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NETWORK PHARMACOLOGY AND MOLECULAR DOCKING STUDY TO REVEAL THE POTENTIAL ANTICANCER ACTIVITY OF OSCILLATOXIN D, E, AND F MARINE CYTOTOXINS

Dewi Luthfiana[1], Maratu Soleha[2], Andri Prasetiyo[3], Wisnu A. Kusuma[4,5],
Rizka Fatriani[5], Lina Nurfadhila[6], Norainny Yunitasari[7], Ahmad H. Ahkam[8],
Teresa L. Wargasetia[9], Rizal Irfandi[10], Arif N. M. Ansori[11,12], Viol D. Kharisma[13,14],
Sin W. Naw[15], Emdad Ullah[16], Vikash Jakhmola[11], Rahadian Zainul[17]*

[1] Bioinformatics Research Center, Indonesian Institute of Bioinformatics (INBIO), Malang, Indonesia
[2] National Research and Innovation Agency, Banten, Indonesia
[3] Department of Pharmaceutical Science, Faculty of Pharmacy, Pancasila University, South Jakarta, Indonesia
[4] Department of Computer Science, Faculty Mathematics and Natural Sciences, IPB University, Bogor, Indonesia
[5] Tropical Biopharmaca Research Center, IPB University, Bogor, Indonesia
[6] Department of Pharmacy, Faculty of Health Sciences, Singaperbangsa Karawang University, Karawang, Indonesia
[7] Faculty of Health, University of Muhammadiyah Gresik, Gresik, Indonesia
[8] Faculty of Pharmacy, Padjadjaran University, Sumedang, Indonesia
[9] Faculty of Medicine, Maranatha Christian University, Bandung, Indonesia
[10] Department of Biology Education, Faculty of Teacher Training and Education, Universitas Puangrimaggalatung, Sengkang, Indonesia
[11] Uttaranchal Institute of Pharmaceutical Sciences, Uttaranchal University, Dehradun, India
[12] Postgraduate School, Universitas Airlangga, Surabaya, Indonesia
[13] Department of Biology, Faculty of Science and Technology, Universitas Airlangga, Surabaya, Indonesia
[14] Division of Molecular Biology and Genetics, Generasi Biologi Indonesia Foundation, Gresik, Indonesia
[15] Department of Chemistry, Myitkyina University, Myitkyina, Myanmar
[16] Department of Chemistry, Mississippi State University, Mississippi, United States
[17] Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang, Padang, Indonesia

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mechanism of action, molecular docking, network pharmacology, oscillatoxins

ABSTRACT

Oscillatoxins (OTXs) are cytotoxins produced by some marine cyanobacteria. Their unique structures show a great potency as an anticancer agent. The limited availability of OTX derivatives in nature provides little information about their biological activity. Some of OTX activities have been tested in the *in vitro* or *in vivo* studies toward cancer cell lines, but their exact mechanism of action on the target is unclear. In this study, we used the network pharmacology analysis method to predict the target and mechanism of action of oscillatoxin D (OTX-D), 30 methyl oscillatoxin D (30-methyl-OTX-D), oscillatoxin E (OTX-E), and oscillatoxin F (OTX-F). There are 20 possible targets of the four compounds toward cancer, and the main targets of them are PIK3CA, CDK1, and MTOR. This was also followed by the molecular docking study to understand the interaction between the four compounds and their targets. Molecular docking showed that the four compounds interacted well with the key targets. In this study, four derivatives of OTXs and their three key targets for the anticancer action were revealed suggesting multiple signaling pathways, including PD-L1 expression and PD-1 checkpoint pathway in cancer, proteoglycans in cancer, and pathways in cancer, establishing a theoretical framework for the further experimental study.

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ИССЛЕДОВАНИЕ МЕТОДОМ СЕТЕВОЙ ФАРМАКОЛОГИИ И МОЛЕКУЛЯРНОГО ДОКИНГА ДЛЯ ВЫЯВЛЕНИЯ ПОТЕНЦИАЛЬНОЙ ПРОТИВОРАКОВОЙ АКТИВНОСТИ МОРСКИХ ЦИТОТОКСИНОВ — ОСЦИЛЛАТОКСИНОВ D, E, И F

Лютфиана Д.[1], Салеха М.[2], Прасетийо А.[3], Кусума В. А.[4,5], Фатриани Р.[5], Нурфадхила Л.[6], Юнитасари Н.[7], Ахкам А. Х.[8], Варгасетия Т. Л.[9], Ирфанди Р.[10], Ансори А. Н.М.[11,12], Харишма В. Д.[13,14], Нау С. В.[15], Улла Э.[16], Яхмола В.[11], Зайнул Р.[17]*

[1] Исследовательский центр биоинформатики Индонезийского института биоинформатики (INBIO), Маланг, Индонезия
[2] Национальное агентство исследований и инноваций, Бантен, Индонезия
[3] Отделение фармацевтических наук, фармацевтический факультет, Университет Панкасила, Южная Джакарта, Индонезия
[4] Кафедра компьютерных наук, факультет математики и естественных наук, Университет IPB, Богор, Индонезия
[5] Исследовательский центр тропической биофармацевтики, Университет ИПБ, Богор, Индонезия
[6] Кафедра фармации, факультет медицинских наук, Сингапурский университет Бангса Караванг, Караванг, Индонезия
[7] Факультет здравоохранения, Университет Мухаммадии Гресик, Гресик, Индонезия
[8] Фармацевтический факультет Университета Паджаджаран, Сумеданг, Индонезия
[9] Факультет медицины, Христианский университет Мараната, Бандунг, Индонезия
[10] Кафедра биологического образования, факультет подготовки учителей и просвещения, Университет Пуангримаггалатунг, Сенгканг, Индонезия
[11] Уттаранчальский институт фармацевтических наук, Университет Уттаранчал, Дехрадун, Индия
[12] Департамент аспирантуры, Университет Айрланга, Сурабая, Индонезия
[13] Кафедра биологии, факультет науки и техники, Университет Айрланга, Сурабая, Индонезия
[14] Отдел молекулярной биологии и генетики, Индонезийский фонд Generasi Biologi, Гресик, Индонезия
[15] Кафедра химии, Университет Мьиткьина, Мьиткьина, Мьянма
[16] Химический факультет, Университет штата Миссисипи, Миссисипи, США
[17] Кафедра химии, факультет математики и естественных наук, Университет Негери Паданг, Паданг, Индонезия

КЛЮЧЕВЫЕ СЛОВА:
механизм действия, молекулярный докинг, сетевая фармакология, осциллатоксины

АННОТАЦИЯ

Осциллатоксины (OTXs) — это цитотоксины, продуцируемые некоторыми морскими цианобактериями. Их уникальные структуры показывают высокую эффективность в качестве противораковых средств. Ограниченная доступность производных OTXs в природе дает мало информации об их биологической активности. Было тестировано несколько активностей OTXs в исследованиях *in vitro* или *in vivo* в отношении линий раковых клеток, но их точный механизм действия на мишень не ясен. В данном исследовании мы использовали метод сетевой фармакологии для прогнозирования мишеней и механизмов действия осциллатоксина D (OTX-D), 30 метил-осциллатоксина D (30-метил-OTX-D), осциллатоксина E (OTX-E), и осциллатоксина F (OTX-F). Существуют 20 возможных мишеней четырех соединений против рака и их основными мишенями являются PIK3CA, CDK1 и MTOR. Затем было проведено исследование методом молекулярного докинга для понимания взаимодействия между 4 соединениями и их мишенями. Молекулярный докинг показал, что 4 соединения хорошо взаимодействовали с ключевыми мишенями. В данной работе было выявлено 4 производных OTXs и 3 ключевых мишени для противоракового действия, указывая на множественные сигнальные пути, включая путь экспрессии PD-L1 и контрольной точки PD-1 при раке, протеогликаны при раке и пути при раке, устанавливая теоретические рамки для дальнейшего экспериментального исследования.

1. Introduction

Marine natural products have abundant sources of biologically active agents. Oscillatoxins (OTXs), as one of the examples, are marine cytotoxins resulting from some cyanobacterial species, including *Lyngbya, Schizothrix,* and *Oscillatoria* spp. OTXs have the characteristic feature of the spiro-ether skeleton. However, their availability from natural sources is limited, thus the biological profile of OTX derivatives is also still scarce. More recently, Araki's group conducted the total synthesis of OTXs, which resulted in OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F [1]. Even though the experimental analysis was conducted toward cancer cell lines, the mechanism of action and the specific target of each compound remain unclear, so target identification is required.

In the drug development, target identification aids understanding drug mechanism of action and side effects, thus accelerating the discovery-to-market process. Insufficient knowledge of drug mechanism of action including its target is one of the main causes of a failure of potential drug candidates in clinical trials. In addition, understanding drug target can minimize drug's lack of efficacy and the occurrence of off-target effects, which often cause drug side effects [2,3]. As such, more stringent methods are required to validate the targets of potential drugs prior to being progressed to the clinic.

This study predicted the potential target and pharmacological activity of OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F through network pharmacological analysis and molecular docking. In network analysis we studied the interaction between OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F and their potential targets. Network pharmacology is a study to predict the pathway between possible multiple targets and compounds by clustering protein in relation to several proteins by measuring parameters such as betweenness centrality, degree, and closeness centrality. In molecular docking, we investigated the interaction and binding energy of OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F toward the targets. Before conducting docking simulation, we determined the main targets based on the overlapping targets resulted from network pharmacology analysis.

In this study, network pharmacology analysis and molecular docking were used as a preliminary study to screen the activities of OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F towards receptors in cancer pathways. Then, the results can be followed by a wet lab experiment either *in vitro* or *in vivo*.

2. Materials and methods

2.1. Sample retrieval

The chemical compounds of oscillatoxins comprised of oscillatoxin D (CID: 101283546), 30-methyl-oscillatoxin D (CID: 185389), oscillatoxin E (CID: 156582093), and oscillatoxin F (CID: 156582092) obtained from PubChem [4] (Figure 1A, 1B, 1C, and 1D). All of the compounds were drawn manually using the SwissADME website [5] to obtain a SMILES code, then inserted to ChemSpider [6] to validate the structure's name.

