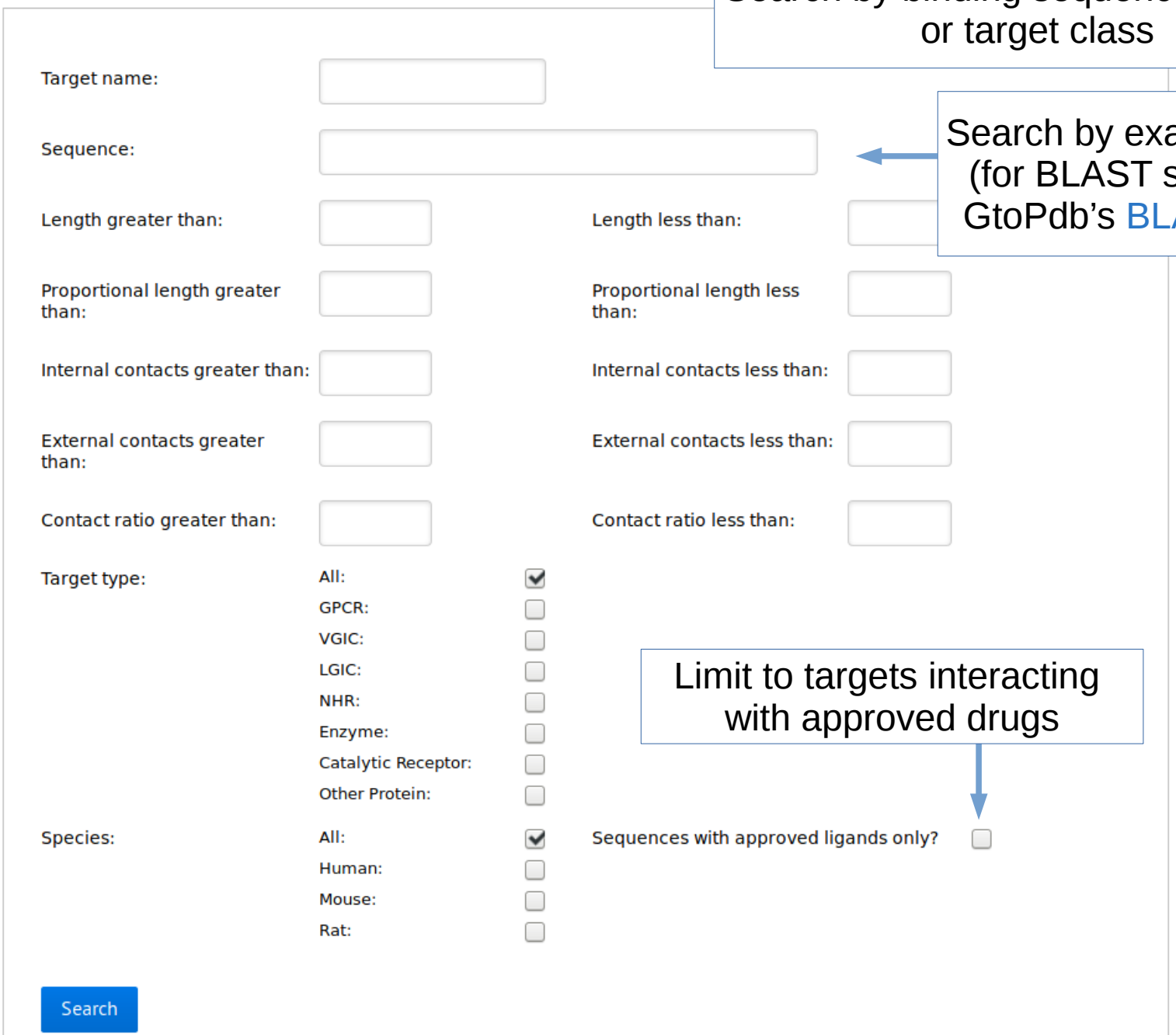
All: ☑
Synthetic organic: ☐
Metabolite: ☐
Natural product: ☐
Peptide: ☐
Inorganic: ☐
Antibody: ☐

