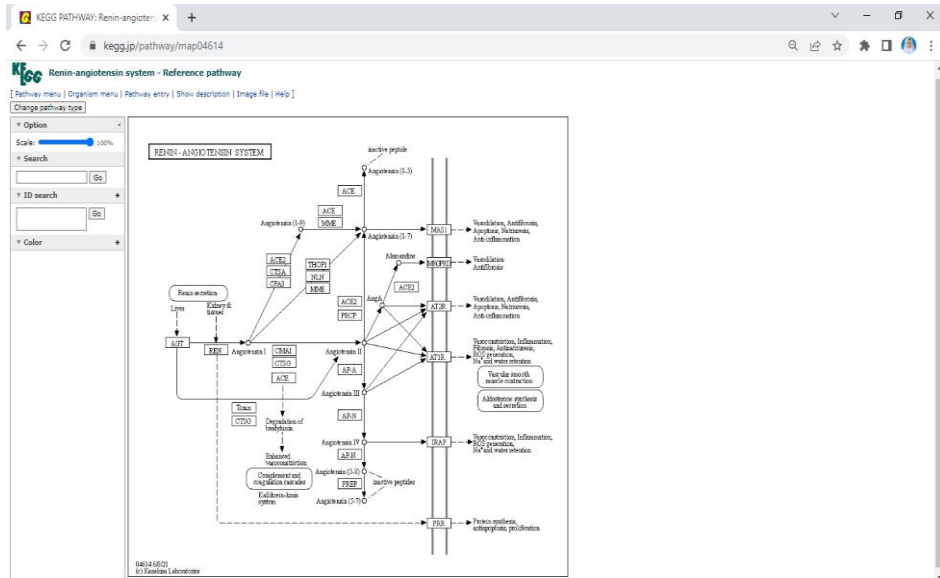
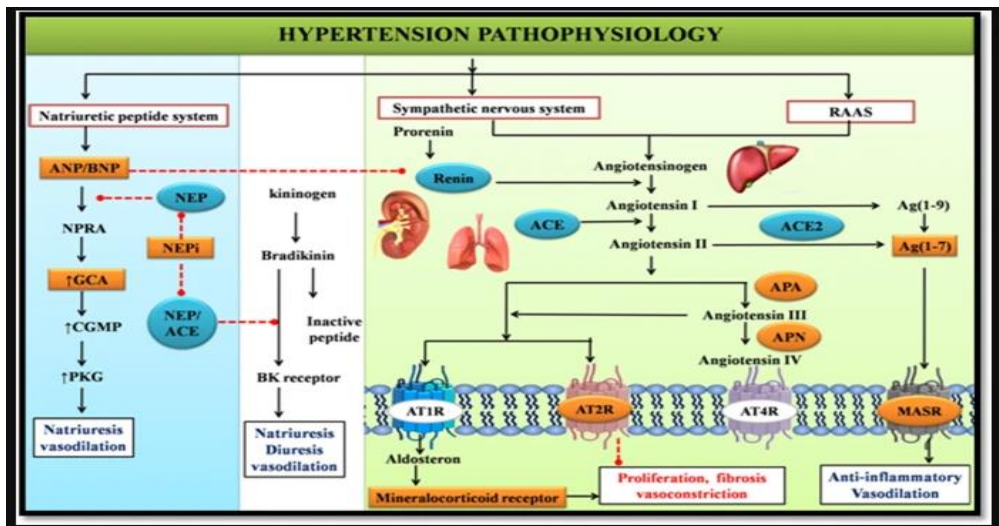