2.2. Network Pharmacological Analysis

The Swiss Target Prediction database [7] and the SuperPred database [8] were used to collect the gene targets from 30-methyl oscillatoxin D, oscillatoxin D, oscillatoxin E, and oscillatoxin F compounds. Protein-Pro-

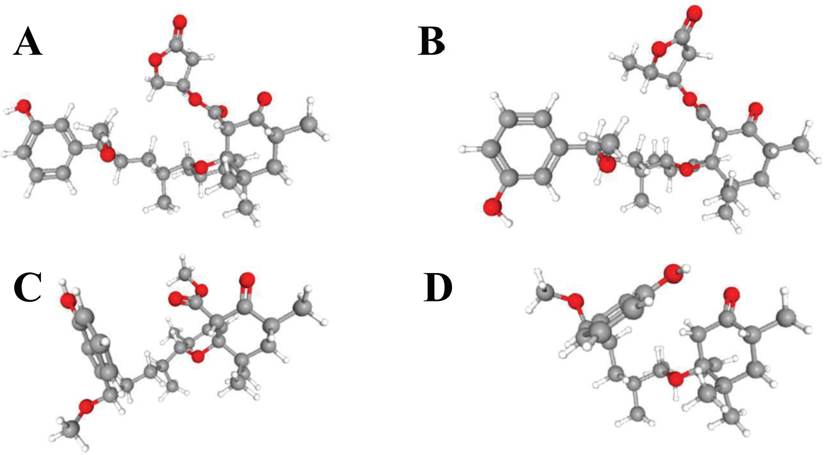


Figure 1. **Chemical compounds of oscillatoxin derivatives. A: oscillatoxin D (CID: 101283546); B: 30-methyl-oscillatoxin D (CID: 185389); C: oscillatoxin E (CID: 156582093), and D: oscillatoxin F (CID: 156582092)**

Рисунок 1. **Химические соединения производных осциллатоксина. A: осциллатоксин D (CID: 101283546); B: 30-метил-осциллатоксин D (CID: 185389); C: осциллатоксин E (CID: 156582093), и D: осциллатоксин F (CID: 156582092)**

tein Interaction Networks (PPI) were created using the STRING database [9] with the restriction of «Homo sapiens» and the following parameters: entire STRING network for network type, high confidence of 0.700 for the necessary score, and medium 5% for FDR stringency. Based on values for degree, betweenness centrality, and closeness centrality, the PPI network was examined using Cytoscape v3.8.2 software [10]. Based on the 20 target proteins with the highest overall centrality value, the sub-network was chosen. A web-based gateway for Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis was Metascape [11]. Afterward, the Pathway Enrichment-Protein Network used Cytoscape v3.8.2 software [10] to visualize the findings of the enrichment study.

2.3. Selection of the protein receptor and control ligand

Four proteins were selected as docking target proteins from four synthesized oscillatoxin compounds, namely CDK1 (PDB ID: 6GU2), PIK3CA (PDB ID: 4JPS), and FKBP/MTOR (PDB ID: 1C9H). The control compound used was a standard drug registered in DrugBank [12], acted as an inhibitor, and was the original ligand of the target protein PDB. CDK1 and MTOR were chosen because they are target proteins from the SwissTargetPrediction and SuperPred databases, and PIK3CA was chosen to replace PIK3R1. This is because there are no experimental results showing PIK3R1 (Uniprot: P27986) to be the target of ligand inhibitors. In addition, PIK3R1 (p85) interacts directly with PIK3CA (p110) and builds PIK3 class I, where p110 is the catalytic domain and p85 is the regulatory domain [13]. Under these assumptions, it is still relevant to investigate the inhibitory effects of PIK3CA. The control compounds used in this study sequentially were Alvocidib/Flavapiridol (CID: 6602328), Alpelisib (CID: 56649450), and Sirolimus/Rapamycin (DrugBank: DB00877).

2.4. Receptor and Ligand Preparation

Receptors were prepared using Biovia Discovery Studio (ver. 19.1.0. Dassault Systemes Biovia) to remove the other ligands and water structures. The prepared receptor was then loaded into PyRx (ver. 0.9.2) and converted to autodock macromolecule format. Oscillatoxin ligand was also loaded in PyRx (ver. 0.9.2), then preparation was done by minimizing the energy based on the Universal Force Field and conversion to Autodock format (.pdbqt) was carried out in OpenBabel [14].

2.5. Molecular Docking Analysis

Molecular docking analysis was carried out using AutodockVina on PyRx (ver. 0.9.2.) The ligand was docked to the protein in rigid conditions at the control ligand binding site, with grid coordinates: CDK1, Center X: 328.447, Y: 214.494, Z: 192.322. Dimensions X: 22,808, Y: 21,990, Z: 20,955; PIK3CA, Center X: –0.276, Y: –8.268, Z: 18.500. Dimensions X: 21,715, Y: 22,604, Z: 23,597; FKBP1/MTOR, Center X: –19.054, Y: –5.071, Z: 192.322. Dimensions X: 23,607, Y: 21,714, Z: 23,078. Then, binding energy scores were recorded, and the representative one was visualized using Biovia Discovery Studio (ver. 19.1.0. Dassault Systemes Biovia). The docking process was done in an environment without water molecules. This was done to reduce the possibility of errors in the computational process due to the presence of water molecules [15]. However, the inclusion of water molecules in certain computational ligands can enrich them substantially and does not affect other ligands [16].

2.6. Chemical interaction and molecular visualization

2D visualization and interaction analysis were performed using Biovia Discovery Studio (ver 19.1.0. Dassault Systemes Biovia), and 2D visualization was performed using LigPlot+ © (ver.2.2.4. Roman Lakoskwi) [17].

3. Results

3.1. Construction and Analysis of the PPI Network

The number of target proteins obtained from the Swiss Target Prediction and SuperPred databases was 234 and 147, respectively. The target proteins were combined, and 341 proteins related to 30-methyl oscillatoxin D, oscillatoxin D, oscillatoxin E, and oscillatoxin F were found. The PPI network of 341 proteins was constructed using STRING and analyzed using Cytoscape software. PPI network analysis showed that out of 341 proteins, 283 proteins **(Supplementary Material)** interacted with each other with 1396 edges. The sub-network was selected based on the 20 proteins that had the highest overall centrality values, namely EGFR, STAT3, AKT1, ESR1, MAPK3, PIK3R1, APP, HSP90AB1, PIK3CA, JAK2, CASP3, NFKB1, FYN, MTOR, CDK1, HIF1A, LYN, HDAC1, MAPK14, and PTPN11 (Table 1).

Table 1. **PPI network analysis of 20 target proteins arranged by highest overall centrality with betweenness centrality, degree, and closeness centrality values**

Таблица 1. **Анализ сети PPI 20 целевых белков, упорядоченных по наивысшей общей центральности с уровнями центральности по посредничеству, по степени и центральности по близости**

No.	Name	Betweenness centrality	Closeness centrality	Degree	Overall centrality
1	EGFR	0.085069154	0.904761905	17	1.690852601
2	STAT3	0.071370767	0.904761905	17	1.690011254
3	AKT1	0.035941917	0.826086957	15	1.467265844
4	ESR1	0.03418289	0.76	13	1.305335287
5	MAPK3	0.042214543	0.791666667	14	1.238364503
6	PIK3R1	0.00850527	0.703703704	11	1.218657054
7	APP	0.004056648	0.575757576	5	1.188040767
8	HSP90AB1	0.017024042	0.655172414	9	1.136891746
9	PIK3CA	0.00850527	0.703703704	11	1.128962776
10	JAK2	0.00873269	0.678571429	10	1.107346493
11	CASP3	0.022082985	0.655172414	9	1.101921322
12	NFKB1	0.043253968	0.730769231	12	1.079738683
13	FYN	0.02289056	0.703703704	11	1.042095396
14	MTOR	0.009879075	0.678571429	10	1.023378462
15	CDK1	0.009607352	0.575757576	5	0.992376837
16	HIF1A	0.012043999	0.655172414	9	0.977125765
17	LYN	0.029646085	0.730769231	12	0.955158012
18	HDAC1	0.008479532	0.575757576	5	0.939202933
19	MAPK14	0.007247496	0.655172414	9	0.92794097
20	PTPN11	0.004645874	0.678571429	10	0.913589597

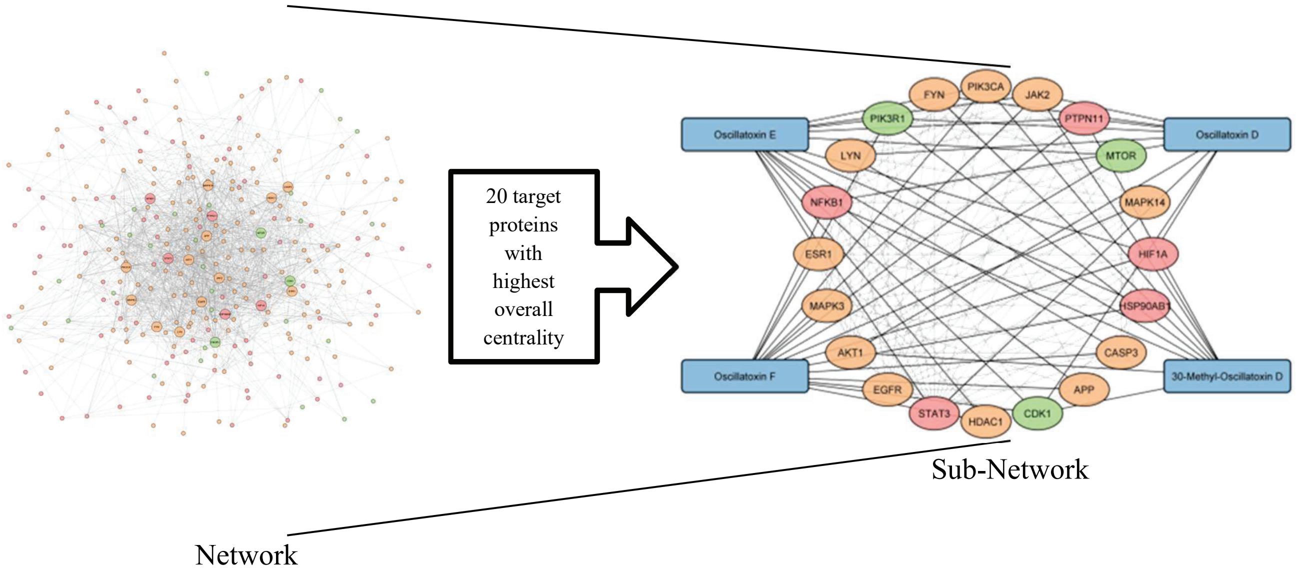


Figure 2. **Topological features of the PPI network and sub-network with high confidence: the orange nodes represent proteins from the Swiss Target Prediction database, the red nodes represent proteins from the SuperPred database, and the green nodes represent proteins from both**

Рисунок 2. **Топологические характеристики сети и подсети PPI с высокой достоверностью: оранжевые узлы представляют белки из базы данных Swiss Target Prediction, красные узлы представляют белки из базы данных SuperPred, а зелёные узлы представляют белки из обеих баз данных**

3.2. Enrichment analysis

Enrichment analysis, including GO and KEGG Pathway, was performed to explore biological processes, components, functions, and signaling pathways related to sub-network protein targets (Figure 2). The lowest LogP (the p-value in log base 10) of GO and KEGG Pathway is shown in Figure 3 and Figure 4. Based on the 20 target proteins selected, AKT1, PIK3CA, PIK3R1, JAK2, MAPK3, MTOR, CDK1, MAPK14, EGFR, and HIF1A are the proteins involved in more than 200 enrichment analyses, with a cutoff of three proteins for each enrichment.

3.3. Molecular Docking Results

Previous studies succeeded in synthesizing derivatives of oscillatoxins (OTXs), including OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F [1]. The structure of the synthesized compounds can be seen in Figure 5. The four synthesized compounds were estimated to have different activities. The activity of these synthesized compounds was analyzed *in silico*, namely through molecular docking analysis. Molecular docking analysis can be used to determine the effectiveness of a drug in the therapy of a disease [18]. The four synthesized products were tested on several signaling pathways, including CDK1, PIK3CA, and FKCBP12/MTOR. PDB ID was used for inhibition testing on the three signaling pathways, respectively, using 6GU2, 4JPS, and 1C9H.