Approved ligands only? ☐

Limit to approved drugs only

Search

Search Sequences



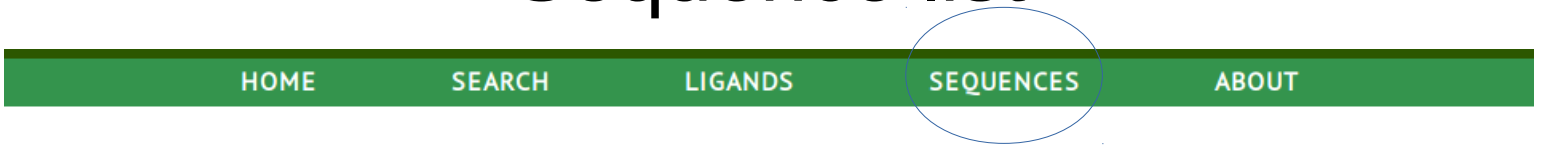
Search by binding sequence property or target class

Search by exact* sequence (for BLAST searches try GtoPdb's BLAST feature)

Limit to targets interacting with approved drugs

*Note this will only match sequences stored in synPHARM, i.e. sequences extracted from PDB entries, which may often differ from the native protein sequence (the N and C termini can be truncated and sometimes residues differ or are undefined)

Sequence list



All Drug Responsive Sequences

All | Approved drugs | Short | Long | Human | Non-Human | Small proportional length

Filter list by clicking on tabs at the top

Sort list by clicking on column headers

All drug-responsive elements which respond to a Guide to PHARMACOLOGY ligand (540).

ID	Target	Species	Ligand	Length	Proportional length
1190	M_2 receptor	Human	[^{3}H]QNB	303	64.7%
1460	A_{2A} receptor	Human	CGS 21680	195	59.7%
1467	A_{2A} receptor	Human	NECA	195	59.7%
1469	A_{2A} receptor	Human	[^{3}H]CGS 21680	195	59.7%
1470	A_{2A} receptor	Human	[^{3}H]NECA	195	59.7%
1490	A_{2A} receptor	Human	xanthine amine congener	194	58.7%
1491	A_{2A} receptor	Human	ZM-241385	250	51.0%
1494	A_{2A} receptor	Human	[^{3}H]XAC	194	58.7%
1495	A_{2A} receptor	Human	caffeine	107	32.2%
1862	β_2-adrenoceptor	Human	(-)-adrenaline	176	37.3%
1873	β_2-adrenoceptor	Human	ICI 118551	332	67.6%
1879	β_2-adrenoceptor	Human	alprenolol	336	68.4%
1888	β_2-adrenoceptor	Human	timolol	335	68.2%
2181	CaS receptor	Human	Ca^{2+}	8	1.1%
2310	CCR5	Human	[^{3}H]maraviroc	298	71.7%
2313	CCR5	Human	maraviroc	298	71.7%
2478	CRF_2 receptor	Human	urocortin 1	424	87.8%
2633	D_3 receptor	Human	eticlopride	327	67.8%

Approved drugs = sequences responding to approved drugs
Short = sequences <100 residues in length
Long = sequences >= 100 residues in length
Small proportional length = sequences <30% of original chain length

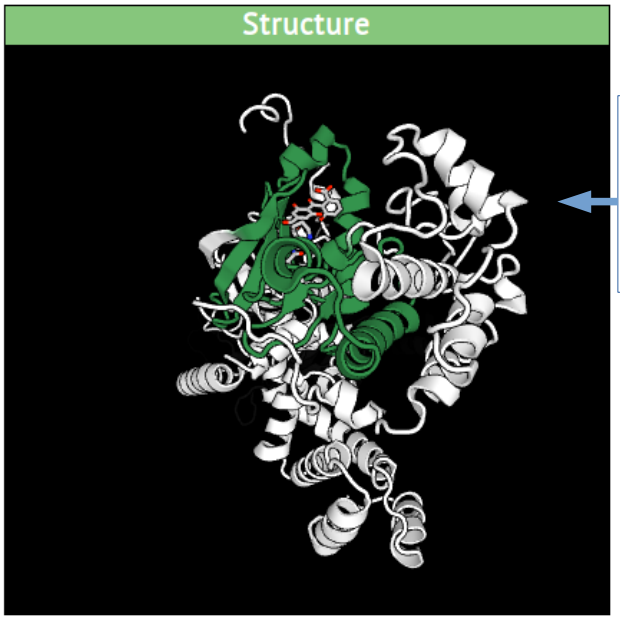
Sequence example

Human beta adrenergic receptor kinase 1

with balanol
GtoP Target: beta adrenergic receptor kinase 1

Links to the synPHARM ligand page, and to the GtoPdb target page for more data on this target