LAMPIRAN

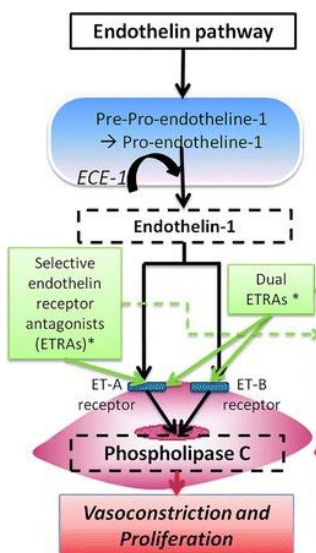
Lampiran 1. Identifikasi protein target



Sistem renin angiotensin-aldosteron



Patofisiologi hipertensi



Endothelin pathway in hypertension

Lampiran 2. Kandungan senyawa kimia dari KNAPSAcK

KNAPSAcK Core System

Not secure | knapsackfamily.com/knapsack_core/top.php

KNAPSAcK Core System

Link to Top page:
http://www.knapsackfamily.com/knapsack_core/top.php

Incorporation to program:
http://www.knapsackfamily.com/knapsack_core/info.php?name={item}&word={keyword}
 Here, {item} must be selected from one of the following words; "organism", "metabolite", "formula", "C_ID", and "CAS_ID".

<Example 1>
 Information on the metabolite assigned to C00000001 (a C_ID) can be retrieved by
http://www.knapsackfamily.com/knapsack_core/info.php?name=C_ID&word=C00000001

<Example 2>
 The reported metabolites in Bacillus (an organism) can be retrieved by
http://www.knapsackfamily.com/knapsack_core/info.php?name=organism&word=bacillus

Words for organisms or metabolites can be retrieved by providing at least three characters that forward matches with their strings.

CAUTION: (C) Any content included in KNAPSAcK database cannot be re-distributed or used for commercial purposes by any user without contacting with KNAPSAcK DB group (skanaya[at]gic.naist.jp).

[Instruction Manual/Japanese](#) [Instruction Manual/English](#)

Select by ...
 ALL Types Organism Metabolite Molecular formula
 C_ID CAS_ID INCHI-KEY INCHI-CODE SMILES

KNAPsACK Metabolite Informa: x

Not secure | knapsackfamily.com/knapsack_core/result.php?name=all&word=apium%20graveolens

input type = all, input word = apium graveolens

Number of matched data: 310

Cl ID	CAS ID	Metabolite	Molecular formula	MW	Organism or InchiKey etc.
C:00000010	118-34-3	Syringin	C17H24O9	372.14203237	Apium graveolens
C:000000149	6750-60-3	Espatulenol	C15H24O	220.18271539	Apium graveolens
C:000000152	7400-08-0	p-Coumaric acid	C9H8O3	164.04734412	Apium graveolens
C:000000154	29803-82-5	trans-p-Menth-2-en-1-ol	C10H18O	154.1357652	Apium graveolens
C:000000163	473-16-5	alpha-Eudesmol	C15H26O	222.19836545	Apium graveolens
C:000000164	473-15-4	beta-Eudesmol	C15H26O	222.19836545	Apium graveolens
C:000000184	2867-05-2	alpha-Thujene	C10H16	136.12520051	Apium graveolens
C:000000212	23255-59-6	Lunularic acid	C15H14O4	258.08920894	Apium graveolens
C:000000242	19883-27-3	(3E,5Z)-1,3,5-Undecatriene	C11H18	150.14085057	Apium graveolens
C:000000287	66-97-7	Ficucin	C11H6O3	186.03169406	Apium graveolens
C:000000300	523-59-1	Seselin	C14H12O3	228.07864425	Apium graveolens
C:000000353	6789-80-6	cis-3-Hexenal	C8H14O	96.07316494	Apium graveolens
C:000000356	928-96-1	cis-3-Hexen-1-ol	C8H16O	100.08881501	Apium graveolens
C:000000357	66-25-1	Hexanal	C6H12O	100.08881501	Apium graveolens
C:000000375	484-20-8	Bergapten	C12H8O4	216.04225874	Apium graveolens
C:000000376	298-81-7	Xanthotoxin	C12H8O4	216.04225874	Apium graveolens
C:000000583	482-27-9	Isopimpinellin	C13H10O5	246.05282343	Apium graveolens
C:000000615	501-16-6	Caffeic acid	C9H8O4	180.04225874	Apium graveolens
C:000000619	97-53-0	Eugenol	C10H12O2	164.08372963	Apium graveolens
C:000000674	491-70-3	Luteolin	C15H10O6	286.04773805	Apium graveolens
C:000000805	80-56-8	alpha-Pinene	C10H16	136.12520051	Apium graveolens
C:000000816	127-91-3	beta-Pinene	C10H16	136.12520051	Apium graveolens
C:000000819	76-22-2	(+)-Camphor	C10H16O	152.12011513	Apium graveolens
C:000000823	138-86-3	Limonene	C10H16	136.12520051	Apium graveolens
C:000000839	13466-78-9	3-Carene	C10H16	136.12520051	Apium graveolens
C:000000843	3330-55-4	cis-beta-Ocimene	C10H16	136.12520051	Apium graveolens
C:000000853	123-35-3	beta-Myrcene	C10H16	136.12520051	Apium graveolens
C:000000861	586-62-9	alpha-Terpinolene	C10H16	136.12520051	Apium graveolens
C:000000862	3779-61-1	trans-beta-Ocimene	C10H16	136.12520051	Apium graveolens
C:000000847	154-23-4	(+)-Catechin	C15H14O6	290.07903818	Apium graveolens
C:000000956	490-46-0	(-)-Epicatechin	C15H14O6	290.07903818	Apium graveolens