The result of the molecular docking analysis of the four synthesized compounds can be seen in Table 2. The interaction of four synthesized OTX with CDK1 (PDB ID: 6GU2) has a lower potential to occur than the control compound Alvocidib/Flavopyridol (CID: 6602328), with OTX-E interactions requiring the highest binding energy. The binding site of Alvocidib (CID: 6602328) is known to interact with the catalytic domain of PIK3CA, which is spread from the residue Ile10 to Asp146 (Figure 7) [19]. Based on the results of the molecular docking analysis, Alvocidib (CID: 6602328) formed hydrogen bonds in the Glu81 and Leu83 residues and 13 hydrophobic bonds in the surrounding residues. Meanwhile, OTX-D

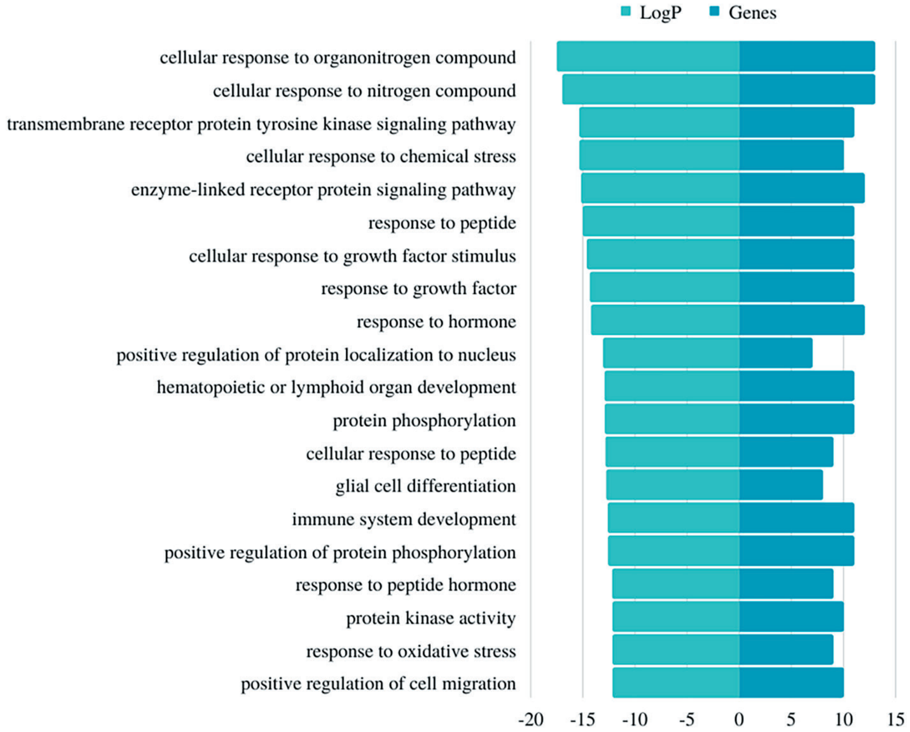


Figure 3. **Gene Ontology chart of 20 enrichments with the lowest LogP and the number of proteins from each GO**

Рисунок 3. **Диаграмма генной онтологии (GO) 20 обогащений с наименьшим LogP и количеством белков от каждой GO**

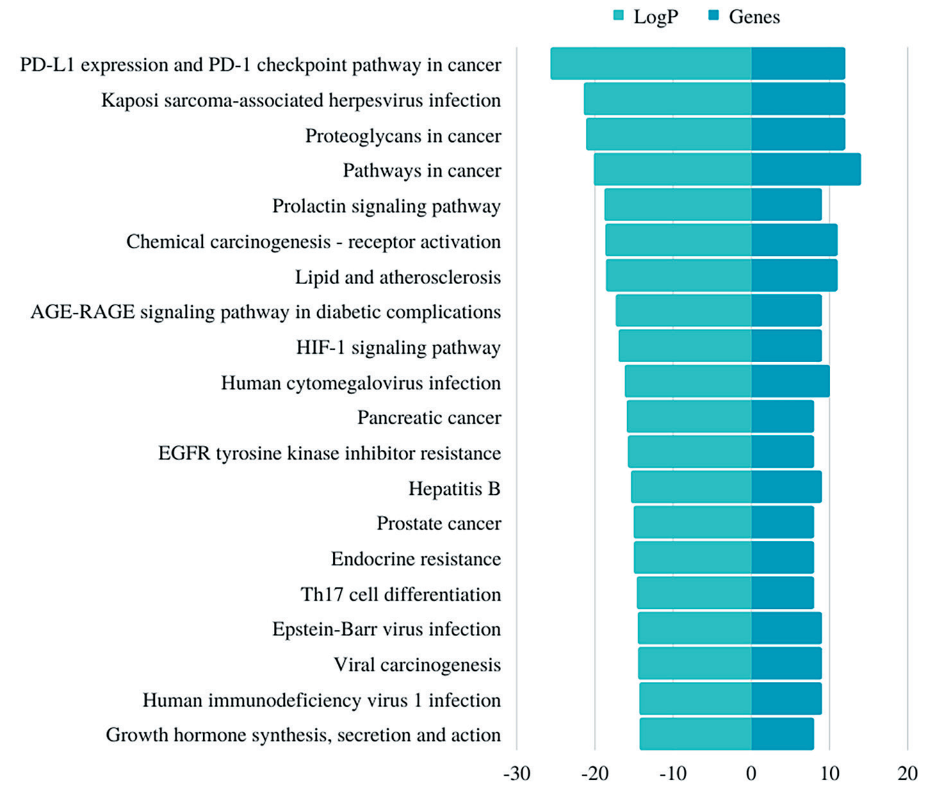
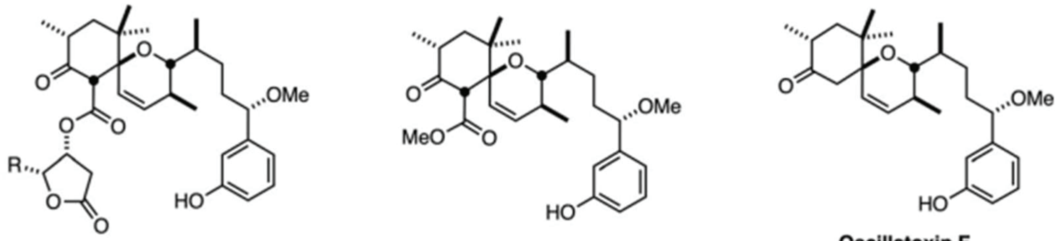


Figure 4. **KEGG Pathway chart of 20 enrichments with the lowest LogP and the number of proteins from each pathway**
Рисунок 4. **Диаграмма пути KEGG 20 обогащений с наименьшим LogP и количеством белков от каждого пути**



Oscillatoxin D: R = H
30-Me-oscillatoxin D: R = Me

Oscillatoxin E

Oscillatoxin F

Figure 5. **The results of the synthesis of OTX compounds from Araki et al. [1]**
Рисунок 5. **Результаты синтеза соединений ОТХ из работы Araki et al. [1]**

had the lowest binding energy score compared to the other synthesized compounds, forming hydrogen bonds in Ile10, Lys33, and Leu83 residues, as well as 10 hydrophobic bonds.

Table 2. **The results of binding energy (Ei) of the molecular docking analysis for four synthesized compounds (kcal/mol)**
Таблица 2. **Результаты энергии связывания (Ei) в анализе методом молекулярного докинга для четырех синтезированных соединений (ккал/моль)**

Signaling pathway	Binding energy (Ei) (kcal/mol)				
	Control	OTX-D	OTX-E	OTX-F	30-methyl-OTX-D
CDK1	−9.6	−9.3	−8.3	−9.2	−9.2
PIK3CA	−10.4	−7.9	−8.3	−8.4	−8.5
FKCBP12/ MTOR	−6.6	−7.5	−6.6	−7.5	−7.7

Table 3. **The number of hydrogen bonds and amino acid residues of the three synthesized compounds**
Таблица 3. **Количество водородных связей и аминокислотных остатков трёх синтезированных соединений**

Synthesized compounds	Number of hydrogen bonds	Amino acid residues
OTX-D	4	ARG42 (2), ILE56, TYR82
OTX-F	2	TYR26, ALA81
30-methyl-OTX-D	2	LYS44, ILE56

In addition, it is known that the number of hydrogen bonds is not always the reason for the low binding energy score in an interaction. The binding energy of molecular docking results is determined by various aspects of scoring and simplification by the software algorithm, such as the presence and type of hydrogen, electrostatic interactions, and van der Waals bonds, which include the presence of water molecules [20]. Thus, compounds with a low score difference are considered to have a similar probability of performing similar activities in the body due to the complexity of the human body systems. To conclude, OTX-D, OTX-F, and 30-methyl-OTX-D have the potential to become PIK3CA inhibitors, as well as Alvocidib.

The interaction of four synthesized OTXs with PIK3CA (PDB ID: 4JPS) has a lower potential to occur than the control compound Alpelisib (CID: 56649450), with OTX-D interactions requiring the highest binding energy. Alpelisib (CID: 56649450) binds to the ATP pocket in the kinase domain, with massive contacts with the P-loop and hinge region [21]. Alpelisib showed a good binding bond through interaction with the hydrogen bond network including three molecules of water and Tyr836, Asp810, Asp933 and Lys802 side chains. Moreover, Lys802 made a hydrogen bond interaction with one fluorine atom of the trifluoromethyl of Alpelisib. Amide group and residue of Gln859 and Val851 performed a pair of donor-acceptor hydrogen bonds (Figure 8) [22]. Based on the results of molecular docking analysis, Alpelisib (CID: 56649450) formed hydrogen bonds in the Gln859 and Ser854 residues and 11 hydrophobic bonds in the surrounding residues. Meanwhile, 30-methyl-OTX-D had the lowest binding energy score compared to the other synthesized compounds, forming hydrogen bonds in Lys802, Asp805, Val851, and Asp933 residues,