Structure



Rotatable, scalable 3D image of the interaction structure

Sequence

IGRgGFGeVygcrkadtgkmyAmKcldkkrikmkqgetlalnErimlslvstgdcpfivcmsyafhtpdklsfilDLMnggdlhyhlsqhgvfseadmrfyaaeiilglehmhnrfvvyrdlkpAniLldehghvriSDlG

< > Reset < >

The binding sequence, with contact residues in bold.
Expand the sequence using the buttons below

Details of the PDB structure the sequence came from, and a link to the RCSB PDB

PDB Details

PDB code	3KRX
HET ID	A690
HET name	BA1
Receptor Chain	A

Other Details

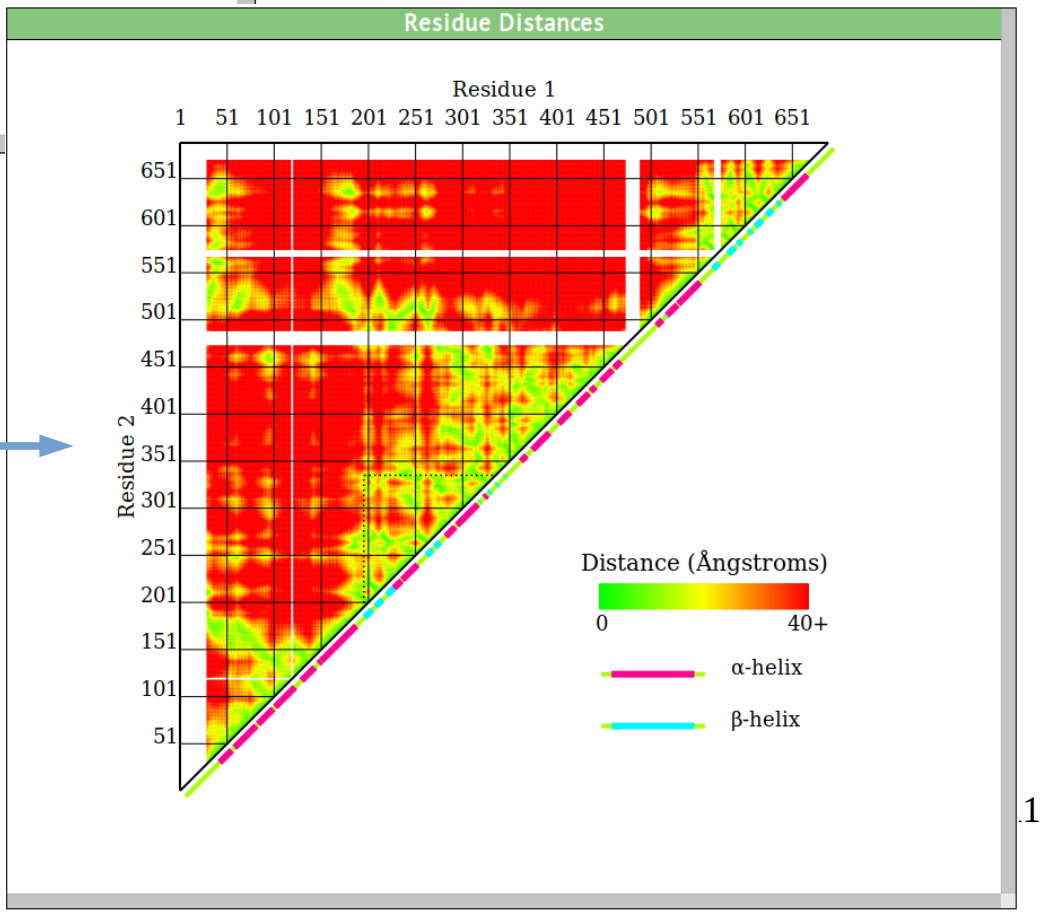
Target Type	Enzyme
Affinity	7.4
Affinity type	pIC50
Sequence length	141
Proportion of original chain length	20.3%
Internal contacts	3511
External contacts	565
Contact ratio	62.1%

Interaction details: **affinity** data from GtoPdb;
proportional sequence length: length of the binding sequence compared with the length of the chain;
contact ratio: ratio of internal contacts to external contacts (higher ratio = more ‘domain-like’ and more likely sequence would fold independently)

Sequence example continued

Feature viewer showing the location of binding residues and secondary structure elements, and a measure of hydrophobicity, along the sequence.