Lampiran 3. Pencarian kandungan kimia dari IJAH analytics

IJAH Analytics

Not secure | ijahapps.cs.ipb.ac.id/#/home

Bogor Agricultural University
INDONESIA JAMU-HERBS

Home Download Upload Ijah1i Help/FAQ Contact About

IJAH Analytics

Search and Predict (Plant - Compound) - (Protein - Disease) Connectivity

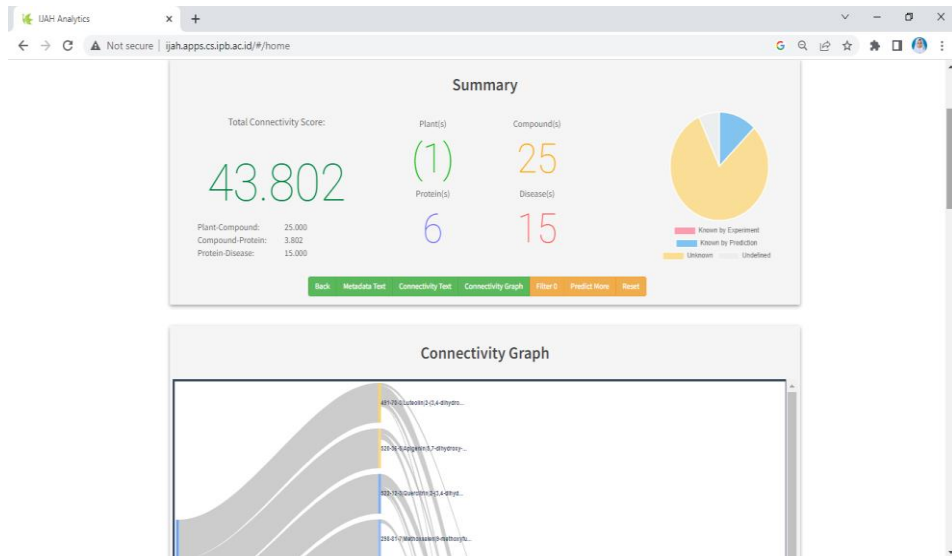
Use-case Examples: Drug-side Target-side Both sides

Drug-Side

Plants (of 4984) Compounds (of 17277)

Target-Side

Proteins (of 3334) Diseases (of 4401)



Lampiran 4. Validasi nama gen

The screenshot shows the UniProt website interface. The main heading is 'Find your protein'. The search bar contains the text 'UniProtKB | ACE'. Below the search bar, there are examples: 'Examples: Insulin, APP, Human, P05067, organism_id:9606'. The page also features navigation links: BLAST, Align, Peptide search, ID mapping, SPARQL, and a top right menu with Release 2022_04, Statistics, and Help.

At the bottom, there are four main categories:

- Proteins: UniProt Knowledgebase
- Species: Proteomes
- Protein Clusters: UniRef
- Sequence Archive: UniParc

Additional buttons for Feedback and Help are visible on the right side of the page.