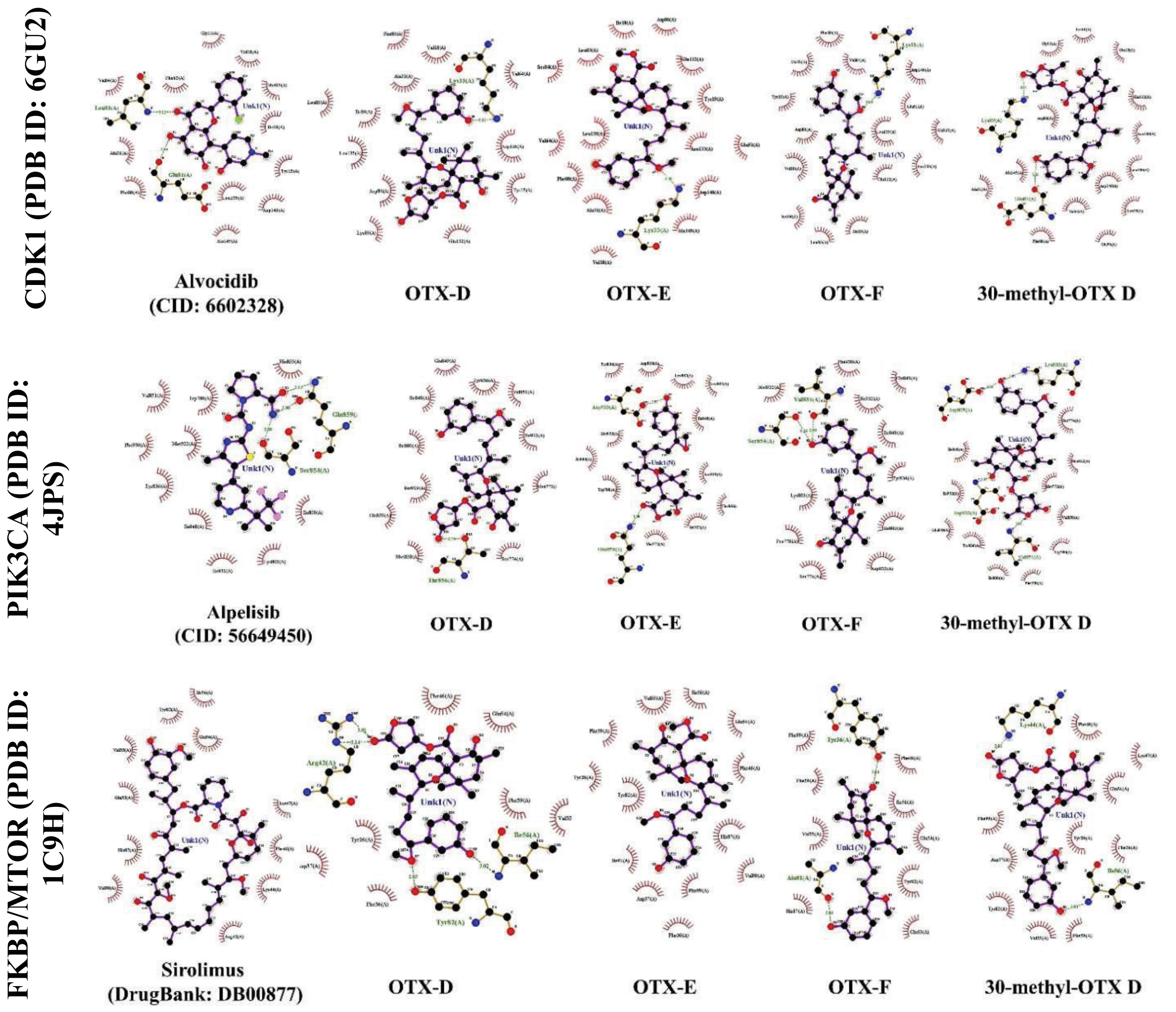


Figure 6. **2D Interaction between four synthesized oscillatoxins compounds with CDK1, PIK3CA, and FKBP/MTOR in comparison with Alvocidib, Alpelisib, and Sirolimus. 2D Visualization conducted with LigPlot+ and the difference of bonds formed belongs to software algorithm**

Рисунок 6. **2D взаимодействия между четырьмя синтезированными соединениями осциллатоксина с CDK1, PIK3CA и FKBP/MTOR по сравнению с Alvocidib, Alpelisib и Sirolimus. 2D визуализация, проведенная с LigPlot+, и различие образованных связей соответствует алгоритму компьютерной программы**

as well as 11 hydrophobic bonds. Based on the binding energy score, it can be said that the potential of the synthesized compound as a PIK3CA inhibitor is relatively weak, so further testing and research are needed.

Furthermore, from the results of the analysis, it can be concluded that the four synthesized compounds had the potential to inhibit the FKCBP12/MTOR signaling pathways. This was because the binding energy of the four compounds synthesized on the FKCBP12/MTOR signaling pathways was better than the binding energy of the control compounds on the FKCBP12/MTOR signaling pathways when binding to the binding site. Moreover, FKCBP12/MTOR has binding sites at Asp37, Gln53, Glu54, Ile56, and Tyr82 when interacting with Sirolimus experimentally, which exerts an inhibitory effect on the MTOR signaling pathway [23]. MTOR signaling pathways can influence gene transcription and protein synthesis to regulate cell growth and proliferation, influence the differentiation of immune cells to participate in immune regulation, and play an important role in tumor metabolism [24]. The type of interaction that occurred between the four synthesized compounds and the FKCBP12/MTOR signaling pathways can be seen in Figure 6. Based on the type of the anticancer inhibition mechanism through the FKCBP12/MTOR signaling pathways, the OTX-E compound had a lower potency than the other three compounds. This was indicated by the value of the binding energy, which was not good, and the absence of hydrogen bonds. The presence of hydrogen bonds affected the binding energy that occurred between the ligand and protein, where the more hydrogen bonds, the better the binding energy [25]. Types of amino acid residues from proteins that formed hydrogen bonds with the three synthesized compounds can be seen in Table 3.

The best interaction potential occurred in 30-methyl-OTX D, which had the lowest binding energy score compared to the other four OTX compounds, including the control compound Sirolimus/Rapamycin (DrugBank: DB00877). A hydrogen bond was also formed in the residues Lys44 and Ile56 during this interaction. Although the interacting residues involved in the hydrogen bonds of 30-methyl-OTX D were different from Sirolimus, hydrophobic bounds were strongly formed in Tyr26, Phe46, Val55, Ile56, Phe59, and Phe99 residues.

4. Discussion

OTXs provide several promising pharmacological activities including the anticancer activity. In 2021, OTX derivatives were obtained through the total synthesis route, which resulted in four compounds including OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F [1]. Generally, the OTX family can activate protein kinase C (PKC), which plays important roles in inflammation action, tumor promotion, and cell growth inhibition [26]. PKCδ is not the appropriate target molecule for the OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F. Such conditions imply that as part of their unique activities, OTXs target molecules that have not yet been recognized. Therefore, further investigation of OTX target protein was conducted in this study.

In drug discovery, target identification is the primary step to determine drug mechanisms of action and side effects, thus accelerating the discovery-to-market process. Understanding of drug targets can help improve drug efficacy and manage the occurrence of undesired effects, which often cause drug side effects [27]. In this study, possible protein targets were determined by the network pharmacological analysis method, followed by the molecular docking study to illustrate the interaction between the com-

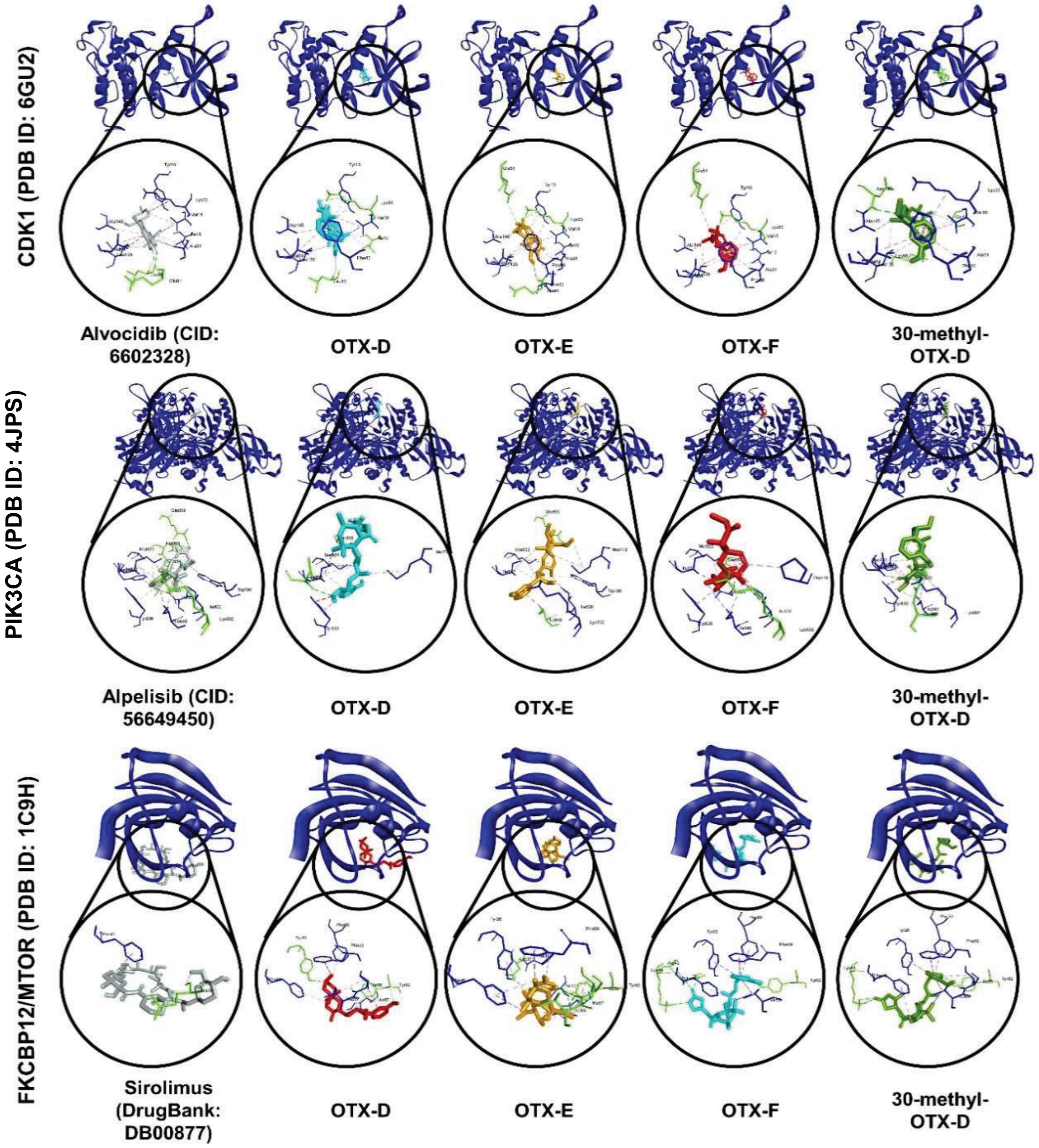


Figure 7. **Binding sites of CDK1, PIK3CA, and FKCBP12/MTOR located at the control ligand interaction sites based on laboratory results**

Рисунок 7. **Участки связывания CDK1, PIK3CA и FKCBP12/MTOR, расположенные на участках взаимодействия контрольного лиганда на основании лабораторных результатов**

pounds and protein targets. We predicted that there were 20 target proteins of OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F, and then we determined that the key targets of the four compounds were PIK3CA, CDK1, and MTOR.

To reveal the anticancer potential of oscillatoxins, gene ontology and KEGG pathway enrichment analyses were performed. According to Figure 4, the result indicates that there are significantly enriched cancer-related terms such as cellular response to organonitrogen compound, cellular response to nitrogen compound, transmembrane receptor protein tyrosine kinase signaling pathway, cellular response to growth factor stimulus, response to growth factor, positive regulation of cell migration, response to hormone, and response to oxidative stress. Nitrogen is part of energy transfer compounds such as ATP (adenosine triphosphate), which allows cells to conserve and use the energy released by metabolism. Disrupting cellular responses to nitrogen disrupts cellular metabolism and cell formation [28]. Many dysregulations in cell mechanisms are related to cancer growth. Aberrantly activated receptor tyrosine kinases (RTKs) lead to human cancers [29]. Chromosomal instability and genetic mutations drive cancer cell migration and invasion [30]. Mutation in the hormone receptor influences a breast tumor's response to chemotherapy [31]. Many studies established the role of oxidative stress in cancer initiation and growth [32]. Tyrosine kinases belong to a large class of enzymes called protein kinases, which also bind phosphates to other amino acids such as serine and threonine. Phosphorylation of proteins by kinases is an important mechanism for the regulation of intracellular signaling (signal transduction) and cellular activities such as cell division. Protein kinases can mutate and lead to uncontrolled cell growth, a necessary step in cancer development [33]. Understanding of these mechanisms has important implications for discovery of anti-cancer drugs.