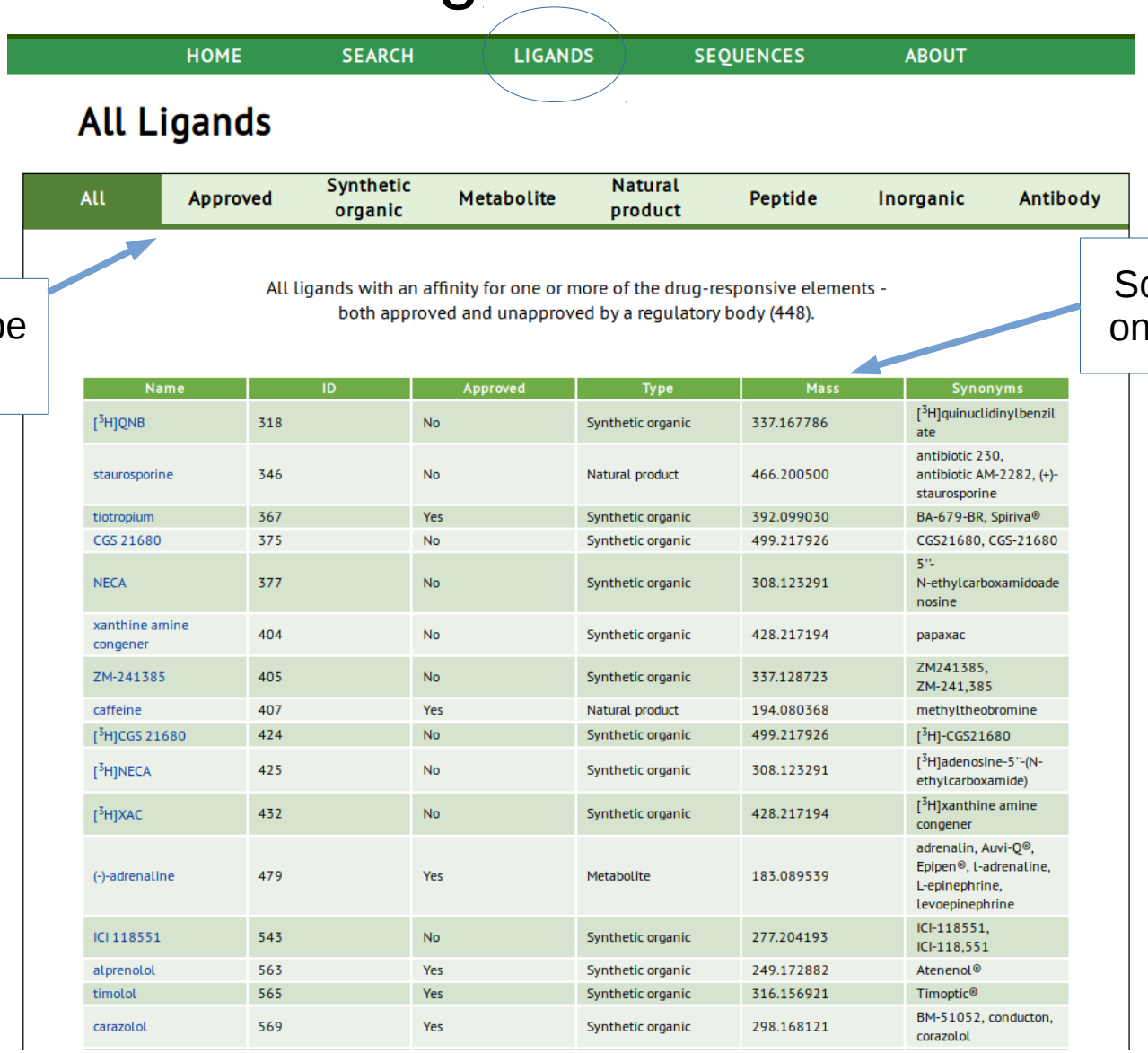
Zoom in by holding the left mouse button and dragging over the sequence.