ACE in UniProtKB search (16814) x

uniprot.org/uniprotkb?query=ACE

UniProtKB ACE

Status

- Reviewed (Swiss-Prot) (512)
- Unreviewed (TrEMBL) (16,302)

Popular organisms

- Human (53)
- Mouse (28)
- Fruit fly (19)
- Rat (18)
- Zebrafish (16)

Taxonomy

Filter by taxonomy

Proteins with

- 3D structure (53)
- Active site (788)

UniProtKB 16,814 results

or search "ACE" as a Organism, Taxonomy, Strain, Gene Name, Protein Name, Author, or Disease

BLAST Align Map IDs Download Add View: Cards Table Customize columns Share

Entry	Entry Name	Protein Names	Gene Names	Organism	Length
<input type="checkbox"/> Q10751	ACE_CHICK	Angiotensin-converting enzyme[...]	ACE, DCP1	Gallus gallus (Chicken)	1,281 AA
<input type="checkbox"/> P12821	ACE_HUMAN	Angiotensin-converting enzyme[...]	ACE, DCP, DCP1	Homo sapiens (Human)	1,306 AA
<input type="checkbox"/> P12820	ACE_BOVIN	Angiotensin-converting enzyme[...]	ACE, DCP1	Bos taurus (Bovine)	1,306 AA
<input type="checkbox"/> P09470	ACE_MOUSE	Angiotensin-converting enzyme[...]	Ace, Dcp1	Mus musculus (Mouse)	1,312 AA
<input type="checkbox"/> F1RRW5	ACE_PIG	Angiotensin-converting enzyme[...]	ACE	Sus scrofa (Pig)	1,309 AA
<input type="checkbox"/> P47820	ACE_RAT	Angiotensin-converting enzyme[...]	Ace, Dcp1	Rattus norvegicus (Rat)	1,313 AA

Angiotensin-converting enzyme

EDNRA in UniProtKB search (601) x

uniprot.org/uniprotkb?query=EDNRA

UniProtKB EDNRA

Status

- Reviewed (Swiss-Prot) (34)
- Unreviewed (TrEMBL) (567)

Popular organisms

- Rat (12)
- Zebrafish (8)
- Human (6)
- Mouse (5)
- Bovine (3)

Taxonomy

Filter by taxonomy

Proteins with

- 3D structure (8)
- Active site (6)
- Activity regulation (4)

UniProtKB 601 results

or search "EDNRA" as a Gene Name, Protein family, or Protein Name

BLAST Align Map IDs Download Add View: Cards Table Customize columns Share

Entry	Entry Name	Protein Names	Gene Names	Organism	Length
<input type="checkbox"/> P25101	EDNRA_HUMAN	Endothelin-1 receptor[...]	EDNRA, ETA, ETRA	Homo sapiens (Human)	427 AA
<input type="checkbox"/> P21450	EDNRA_BOVIN	Endothelin-1 receptor[...]	EDNRA	Bos taurus (Bovine)	427 AA
<input type="checkbox"/> P26684	EDNRA_RAT	Endothelin-1 receptor[...]	Ednra	Rattus norvegicus (Rat)	426 AA
<input type="checkbox"/> Q61614	EDNRA_MOUSE	Endothelin-1 receptor[...]	Ednra, Gpcr10	Mus musculus (Mouse)	427 AA
<input type="checkbox"/> Q95L55	EDNRA_SHEEP	Endothelin-1 receptor[...]	EDNRA	Ovis aries (Sheep)	427 AA
<input type="checkbox"/> QSKSU9	EDNRA_CANLF	Endothelin-1 receptor[...]	EDNRA	Canis lupus familiaris (Dog) (Canis familiaris)	426 AA

Endothelin Receptor Type A

Lampiran 5. Percarian aktivitas biologi kandungan senyawa

PubChem National Library of Medicine
National Center for Biotechnology Information

PubChem About Posts Submit Contact

Explore Chemistry

Quickly find chemical information from authoritative sources

apigenin

Compound	Gene	Taxonomy
apigenin	apelin	English grain aphid
APIGENIN (CONSTITUENT OF CHA...	neogenin	
Apigeninidin	myogenin	
Apigenin triacetate	neogenin 1	
Apigenin 7-glucoside	adipogenin	
Apigenin 7,4'-dimethyl ether	anjoogenin	