Further KEGG enrichment analysis of the target proteins showed that compounds OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F are mainly involved in PD-L1 expression and PD-1 checkpoint pathway in cancer, proteoglycans in cancer, and pathways in cancer. Molecular docking also illustrated that OTX derivatives were well combined with the target proteins. PIK3CA, CDK1, and MTOR are important targets associated with the cancer diseases. By having the antiproliferative activity in DMS114 lung cancer cell lines [1], OTX-F may target PIK3CA, CDK1, and MTOR. Other three compounds generally also target PIK3CA, CDK1, and MTOR. Even though they lack the antiproliferative activity in DMS114 cells, the targets may be expressed in other types of cancers. Compounds OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F also target NFKB1, JAK2, PTPN11, MAPK14, MAPK3, AKT1, EGFR, HIF1A, STAT3, ESR1, PIK3R1, LYN, HDAC1, FYN, HSP90AB1, CASP3, and APP.

Various potential targets of OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F in the cancer cells demonstrated that they offered the promising pharmacological activities, which might be the fundamental theory in the further study.

5. Conclusion

This study revealed 20 potential protein targets and three key target proteins of OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F, which are involved in various signaling pathways, including PD-L1 expression and PD-1 checkpoint pathway in cancer, proteoglycans in cancer, and pathways in cancer. These three main targets are PIK3CA, CDK1, and MTOR. To date, there are several experimental studies on the effect of oscillatoxin derivatives; however, the exact mechanism of action and the target proteins remain unclear. Therefore, this study determined the protein targets and provides the prediction of mechanism of compounds OTX-D, 30-methyl-OTX-D, OTX-E, and OTX-F through network pharmacological analysis and molecular docking study. To support the result of this study, an experimental study is required to validate the target of oscillatoxins.

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AUTHOR INFORMATION	СВЕДЕНИЯ ОБ АВТОРАХ
Affiliation	**Принадлежность к организации**
Dewi Luthfiana, Bachelor of Science, Researcher, Bioinformatics Research Center, Indonesian Institute of Bioinformatics (INBIO) Pakisaji, Kab.Malang, Jawa Timur, Indonesia, 65162 Tel.: +628–533–645–32–24 E-mail: dewiluthfiana7@gmail.com ORCID: https://orcid.org/0000–0001–6109–5283	**Лютфиана Дэви** — бакалавр, научный сотрудник, Исследовательский центр биоинформатики, Индонезийский институт биоинформатики 65162, Индонезия, Восточная Ява, регентство Маланг, Пакисаджи Тел.: +628–533–645–32–24 E-mail: dewiluthfiana7@gmail.com ORCID: https://orcid.org/0000–0001–6109–5283
Maratu Soleha, Master of Biotechnology, Researcher, National Research and Innovation Agency Gedung B. J. Habibie, Jl. M. H. Thamrin No. 8, Jakarta Pusat, Indonesia, 10340 Tel.: +628–953–452–30–62 E-mail: maratu1508@gmail.com ORCID: https://orcid.org/0009–0007–3119–4951	**Солеха Марату** — магистр биотехнологии, научный сотрудник, Национальное агентство исследований и инноваций 10340, Индонезия, Центральная Джакарта, ул. М. Х. Тамрин, 8, Здание Б. Дж. Хабиби Тел.: +628–953–452–30–62 E-mail: maratu1508@gmail.com ORCID: https://orcid.org/0009–0007–3119–4951
Andri Prasetiyo, Doctor in Pharmaceutical Science, Assistant Professor, Department of Pharmaceutical Science, Faculty of Pharmacy, Pancasila University Jalan Raya Lenteng Agung No.56–80, Srengseng Sawah, Jagakarsa, Jakarta 12640, Indonesia Tel.: +628–128–654–61–48 E-mail: andriprasetiyo@univpancasila.ac.id ORCID: https://orcid.org/0000–0002–9936–6058	**Прасетийо Андри** — доктор фармацевтических наук, старший преподаватель, кафедра фармацевтических наук, фармацевтический факультета, Университет Панкасила 12640, Индонезия, Джакарта, ул. Джалан Райя Лентенг Агунг, 56 Тел.: +628–128–654–61–48 E-mail: andriprasetiyo@univpancasila.ac.id ORCID: https://orcid.org/0000–0002–9936–6058

Wisnu A. Kusuma, PhD in Computer Science, Associate Professor, Department of Computer Science, Faculty Mathematics and Natural Sciences, IPB University Jln. Meranti, Kampus IPB Darmaga, Bogor, Indonesia, 16680 Tropical Biopharmaca Research Center, IPB University Jl. Taman Kencana No. 3, Bogor, Indonesia, 16128 Tel.: +622–518–37–35–61 E-mail: ananta@apps.ipb.ac.id ORCID: https://orcid.org/0000–0002–3682–244X	**Кусума Висну Ананта** — PhD компьютерных наук, адъюнкт-профессор, кафедра компьютерных наук, факультет математики и естественных наук, Университет ИПБ 16680, Индонезия, Богор, кампус IBP Дагмара, улица Меранти Исследовательский центр тропической биофармацевтики, Университет ИПБ 16128, Индонезия, Богор, ул. Таман Кенсана, 3 Тел.: +622–518–37–35–61 E-mail: ananta@apps.ipb.ac.id ORCID: https://orcid.org/0000–0002–3682–244X
Rizka Fatriani, Master in Biology, Research Assistant, Tropical Biopharmaca Research Center, IPB University Jl. Taman Kencana No. 3, Bogor, Indonesia, 16128 Tel.: +622–518–37–35–61 E-mail: fatrianirizka@gmail.com	**Фатриани Ризка** — магистр биологии, научный сотрудник, Исследовательский центр тропической биофармацевтики, Университет ИПБ 16128, Индонезия, Богор, ул. Таман Кенсана, 3 Тел.: +622–518–37–35–61 E-mail: fatrianirizka@gmail.com
Lina Nurfadhila, Master in Pharmaceutical Science, Lecturer, Faculty of Health Sciences, University of Singaperbangsa Karawang Jl. HS. Ronggo Waluyo, Karawang, West Java, Indonesia, 41363 Tel.: +628–572–343–23–10 E-mail: lina.nurfadhila@fikes.unsika.ac.id ORCID: https://orcid.org/0000–0001–8629–6866	**Нурфадхила Лина** — магистр фармацевтических наук, преподаватель, факультет медицинских наук, Сингапурский университет Банга Караванг 41363, Индонезия, Западная Ява, Касаванг, улица Ронгго Валуйя Тел.: +628–572–343–23–10 E-mail: lina.nurfadhila@fikes.unsika.ac.id ORCID: https://orcid.org/0000–0001–8629–6866
Norainny Yunitasari, Doctor in Chemistry, Lecturer, Faculty of Health, University of Muhammadiyah Gresik Jl. Proklamasi 54, Gresik, East Java, Indonesia, 61121 Tel.: +628–123–442–26–26 E-mail: yunitasari060688@gmail.com ORCID: https://orchid.org/0000–0002–1861–0953	**Юнитасари Норайни** — доктор химических наук, преподаватель, факультет здравоохранения, Университет Мухаммадии Гресик 61121, Индонезия, Восточная Ява, Гресик, ул. Прокламации, 54 Тел.: +628–123–442–26–26 E-mail: yunitasari060688@gmail.com ORCID: https://orchid.org/0000–0002–1861–0953
Ahmad H. Ahkam, Master student in Pharmacology, Faculty of Pharmacy, Padjadjaran University Jl. Ir. Soekarno km.21, Kab. Sumedang, West Java, Indonesia, 40132 Tel.: +628–521–988–34–77 E-mail: ahmad23011@mail.unpad.ac.id	**Ахкам Ахмад Х.** — магистрант по фармакологии, фармацевтический факультет, Паджаджаранский университет 40132, Индонезия, Западная Ява, регентство Сумеданг, ул. Сухарно, 21 км Тел.: +628–521–988–34–77 E-mail: ahmad23011@mail.unpad.ac.id
Teresa L. Wargasetia, Doctor in Medical Science, Associate Professor, Faculty of Medicine, Maranatha Christian University Jl. Prof. drg. Surya Sumantri, M.P.H. No. 65 Bandung, West Java, Indonesia, 40164 Tel.: +622–220–121–86 E-mail: Teresa.lw@med.maranatha.edu ORCID: https://orcid.org/0000–0002–3433–3300	**Варгасетия Тереза Лилиана** — доктор медицинских наук, адъюнкт-профессор, медицинский факультет, Христианский университет Маранаты 40164, Индонезия, Западная Ява, Бандунг, ул. Профессора Сурия Сумантри, 65 Тел.: +622–220–121–86 E-mail: Teresa.lw@med.maranatha.edu ORCID: https://orcid.org/0000–0002–3433–3300
Rizal Irfandi, Master of Chemistry, Assistant Professor, Department of Biology Education, Faculty of Teacher Training and Education, Universitas Puangrimaggalatung Jalan Puangrimaggalatung No 27, Sengkang, Indonesia, 90915 Tel.: +628–239–364–43–53 E-mail: rizalirfandi043@gmail.com ORCID: https://orcid.org/0000–0002–4845–3397	**Ирфанди Ризал**, Магистр химии, старший преподаватель, кафедра биологического образования факультета подготовки учителей и просвещения, Университет Пуангримаггалатунг 90915, Индонезия, Сенгканг, ул. Джалан Пуангримаггалатунг, 27 Тел.: +628–239–364–43–53 E-mail: rizalirfandi043@gmail.com ORCID: https://orcid.org/0000–0002–4845–3397
Arif N. M. Ansori, PhD in Veterinary Science, Researcher, Postgraduate School, Universitas Airlangga Jl. Mulyorejo, Kec. Mulyorejo, Surabaya, East Java, 60115, Indonesia Tel.: +628–214–464–78–32 E-mail: ansori.anm@gmail.com ORCID: https://orcid.org/0000–0002–1279–3904	**Анзори Ариф Нур Мухаммад** — PhD, Доктор ветеринарных наук, научный сотрудник, департамент аспирантуры, Университет Айрланга 60115, Индонезия, Восточная Ява, Сурабая, округ Мулиорехо, ул. Мулиорехо Тел.: +628–214–464–78–32 E-mail: ansori.anm@gmail.com ORCID: https://orcid.org/0000–0002–1279–3904
Viol D. Kharisma, Master of Science, PhD Student, Department of Biology, Faculty of Science and Technology, Universitas Airlangga Jl. Mulyorejo, Kec. Mulyorejo, Surabaya, East Java, 60115, Indonesia Tel.: +628–121–78–70–02 E-mail: viol.dhea.kharisma-2022@fst.unair.ac.id ORCID: https://orcid.org/0000–0001–9060–0429	**Харишма Виол Дхеа** — магистр наук, аспирант, кафедра биологии, факультет науки и техники, Университет Айрланга 60115, Индонезия, Восточная Ява, Сурабая, округ Мулиорехо, ул. Мулиорехо Тел.: +628–121–78–70–02 E-mail: viol.dhea.kharisma-2022@fst.unair.ac.id ORCID: https://orcid.org/0000–0001–9060–0429
Sin W. Naw, Master of Science, Lecturer, Department of Chemistry, Myitkyina University CC95+FWM, Myitkyina, Myanmar Tel.: +959–440–00–71–12 E-mail: maripsinwarnaw94@gmail.com ORCID: https://orcid.org/0000–0002–5985–361X	**Нау Син Во** — магистр наук, преподаватель, химический факультет, Университет Мьиткьина Мьянма, Мьиткьина, CC95+FWM, Тел.: +959–440–00–71–12 E-mail: maripsinwarnaw94@gmail.com ORCID: https://orcid.org/0000–0002–5985–361X
Emdad Ullah, Master of Science, PhD Student, Department of Chemistry, Mississippi State University 310 President Cir, Mississippi, Mississippi State, United States MS39762 Tel.: +1–662–617–56–70 E-mail: emdadsami@yahoo.com ORCID: https://orcid.org/0000–0002–1683–2501	**Улла Эмдат** — магистр наук, аспирант, химический факультет, Университет штата Миссисипи MS39762, США, штат Миссисипи, Миссисипи, Президентский центр, 310 Тел.: +1–662–617–56–70 E-mail: emdadsami@yahoo.com ORCID: https://orcid.org/0000–0002–1683–2501
Vikash Jakhmola, Professor, Professor, Uttaranchal Institute of Pharmaceutical Sciences, Uttaranchal University Chakrata Rd, Prem Nagar, Dehradun, Uttarakhand, 248007, India Tel.: +918–126–00–96–20 E-mail: jakhmola.1979@gmail.com ORCID: https://orcid.org/0000–0002–8108–006X	**Яхмола Викаш** — профессор, Уттаранчальский институт фармацевтических наук, Уттаранчальский университет 248007, Индия, Уттаракханд, Дехрадун, ул. Чакрата Тел.: +918–126–00–96–20 E-mail: jakhmola.1979@gmail.com ORCID: https://orcid.org/0000–0002–8108–006X