Residue distance matrix with sequence shown as a dotted line.
Green = nearby residues
Red = distant residues
Gives an indication of sequence ‘globularity’ - if area within dotted line is greener than surrounding area, the sequence is compact.

White regions indicate residues were missing in the PDB file.

Ligand list



Name	ID	Approved	Type	Mass	Synonyms
[^{3}H]QNB	318	No	Synthetic organic	337.167786	[^{3}H]quinuclidinylbenzilate
staurosporine	346	No	Natural product	466.200500	antibiotic 230, antibiotic AM-2282, (+)-staurosporine
tiotropium	367	Yes	Synthetic organic	392.099030	BA-679-BR, Spiriva®
CGS 21680	375	No	Synthetic organic	499.217926	CGS21680, CGS-21680
NECA	377	No	Synthetic organic	308.123291	5''-N-ethylcarboxamidoadenosine
xanthine amine congener	404	No	Synthetic organic	428.217194	papaxac
ZM-241385	405	No	Synthetic organic	337.128723	ZM241385, ZM-241,385
caffeine	407	Yes	Natural product	194.080368	methyltheobromine
[^{3}H]CGS 21680	424	No	Synthetic organic	499.217926	[^{3}H]-CGS21680
[^{3}H]NECA	425	No	Synthetic organic	308.123291	[^{3}H]adenosine-5''-(N-ethylcarboxamide)
[^{3}H]XAC	432	No	Synthetic organic	428.217194	[^{3}H]xanthine amine congener
(-)-adrenaline	479	Yes	Metabolite	183.089539	adrenalin, Auvi-Q®, Epipen®, l-adrenaline, L-epinephrine, levoepinephrine
ICI 118551	543	No	Synthetic organic	277.204193	ICI-118551, ICI-118,551
alprenolol	563	Yes	Synthetic organic	249.172882	Atenenol®
timolol	565	Yes	Synthetic organic	316.156921	Timoptic®
carazolol	569	Yes	Synthetic organic	298.168121	BM-51052, conducton, corazolol

Filter list by ligand type by clicking on tabs

Sort list by clicking on column headers

Approved = ligands approved for use as drugs by a regulatory body
Synthetic organic = low molecular weight synthetic or semi-synthetic compounds
Metabolite = non-peptidic, biogenic compounds produced by animal life processes, e.g. hormones
Natural product = non-peptidic, biogenic compounds derived from other living organisms
Peptide = synthetic, semi-synthetic and natural peptides
Inorganic = ions and other inorganic compounds
Antibody = experimental and therapeutic monoclonal antibodies

Ligand example

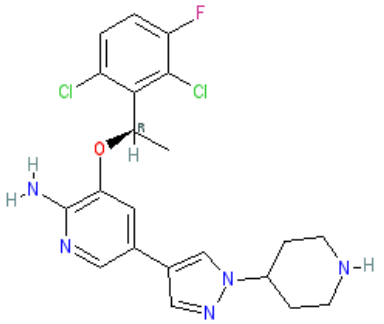
crizotinib

Guide to PHARMACOLOGY ID: 4903
CAS Registry No. - 877399-52-5
ChEMBL Ligand - CHEMBL601719
PubChem CID - 11626560
RCSB PDB Ligand - VGH&sid=2XP2
Wikipedia - Crizotinib

Links to other resources with further data on this ligand. The GtoPdb ligand page contains a more extensive set of out-links.

2D image of the ligand structure

Structure



Molecular Details

Molecular mass (Da)	449.11853
Hydrogen bond acceptors	5
Hydrogen bond donors	2
Polar surface area (A^2)	77.99
Lipinski rules broken	0
logP	2.834

Calculated molecular properties (for definitions see GtoPdb help)

Other Details

Ligand type	Synthetic organic
Radiolabelled	No
Approved	Yes
Approval Source	FDA (2011), EMA (2012)

Ligand class and drug approval status

Responsive Sequences

MET proto-oncogene, receptor tyrosine kinase (147 residues)

anaplastic lymphoma receptor tyrosine kinase (123 residues)

MET proto-oncogene, receptor tyrosine kinase (147 residues)

Sequences this ligand binds to in synPHARM (click on the link to go to the sequence page)