Apigenin | C15H10O5 - PubChem

pubchem.ncbi.nlm.nih.gov/compound/5280443

PubChem National Library of Medicine
National Center for Biotechnology Information

PubChem About Posts Submit Contact Search PubChem

COMPOUND SUMMARY

Apigenin

PubChem CID: 5280443

Structure

2D 3D

Find Similar Structures

Chemical Safety

Irritant

Cite Download

CONTENTS

- 9 Use and Manufacturing
- 10 Identification
- 11 Safety and Hazards
- 12 Toxicity
- 13 Associated Disorders and Diseases
- 14 Literature
- 15 Patents
- 16 Interactions and Pathways
- 17 Biological Test Results
- 18 Taxonomy

Apigenin | C15H10O5 - PubChem

pubchem.ncbi.nlm.nih.gov/compound/5280443#section=Biological-Test-Results

PubChem Apigenin (Compound)

17 Biological Test Results

17.1 BioAssay Results

3,457 Items View More Rows & Details Download

Activity	Activity Value, μM	Activity Type	Target Name	BioAssay Name	BioAssay AID
Inconclusive	0.0071	Potency	NR3C1 - nuclear receptor subfamily 3 group C member 1 (human)	qHTS assay for small molecule agonists of glucocorticoid receptor signaling	588532
Active	0.008	Vmax	LOX11 - seed linoleate 13S-lipoxygenase-1 (soybean)	Activity at soybean LOX-1 using linoleic acid as substrate at 100 μM preincubated for 5 mins followed by substrate addition by Michaelis-Menten plot	1063897

CONTENTS

- 9 Use and Manufacturing
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- 11 Safety and Hazards
- 12 Toxicity
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- 16 Interactions and Pathways
- 17 Biological Test Results
- 18 Taxonomy
- 19 Classification
- 20 Information Sources

Lampiran 6. Interaksi protein-protein

STRING: functional protein asso. x

string-db.org/cgi/input?sessionId=b1298xrlsMK2&input_page_show_search=on

version: 11.5 LOGIN REGISTER SURVEY

STRING Search Download Help My Data

Protein by name > SEARCH

Protein by sequence >

Multiple proteins >

Multiple sequences >

Proteins with Values/Ranks >

Protein families ("COGs") >

Annotate your proteome **New** >

Organisms >

Examples >

Random entry >

Single Protein by Name / Identifier

Protein Name: (examples: #1 #2 #3)
ACE2

Organisms: auto-detect

Advanced Settings

SEARCH

searching - STRING-functional | x

string-db.org/cgi/network?pollingId=bqBvEuth4er&sessionId=b129BrLsMKZ

Version: 11.5 LOGIN REGISTER SURVEY

STRING Search Download Help My Data

There are several matches for 'ACE2'. Please select one from the list below and press Continue to proceed.