Rahadian Zainul, Professor in Chemistry, Professor, Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang
Jl. Prof. Dr. Hamka, Air Tawar Bar., Kec. Padang Utara, Kota Padang, Sumatera Barat, Indonesia, 25171
Tel.: +628–126–138–53–85
E-mail: rahadianzmsiphd@fmipa.unp.ac.id
ORCID: https://orcid.org/ 0000–0002–3740–3597
* corresponding author

Зайнул Рахадин — профессор химии, профессор, кафедра химии, факультет математики и естественных наук, Университет Негери Паданг
21171, Индонезия, Западная Суматра, округ Паданг Утара, Патанг, ул. Профессора, доктора Хамка
Тел.: +628–126–138–53–85
E-mail: rahadianzmsiphd@fmipa.unp.ac.id
ORCID: https://orcid.org/ 0000–0002–3740–3597
* автор для контактов

Contribution	Критерии авторства
The author has the sole responsibility for writing the manuscript and is responsible for plagiarism.	Автор имеет единоличное отношение к написанию рукописи и несет ответственность за плагиат
Conflict of interest	**Конфликт интересов**
The author declare no conflict of interest.	Автор заявляет об отсутствии конфликта интересов.

SUPPLEMENTARY MATERIAL

Supplementary 1. The list of gene and protein names associated with 30-methyl oscillatoxin D, oscillatoxin D, oscillatoxin E, and oscillatoxin F compounds

No	Gene Name	Protein Name
1	EGFR	Epidermal growth factor receptor
2	STAT3	Signal transducer and activator of transcription 3
3	AKT1	RAC-alpha serine/threonine-protein kinase
4	ESR1	Estrogen receptor
5	MAPK3	Mitogen-activated protein kinase 3
6	PIK3R1	Phosphoinositide-3-kinase regulatory subunit alpha/beta/delta
7	APP	Amyloid-beta A4 protein
8	HSP90AB1	Heat shock protein 90 alpha family class b member 1
9	PIK3CA	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform
10	JAK2	Tyrosine-protein kinase JAK2
11	CASP3	Caspase-3
12	NFKB1	Nuclear factor NF-kappa-B p105 subunit
13	FYN	Tyrosine-protein kinase Fyn
14	MTOR	Serine/threonine-protein kinase mTOR
15	CDK1	Cyclin-dependent kinase 1
16	HIF1A	Hypoxia-inducible factor 1-alpha
17	LYN	Lyn proto-oncogene, src family tyrosine kinase
18	HDAC1	Histone deacetylase 1/2
19	MAPK14	Mitogen-activated protein kinase 14
20	PTPN11	Tyrosine-protein phosphatase non-receptor type 11
21	MDM2	E3 ubiquitin-protein ligase Mdm2
22	GSK3B	Glycogen synthase kinase-3 beta
23	TLR4	Toll-like receptor 4
24	ERBB2	Receptor tyrosine-protein kinase erbB-2
25	ITGB1	Integrin beta-1
26	JAK1	Tyrosine-protein kinase JAK1
27	PIK3CD	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit delta isoform
28	CDK2	Cyclin-dependent kinase 2
29	PRKCA	Protein kinase C alpha type
30	PIK3CB	Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha/beta/delta
31	RXRA	Retinoic acid receptor RXR-alpha
32	EPHB2	Ephrin type-B receptor 2
33	ABL1	Tyrosine-protein kinase ABL1
34	YES1	Yes proto-oncogene 1, src family tyrosine kinase
35	CDC25C	M-phase inducer phosphatase 3
36	CCNA2	Cyclin-A2
37	PRKCD	Protein kinase C delta type
38	GRIN1	Glutamate receptor ionotropic, NMDA 1
39	PDPK1	3-phosphoinositide-dependent protein kinase 1
40	IGF1R	Insulin-like growth factor 1 receptor
41	CCNB1	G2/mitotic-specific cyclin-B1
42	MMP9	Matrix metalloproteinase-9
43	HCK	Tyrosine-protein kinase HCK
44	SYK	Spleen associated tyrosine kinase
45	EZH2	Histone-lysine N-methyltransferase EZH2
46	HDAC2	Histone deacetylase 1/2
47	PDGFRB	Platelet-derived growth factor receptor beta
48	JAK3	Tyrosine-protein kinase JAK3
49	PTK2B	Protein-tyrosine kinase 2-beta
50	FGR	Fgr proto-oncogene, src family tyrosine kinase
51	CAMK2A	Calcium/calmodulin-dependent protein kinase type II subunit alpha
52	PARP1	Poly [ADP-ribose] polymerase 1
53	PIK3CG	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit gamma isoform
54	IKBKB	Inhibitor of nuclear factor kappa-B kinase subunit beta
55	CASP8	Caspase-8
56	CCNE1	G1/S-specific cyclin-E1
57	CAMK2D	Calcium/calmodulin-dependent protein kinase type II subunit delta
58	GRM5	Metabotropic glutamate receptor 5
59	ESR2	Estrogen receptor beta
60	PRKDC	DNA-dependent protein kinase catalytic subunit
61	PGR	Progesterone receptor
62	ITGB3	Integrin beta-3
63	FKBP5	Peptidyl-prolyl cis-trans isomerase FKBP5
64	PTPN1	Tyrosine-protein phosphatase non-receptor type 1
65	MAP2K2	Dual specificity mitogen-activated protein kinase kinase 2
66	CHEK1	Serine/threonine-protein kinase Chk1
67	LRRK2	Leucine-rich repeat serine/threonine-protein kinase 2
68	BCL2	Apoptosis regulator Bcl-2
69	CDK9	Cyclin-dependent kinase 9
70	HDAC3	Histone deacetylase 3
71	CCNB2	G2/mitotic-specific cyclin-B2
72	MMP2	Matrix metalloproteinase-2 (gelatinase a)
73	BLK	Tyrosine-protein kinase Blk
74	CDK5	Cyclin-dependent-like kinase 5
75	AURKA	Aurora kinase A
76	HDAC6	Histone deacetylase 6
77	NTRK1	High affinity nerve growth factor receptor
78	AURKB	Aurora kinase B
79	ZAP70	Tyrosine-protein kinase ZAP-70
80	CACNA1C	Voltage-dependent L-type calcium channel subunit alpha-1C
81	PDGFRA	Platelet-derived growth factor receptor alpha
82	ITK	Tyrosine-protein kinase ITK/TSK
83	TOP2A	DNA topoisomerase 2-alpha
84	KIF11	Kinesin-like protein KIF11
85	BRAF	B-raf proto-oncogene serine/threonine-protein kinase
86	PTPN2	Tyrosine-protein phosphatase non-receptor type 2
87	KDM1A	[histone h3]-n6, n6-dimethyl-l-lysine4 fad-dependent demethylase
88	MMP3	Matrix metalloproteinase-3 (stromelysin 1, progelatinase)
89	MAPK10	Mitogen-activated protein kinase 8/9/10 (c-jun n-terminal kinase)
90	ADAM10	Disintegrin and metalloproteinase domain-containing protein 10
91	ADAM17	Disintegrin and metalloproteinase domain-containing protein 17