<- BACK CONTINUE ->

311 matches showing page 1 of 16 - first - previous - next - last

organism	protein
<input checked="" type="checkbox"/> Homo sapiens	ACE2 - Angiotensin-converting enzyme 2; Carboxypeptidase which converts angiotensin I to angiotensin 1-9, a peptide of unknown function, and angiotensin II to angiotensin 1-7, a vasodilator. Also able to hydrolyze apelin-13 and dynorphin-13 with high efficiency. May be an important regulator of heart function
<input type="checkbox"/> Mus musculus	Ace2 - Angiotensin I converting enzyme (peptidyl-dipeptidase a) 2; Angiotensin-converting enzyme 2; Carboxypeptidase which converts angiotensin I to angiotensin 1-9, a peptide of unknown function, and angiotensin II to angiotensin 1-7, a vasodilator. Also able to hydrolyze apelin-13 and dynorphin-13 with high efficiency. May be an important regulator of heart function. May have a protective role in acute lung injury
<input type="checkbox"/> Saccharomyces cerevisiae	ACE2 - Metallothionein expression activator; Transcription factor required for septum destruction after cytokinesis; phosphorylation by Cbk1p blocks nuclear exit during M/G1 transition, causing localization to daughter cell nuclei, and also increases Ace2p activity; phosphorylation by Cdc28p and Pho85p prevents nuclear import during cell cycle phases other than cytokinesis; part of RIM network that regulates cellular polarity and morphogenesis; ACE2 has a paralogs, SWI5, that arose from the whole genome duplication
<input type="checkbox"/> Homo sapiens	HPN - Serine protease hepsin; Serine protease that cleaves extracellular substrates, and contributes to the proteolytic processing of growth factors, such as HGF and MST1/HGLF. Plays a role in cell growth and maintenance of cell morphology. Plays a role in the proteolytic processing of ACE2. Mediates the proteolytic cleavage of urinary UMOD that is required for UMOD polymerization; Belongs to the peptidase S1 family [a.k.a. TMPRSS1, P05981, S01.224]
<input type="checkbox"/> Homo sapiens	TMPPRSS110 - Transmembrane protease serine 110; May play some biological role in the host defense system on the mucous membrane independently of or in cooperation with other substances in airway mucous or bronchial secretions. Plays a role in the proteolytic processing of ACE2. Proteolytically cleaves and activates the human coronavirus 229E (HCoV-229E) spike glycoprotein which facilitate virus-cell membrane fusions; spike proteins are synthesized and maintained in precursor intermediate folding states and proteolysis permits the refolding and subsequent release required to infect a new cell [a.k.a. MAT087, P11680, P05981]

ACE2 protein (human) - STRING | x

string-db.org/cgi/network?taskId=b39TmwuXLO4C&sessionId=b129BrLsMKZ

Version: 11.5 LOGIN REGISTER SURVEY

STRING Search Download Help My Data

Viewers > Legend > Settings > Analysis > Exports > Clusters > More > Less

Lampiran 7. Data protein target dari *Swiss Target Prediction*

The screenshot shows the SwissTargetPrediction website interface. The header includes the SIB logo and navigation links: Home, FAQ, Help, Download, Contact, Disclaimer. A text box explains the website's purpose: "This website allows you to estimate the most probable macromolecular targets of a small molecule, assumed as bioactive. The prediction is founded on a combination of 2D and 3D similarity with a library of 370'000 known actives on more than 3000 proteins from three different species." Below this, there is a "Select a species" section with radio buttons for Homo sapiens (selected), Mus musculus, and Rattus norvegicus. A "Paste a SMILES in this box, or draw a molecule" section contains the SMILES string Oc1=CC=C(C=C1)C1=C(C(=O)C2=C(O)C=C(O)C=C2O1) and a "Predict targets" button. To the right, a chemical structure of the query molecule is displayed.

The screenshot shows the results page for the query molecule. The "Query Molecule" section displays the chemical structure. The "Target Classes" section features a pie chart showing the distribution of target classes for the top 15, top 25, top 50, and all targets. The legend for the pie chart includes: Kinase, Kinase, Cholesterolase, G-proteins/PDZ, Nuclear receptor, Metabotropic, Tyrosine 3-D protein coupled receptor, and Other unrelated proteins. Below the pie chart, there are export options and a search bar. The main results table is as follows:

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Tyrosine-protein kinase SYK	SYK	P43405	CHEMBL2599	Kinase	100%	3 / 3
Glycogen synthase kinase-3 beta	GSK3B	P49641	CHEMBL262	Kinase	100%	3 / 7
Multidrug resistance-associated protein 1	ABCC1	P33527	CHEMBL3004	Primary active transporter	100%	7 / 11
Estradiol 17-beta-dehydrogenase 1	HSD17B1	P14061	CHEMBL1311	Enzyme	100%	9 / 4

Lampiran 8. Data protein target dari SEA

SEA Search Server

Similarity ensemble approach (SEA)

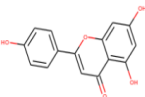
The Similarity ensemble approach relates proteins based on the set-wise chemical similarity among their ligands. It can be used to rapidly search large compound databases and to build cross-target similarity maps.

1C2=CC(=O)C3=C(C=C(C=C3O2)O)O [Try SEA](#)

[Browse Library](#) [Search Library](#)

Browse searchable targets from ChEMBL Submit a search of ChEMBL or custom targets

Results of Job: [search_ae9949f1-2f93-4509-bab0-8ff1fd880e7c](#) [Download](#)

Query	Target Key	Target Name	Description	P-Value	MaxTC
 compound_1	BGLR_RAT	Gusb	Beta-glucuronidase	1.242e-85	1.00
	CP1B1_HUMAN	CYP1B1	Cytochrome P450 1B1	3.521e-56	1.00
	ALDR_RAT	Akr1b1	Aldo-keto reductase family 1 member B1	5.052e-56	1.00
	XDH_HUMAN	XDH	Xanthine dehydrogenase/oxidase	3.25e-43	1.00
	ESR2_HUMAN	ESR2	Estrogen receptor beta	2.226e-32	1.00
	ESR1_HUMAN	ESR1	Estrogen receptor	9.619e-24	1.00
	TNKS1_HUMAN	TNKS	Poly [ADP-ribose] polymerase tankyrase-1	1.281e-22	1.00
	MDR1_HUMAN	ABCB1	ATP-dependent translocase ABCB1	6.184e-22	1.00
	NOX4_HUMAN	NOX4	NADPH oxidase 4	1.135e-	1.00

Lampiran 9. Data protein target dari SuperPred

https://prediction.charite.de/sub/ x +

prediction.charite.de/subpages/target_prediction.php

Super-PRED Home Drug Classification Target Prediction ATC-Tree Statistics FAQ Contact

TARGET PREDICTION

Here you can run a [target prediction](#) for your input compound.

There are different ways to start the classification:

- Search a compound by its name via PubChem
- Draw your structure
- Create a structure by SMILES string
- Load a molecule by clicking on imglink (order)

Pubchem-Name :

e.g. Aspirin

Enter a compound name to search via PubChem

SMILES :

COC1=C2C=CC(=O)OC2=CC3=C1C=CO3

Enter a SMILES string to search by derived structure

https://prediction.charite.de/sub/ x +

prediction.charite.de/subpages/target_result.php

Target Name	ChEMBL-ID	UniProt ID	PDB Visualization	TTD ID	Probability	Model accuracy
Voltage-gated potassium channel subunit Kv1.5	CHEMBL4306	P22460	Not Available	T17569	97.16%	94.03%
DNA-(apurinic or apyrimidinic site) lyase	CHEMBL5619	P27695	6BOW	T13348	96.5%	91.11%
Transcription intermediary factor 1-alpha	CHEMBL3108638	O15164	4YBM	Not Available	91.61%	95.56%
Dual specificity protein kinase CLK4	CHEMBL4203	Q9HAZ1	6FYV	Not Available	91.05%	94.45%
Cathepsin D	CHEMBL2581	P07339	4OD9	T67102	88.94%	98.95%
Dual specificity protein phosphatase 3	CHEMBL2635	P51452	3F81	Not Available	88.43%	94%
DNA topoisomerase II alpha	CHEMBL1806	P11388	6ZY5	T17048	85.85%	89%
Nuclear factor erythroid 2-related factor 2	CHEMBL1075094	Q16236	2FLU	Not Available	85.45%	96%
Arachidonate 12-lipoxygenase	CHEMBL3687	P18054	3D3L	Not Available	84.11%	75.57%

Lampiran 10. Senyawa hasil prediksi dari Swiss Tatget Prediction, SEA, SuperPred

Senyawa	Swiss target prediction Nama protein target	Nilai Probability	SEA Nama protein target	Max Tc	SuperPred Nama protein target	Nilai Probability
Apigenin	TNKS	1	TNKS	1		
	TNKS2	1	TNKS2	1		
			MPO	1		
			DPP4	1		
Luteolin	MMP9	1	MMP9	1		
	TNKS	1	TNKS	1		
	TNKS2	1	TNKS2	1		
			DPP4	1		
Caffeic acid	MMP1	0,72	MMP1	1		
	MMP9	0,72	MMP9	1		
			DPP4	1		
3-n Butylphthalide					ANPEP	82,83%
Bergapten					ANPEP	73,63%

Lampiran 11. Visualisasi network pharmacology menggunakan *Cytoscape*