No	Gene Name	Protein Name
92	HDAC7	Histone deacetylase 7
93	CDK7	Cyclin-dependent kinase 7
94	TRIM24	Transcription intermediary factor 1-alpha
95	PSEN1	Presenilin-1
96	NR1I2	Nuclear receptor subfamily 1 group I member 2
97	IL6ST	Interleukin-6 receptor subunit beta
98	FKBP1A	Peptidyl-prolyl cis-trans isomerase FKBP1A
99	NLRP3	NACHT, LRR and PYD domains-containing protein 3
100	CCNA1	Cyclin-A1
101	NOS2	Nitric-oxide synthase, inducible
102	OPRM1	Mu-type opioid receptor
103	CCNT1	Cyclin-T1
104	CAPN1	Calpain-1 catalytic subunit
105	INSR	Insulin receptor
106	CAMK2G	Calcium/calmodulin-dependent protein kinase type II subunit gamma
107	MMP14	Matrix metalloproteinase-14
108	SLC9A1	Solute carrier family 9 (sodium/hydrogen exchanger), member 1
109	CASP1	Caspase-1
110	HDAC5	Histone deacetylase 4/5
111	NFE2L2	Nuclear factor erythroid 2-related factor 2
112	GRM1	Metabotropic glutamate receptor 1
113	OGT	UDP-N-acetylglucosamine — peptide N-acetylglucosaminyltransferase 110 kDa subunit
114	ROCK1	Rho-associated protein kinase 1
115	CCNH	Cyclin-H
116	CTSD	Cathepsin D
117	MME	Membrane metalloendopeptidase
118	DUT	Deoxyuridine 5'-triphosphate nucleotidohydrolase, mitochondrial
119	CCNB3	G2/mitotic-specific cyclin-B3
120	FPR1	Formyl peptide receptor 1
121	RIPK2	Receptor-interacting serine/threonine-protein kinase 2
122	ATR	Serine/threonine-protein kinase ATR
123	PRKAA1	5'-AMP-activated protein kinase catalytic subunit alpha-1
124	LGALS3	Galectin-3
125	CFTR	Cystic fibrosis transmembrane conductance regulator
126	THRA	Thyroid hormone receptor alpha
127	KEAP1	Kelch-like ECH-associated protein 1
128	RPS6KA1	Ribosomal protein S6 kinase alpha-1
129	WEE1	Wee1-like protein kinase
130	CASP7	Caspase-7
131	CTSB	Cathepsin B
132	HDAC4	Histone deacetylase 4/5
133	BMX	Cytoplasmic tyrosine-protein kinase BMX
134	MARK3	MAP/microtubule affinity-regulating kinase 3
135	PSEN2	Presenilin-2
136	PLK4	Serine/threonine-protein kinase PLK4
137	ROCK2	Rho-associated protein kinase 2
138	MMP1	Matrix metalloproteinase-1 (interstitial collagenase)
139	EIF2AK2	Interferon-induced, double-stranded RNA-activated protein kinase
140	CBX4	E3 SUMO-protein ligase CBX4
141	NCSTN	Nicastrin
142	RPS6KA3	Ribosomal protein S6 kinase alpha-3
143	NR3C2	Mineralocorticoid receptor
144	ADRB1	Beta-1 adrenergic receptor
145	NTRK3	NT-3 growth factor receptor
146	PSENEN	Gamma-secretase subunit PEN-2
147	APH1A	Gamma-secretase subunit APH-1A
148	DRD2	D(2) dopamine receptor
149	PIP5K1A	Phosphatidylinositol 4-phosphate 5-kinase type-1 alpha
150	CSF1R	Macrophage colony-stimulating factor 1 receptor
151	PLK2	Serine/threonine-protein kinase PLK2
152	APEX1	DNA-(apurinic or apyrimidinic site) lyase
153	TBK1	Serine/threonine-protein kinase TBK1
154	PKN1	Serine/threonine-protein kinase N1
155	P2RX7	P2X purinoceptor 7
156	FNTA	Protein farnesyltransferase/geranylgeranyltransferase type-1 subunit alpha
157	EIF2AK3	Eukaryotic translation initiation factor 2-alpha kinase 3
158	APH1B	Aph-1 homolog B, gamma-secretase subunit
159	PDE3B	cGMP-inhibited 3',5'-cyclic phosphodiesterase B
160	PIM1	Serine/threonine-protein kinase pim-1
161	CDK5R1	Cyclin dependent kinase 5 regulatory subunit 1
162	PROC	Vitamin K-dependent protein C
163	MAP3K11	Mitogen-activated protein kinase kinase kinase 11
164	SLC2A1	Solute carrier family 2, facilitated glucose transporter member 1
165	DUSP3	Dual specificity protein phosphatase 3
166	GPBAR1	G-protein coupled bile acid receptor 1
167	MAP3K3	Mitogen-activated protein kinase kinase kinase 3
168	HSD17B10	3-hydroxyacyl-CoA dehydrogenase / 3-hydroxy-2-methylbutyryl-CoA dehydrogenase
169	PIP4K2B	Phosphatidylinositol 5-phosphate 4-kinase type-2 beta
170	PER2	Period circadian protein homolog 2
171	KLF5	Krueppel-like factor 5
172	KCNH2	Potassium voltage-gated channel subfamily H member 2
173	CXCR1	C–X-C chemokine receptor type 1
174	PSMB5	Proteasome subunit beta type-5
175	PSMB9	Proteasome subunit beta type-9
176	PSMB2	Proteasome subunit beta type-2
177	PSMB1	Proteasome subunit beta type-1
178	CCR1	C–C chemokine receptor type 1
179	AGTR1	Type-1 angiotensin II receptor
180	P2RX3	P2X purinoceptor 3
181	HDAC9	Histone deacetylase 9
182	CRHR1	Corticotropin-releasing factor receptor 1
183	FRK	Tyrosine-protein kinase FRK
184	TNK2	Activated CDC42 kinase 1
185	HDAC8	Histone deacetylase 8
186	FPR2	Formyl peptide receptor-like
187	EGLN1	Egl nine homolog 1
188	CACNA1H	Voltage-dependent T-type calcium channel subunit alpha-1H
189	CXCR2	C–X-C chemokine receptor type 2
190	CTSL	Cathepsin L1
191	COMT	Catechol O-methyltransferase
192	TDP1	Tyrosyl-DNA phosphodiesterase 1
193	GCK	Glucokinase
194	CYP3A4	Cytochrome p450 family 3 subfamily a polypeptide 4
195	CTSK	Cathepsin K
196	CNR1	Cannabinoid receptor 1
197	IKBKE	Inhibitor of nuclear factor kappa-B kinase subunit epsilon
198	HMGCR	3-hydroxy-3-methylglutaryl-coenzyme A reductase
199	HTR2A	5-hydroxytryptamine receptor 2A
200	STK4	Serine/threonine-protein kinase 4
201	STK3	Serine/threonine-protein kinase 3
202	ADORA2A	Adenosine A2a receptor
203	BACE2	Beta-site app-cleaving enzyme 2 (memapsin 1)
204	WNT3A	Wingless-type mmtv integration site family, member 3
205	GUSB	Beta-glucuronidase
206	CYP11B2	Steroid 11beta-monooxygenase / corticosterone 18-monooxygenase
207	ROS1	Proto-oncogene tyrosine-protein kinase ROS
208	ANPEP	Alanyl aminopeptidase, membrane
209	FDFT1	Squalene synthase
210	SLC40A1	Solute carrier family 40 member 1
211	DCUN1D1	Defective in cullin neddylation 1 domain containing 1
212	CHRNB4	Neuronal acetylcholine receptor subunit beta-4
213	MMP16	Matrix metalloproteinase-16
214	KDM4A	Lysine-specific demethylase 4A
215	GBA	Glucosylceramidase
216	F13A1	Coagulation factor xiii a1 polypeptide
217	PKN2	Serine/threonine-protein kinase N2
218	MAP3K12	Mitogen-activated protein kinase kinase kinase 12
219	AURKC	Aurora kinase C
220	REN	Renin

No	Gene Name	Protein Name
221	PDE3A	cGMP-inhibited 3',5'-cyclic phosphodiesterase A
222	MAP3K2	Mitogen-activated protein kinase kinase kinase 2
223	GRK4	G protein-coupled receptor kinase 4
224	SCD	Stearoyl-coa desaturase (delta-9 desaturase)
225	GRK5	G protein-coupled receptor kinase 5
226	C5AR1	C5a anaphylatoxin chemotactic receptor 1
227	NAMPT	Nicotinamide phosphoribosyltransferase
228	CACNA1B	Voltage-dependent N-type calcium channel subunit alpha-1B
229	MMP13	Matrix metalloproteinase-13 (collagenase 3)
230	MAOA	Amine oxidase [flavin-containing] A
231	HDAC11	Histone deacetylase 11
232	ADAMTS4	A disintegrin and metalloproteinase with thrombospondin motifs 4
233	ADAMTS5	A disintegrin and metalloproteinase with thrombospondin motifs 5
234	HDAC10	Histone deacetylase 10
235	TNKS2	Tankyrase-2
236	MMP7	Matrix metalloproteinase-7 (matrilysin, uterine)
237	CTSS	Cathepsin S
238	BRD4	Bromodomain-containing protein 4
239	GAK	Cyclin-G-associated kinase
240	CSNK2B	Casein kinase II subunit beta
241	BMP1	Bone morphogenetic protein 1
242	HTR2C	5-hydroxytryptamine receptor 2C
243	PDE10A	cAMP and cAMP-inhibited cGMP 3',5'-cyclic phosphodiesterase 10A
244	FPR3	Formyl peptide receptor-like
245	F10	Coagulation factor X
246	OXTR	Oxytocin receptor
247	EPHX2	Bifunctional epoxide hydrolase 2
248	KCNA5	Potassium voltage-gated channel subfamily A member 5
249	MMP15	Matrix metalloproteinase-15
250	SLC10A2	Ileal sodium/bile acid cotransporter
251	CAMKK1	Calcium/calmodulin-dependent protein kinase kinase 1
252	CAMKK2	Calcium/calmodulin-dependent protein kinase kinase 2
253	CALCRL	Calcitonin gene-related peptide type 1 receptor
254	ABCB11	Atp-binding cassette, subfamily b (mdr/tap), member 11
255	ACVR1B	Activin receptor type-1B
256	KDM4C	Lysine-specific demethylase 4C
257	SAE1	SUMO-activating enzyme subunit 1
258	TRPA1	Transient receptor potential cation channel subfamily A member 1
259	PRCP	Lysosomal Pro-X carboxypeptidase
260	ALOX15	Arachidonate 15-lipoxygenase
261	SIK1	Serine/threonine-protein kinase SIK1
262	AVPR1B	Vasopressin V1b receptor
263	RORB	Rar-related orphan receptor beta
264	DYRK1A	Dual specificity tyrosine-phosphorylation-regulated kinase 1A
265	PGGT1B	Geranylgeranyl transferase type-1 subunit beta
266	KCNA3	Potassium voltage-gated channel subfamily A member 3
267	ADORA1	Adenosine receptor A1
268	GBA2	Non-lysosomal glucosylceramidase
269	CNR2	Cannabinoid receptor 2
270	GPR55	G protein-coupled receptor 55
271	AOC3	Amine oxidase, copper containing 3
272	HSD17B3	Testosterone 17-beta-dehydrogenase 3
273	CYP11B1	Cytochrome p450 family 11 subfamily b member 1
274	DRD3	D(3) dopamine receptor
275	CAMK1	Calcium/calmodulin-dependent protein kinase type 1
276	SCN9A	Sodium channel protein type 9 subunit alpha
277	TFPI	Tissue factor pathway inhibitor
278	F7	Coagulation factor VII
279	AVPR1A	Vasopressin V1a receptor
280	PTGS1	Prostaglandin G/H synthase 1
281	ALOX12	Arachidonate 12-lipoxygenase, 12S-type
282	OPRD1	Delta-type opioid receptor
283	SCN3A	Sodium channel protein type 3 subunit alpha

Supplementary 2. GO and KEGG Pathway Enrichment analysis arranged by the lowest LogP

No.	Category	Description	LogP	Hits
1	KEGG Pathway	PD-L1 expression and PD-1 checkpoint pathway in cancer	−25.60593524	AKT1, MAPK14, EGFR, MTOR, HIF1A, JAK2, NFKB1, PIK3CA, PIK3R1, MAPK3, PTPN11, STAT3
2	KEGG Pathway	Kaposi sarcoma-associated herpesvirus infection	−21.37006059	AKT1, CASP3, MAPK14, MTOR, HIF1A, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
3	KEGG Pathway	Proteoglycans in cancer	−21.07556468	AKT1, CASP3, MAPK14, EGFR, ESR1, MTOR, HIF1A, PIK3CA, PIK3R1, MAPK3, PTPN11, STAT3
4	KEGG Pathway	Pathways in cancer	−20.08993123	AKT1, CASP3, EGFR, ESR1, MTOR, HDAC1, HIF1A, HSP90AB1, JAK2, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
5	KEGG Pathway	Prolactin signaling pathway	−18.72612814	AKT1, MAPK14, ESR1, JAK2, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
6	KEGG Pathway	Chemical carcinogenesis — receptor activation	−18.59800803	AKT1, EGFR, ESR1, MTOR, HSP90AB1, JAK2, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
7	KEGG Pathway	Lipid and atherosclerosis	−18.52961231	AKT1, CASP3, MAPK14, HSP90AB1, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
8	GO Biological Processes	cellular response to organonitrogen compound	−17.45417101	AKT1, APP, CASP3, EGFR, MTOR, FYN, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
9	KEGG Pathway	AGE-RAGE signaling pathway in diabetic complications	−17.2642881	AKT1, CASP3, MAPK14, JAK2, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
10	GO Biological Processes	cellular response to nitrogen compound	−16.92333947	AKT1, APP, CASP3, EGFR, MTOR, FYN, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
11	KEGG Pathway	HIF-1 signaling pathway	−16.91507977	AKT1, EGFR, MTOR, HIF1A, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
12	KEGG Pathway	Human cytomegalovirus infection	−16.12287961	AKT1, CASP3, MAPK14, EGFR, MTOR, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
13	KEGG Pathway	Pancreatic cancer	−15.86530465	AKT1, EGFR, MTOR, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
14	KEGG Pathway	EGFR tyrosine kinase inhibitor resistance	−15.72475938	AKT1, EGFR, MTOR, JAK2, PIK3CA, PIK3R1, MAPK3, STAT3
15	KEGG Pathway	Hepatitis B	−15.32479169	AKT1, CASP3, MAPK14, JAK2, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
16	GO Biological Processes	transmembrane receptor protein tyrosine kinase signaling pathway	−15.29966654	AKT1, CASP3, MAPK14, EGFR, FYN, JAK2, LYN, PIK3CA, PIK3R1, PTPN11, STAT3
17	GO Biological Processes	cellular response to chemical stress	−15.28980435	AKT1, CASP3, CDK1, EGFR, MTOR, FYN, HIF1A, JAK2, PIK3CA, MAPK3
18	GO Biological Processes	enzyme-linked receptor protein signaling pathway	−15.12435263	AKT1, CASP3, MAPK14, EGFR, FYN, JAK2, LYN, PIK3CA, PIK3R1, MAPK3, PTPN11, STAT3
19	KEGG Pathway	Prostate cancer	−14.98405536	AKT1, EGFR, MTOR, HSP90AB1, NFKB1, PIK3CA, PIK3R1, MAPK3
20	GO Biological Processes	response to peptide	−14.95922233	AKT1, APP, MAPK14, MTOR, FYN, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, STAT3
21	KEGG Pathway	Endocrine resistance	−14.94722576	AKT1, MAPK14, EGFR, ESR1, MTOR, PIK3CA, PIK3R1, MAPK3
22	KEGG Pathway	Th17 cell differentiation	−14.5991035	MAPK14, MTOR, HIF1A, HSP90AB1, JAK2, NFKB1, MAPK3, STAT3

No.	Category	Description	LogP	Hits
23	GO Biological Processes	cellular response to growth factor stimulus	−14.58292452	AKT1, APP, CASP3, MAPK14, EGFR, FYN, HDAC1, PIK3CA, MAPK3, PTPN11, STAT3
24	KEGG Pathway	Epstein-Barr virus infection	−14.44825882	AKT1, CASP3, MAPK14, HDAC1, LYN, NFKB1, PIK3CA, PIK3R1, STAT3
25	KEGG Pathway	Viral carcinogenesis	−14.4092556	CASP3, CDK1, HDAC1, LYN, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
26	GO Biological Processes	response to growth factor	−14.28947282	AKT1, APP, CASP3, MAPK14, EGFR, FYN, HDAC1, PIK3CA, MAPK3, PTPN11, STAT3
27	KEGG Pathway	Human immunodeficiency virus 1 infection	−14.25707771	AKT1, CASP3, CDK1, MAPK14, MTOR, NFKB1, PIK3CA, PIK3R1, MAPK3
28	KEGG Pathway	Growth hormone synthesis, secretion and action	−14.22311148	AKT1, MAPK14, MTOR, JAK2, PIK3CA, PIK3R1, MAPK3, STAT3
29	KEGG Pathway	Thyroid hormone signaling pathway	−14.19355861	AKT1, ESR1, MTOR, HDAC1, HIF1A, PIK3CA, PIK3R1, MAPK3
30	GO Biological Processes	response to hormone	−14.17497647	AKT1, CASP3, MAPK14, ESR1, MTOR, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, PTPN11, STAT3
31	KEGG Pathway	Chemical carcinogenesis — reactive oxygen species	−14.05719836	AKT1, MAPK14, EGFR, HIF1A, NFKB1, PIK3CA, PIK3R1, MAPK3, PTPN11
32	KEGG Pathway	Acute myeloid leukemia	−13.83527197	AKT1, MTOR, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
33	KEGG Pathway	Fc epsilon RI signaling pathway	−13.78825694	AKT1, MAPK14, FYN, LYN, PIK3CA, PIK3R1, MAPK3
34	KEGG Pathway	Central carbon metabolism in cancer	−13.69637016	AKT1, EGFR, MTOR, HIF1A, PIK3CA, PIK3R1, MAPK3
35	KEGG Pathway	Phospholipase D signaling pathway	−13.47885587	AKT1, EGFR, MTOR, FYN, PIK3CA, PIK3R1, MAPK3, PTPN11
36	KEGG Pathway	Chronic myeloid leukemia	−13.43640436	AKT1, HDAC1, NFKB1, PIK3CA, PIK3R1, MAPK3, PTPN11
37	KEGG Pathway	Cellular senescence	−13.29282869	AKT1, CDK1, MAPK14, MTOR, NFKB1, PIK3CA, PIK3R1, MAPK3
38	KEGG Pathway	Hepatitis C	−13.27026951	AKT1, CASP3, EGFR, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
39	KEGG Pathway	JAK-STAT signaling pathway	−13.15964942	AKT1, EGFR, MTOR, JAK2, PIK3CA, PIK3R1, PTPN11, STAT3
40	KEGG Pathway	Colorectal cancer	−13.04750006	AKT1, CASP3, EGFR, MTOR, PIK3CA, PIK3R1, MAPK3
41	GO Biological Processes	positive regulation of protein localization to nucleus	−13.01123492	AKT1, CDK1, MAPK14, FYN, HSP90AB1, JAK2, PIK3R1
42	GO Biological Processes	hematopoietic or lymphoid organ development	−12.87683255	APP, CASP3, MAPK14, MTOR, HIF1A, JAK2, LYN, PIK3R1, MAPK3, PTPN11, STAT3
43	GO Biological Processes	protein phosphorylation	−12.86332723	AKT1, APP, CDK1, MAPK14, EGFR, MTOR, FYN, JAK2, LYN, PIK3R1, MAPK3
44	GO Biological Processes	cellular response to peptide	−12.78740546	AKT1, APP, FYN, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, STAT3
45	KEGG Pathway	MicroRNAs in cancer	−12.7620605	CASP3, EGFR, MTOR, HDAC1, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
46	GO Biological Processes	glial cell differentiation	−12.71137655	AKT1, APP, MTOR, HDAC1, LYN, MAPK3, PTPN11, STAT3
47	KEGG Pathway	Choline metabolism in cancer	−12.6387421	AKT1, EGFR, MTOR, HIF1A, PIK3CA, PIK3R1, MAPK3
48	KEGG Pathway	Neutrophil extracellular trap formation	−12.59867169	AKT1, MAPK14, MTOR, HDAC1, NFKB1, PIK3CA, PIK3R1, MAPK3
49	GO Biological Processes	immune system development	−12.56948105	APP, CASP3, MAPK14, MTOR, HIF1A, JAK2, LYN, PIK3R1, MAPK3, PTPN11, STAT3
50	KEGG Pathway	Chemokine signaling pathway	−12.56191468	AKT1, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
51	GO Biological Processes	positive regulation of protein phosphorylation	−12.55054283	AKT1, APP, EGFR, MTOR, FYN, HSP90AB1, JAK2, LYN, PIK3CA, MAPK3, PTPN11
52	KEGG Pathway	Progesterone-mediated oocyte maturation	−12.51396428	AKT1, CDK1, MAPK14, HSP90AB1, PIK3CA, PIK3R1, MAPK3
53	KEGG Pathway	Human papillomavirus infection	−12.5056256	AKT1, CASP3, EGFR, MTOR, HDAC1, NFKB1, PIK3CA, PIK3R1, MAPK3
54	KEGG Pathway	C-type lectin receptor signaling pathway	−12.45346505	AKT1, MAPK14, NFKB1, PIK3CA, PIK3R1, MAPK3, PTPN11
55	KEGG Pathway	T cell receptor signaling pathway	−12.45346505	AKT1, MAPK14, FYN, NFKB1, PIK3CA, PIK3R1, MAPK3
56	KEGG Pathway	Insulin resistance	−12.33600178	AKT1, MTOR, NFKB1, PIK3CA, PIK3R1, PTPN11, STAT3
57	KEGG Pathway	PI3K-Akt signaling pathway	−12.24323633	AKT1, EGFR, MTOR, HSP90AB1, JAK2, NFKB1, PIK3CA, PIK3R1, MAPK3
58	KEGG Pathway	TNF signaling pathway	−12.22295848	AKT1, CASP3, MAPK14, NFKB1, PIK3CA, PIK3R1, MAPK3
59	KEGG Pathway	Toxoplasmosis	−12.22295848	AKT1, CASP3, MAPK14, JAK2, NFKB1, MAPK3, STAT3
60	GO Biological Processes	response to peptide hormone	−12.14528875	AKT1, MAPK14, MTOR, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, STAT3
61	GO Molecular Functions	protein kinase activity	−12.11589619	AKT1, CDK1, MAPK14, EGFR, MTOR, FYN, JAK2, LYN, PIK3CA, MAPK3
62	GO Biological Processes	response to oxidative stress	−12.11319183	AKT1, APP, CASP3, CDK1, EGFR, FYN, HIF1A, JAK2, MAPK3
63	GO Biological Processes	positive regulation of cell migration	−12.10828754	AKT1, APP, EGFR, MTOR, HIF1A, JAK2, LYN, PIK3R1, MAPK3, STAT3
64	KEGG Pathway	Sphingolipid signaling pathway	−12.03482773	AKT1, MAPK14, FYN, NFKB1, PIK3CA, PIK3R1, MAPK3
65	KEGG Pathway	Neurotrophin signaling pathway	−12.03482773	AKT1, MAPK14, NFKB1, PIK3CA, PIK3R1, MAPK3, PTPN11
66	GO Biological Processes	positive regulation of hydrolase activity	−11.93699527	AKT1, APP, EGFR, ESR1, MTOR, FYN, HSP90AB1, JAK2, LYN, STAT3
67	GO Biological Processes	positive regulation of cell motility	−11.91516041	AKT1, APP, EGFR, MTOR, HIF1A, JAK2, LYN, PIK3R1, MAPK3, STAT3
68	KEGG Pathway	Platelet activation	−11.90732075	AKT1, MAPK14, FYN, LYN, PIK3CA, PIK3R1, MAPK3
69	KEGG Pathway	Osteoclast differentiation	−11.80907918	AKT1, MAPK14, FYN, NFKB1, PIK3CA, PIK3R1, MAPK3
70	GO Biological Processes	positive regulation of locomotion	−11.80766272	AKT1, APP, EGFR, MTOR, HIF1A, JAK2, LYN, PIK3R1, MAPK3, STAT3
71	GO Biological Processes	gliogenesis	−11.79564418	AKT1, APP, MTOR, HDAC1, LYN, MAPK3, PTPN11, STAT3
72	KEGG Pathway	Relaxin signaling pathway	−11.78501358	AKT1, MAPK14, EGFR, NFKB1, PIK3CA, PIK3R1, MAPK3
73	KEGG Pathway	FoxO signaling pathway	−11.73745431	AKT1, MAPK14, EGFR, PIK3CA, PIK3R1, MAPK3, STAT3
74	KEGG Pathway	Shigellosis	−11.68080542	AKT1, MAPK14, EGFR, MTOR, NFKB1, PIK3CA, PIK3R1, MAPK3
75	GO Biological Processes	regulation of generation of precursor metabolites and energy	−11.66750111	AKT1, APP, CDK1, MTOR, HIF1A, PIK3CA, STAT3
76	GO Biological Processes	regulation of protein localization to nucleus	−11.64454162	AKT1, CDK1, MAPK14, FYN, HSP90AB1, JAK2, PIK3R1
77	KEGG Pathway	Estrogen signaling pathway	−11.57670035	AKT1, EGFR, ESR1, HSP90AB1, PIK3CA, PIK3R1, MAPK3
78	GO Biological Processes	hemopoiesis	−11.52059297	APP, CASP3, MAPK14, MTOR, HIF1A, JAK2, LYN, PIK3R1, PTPN11, STAT3

No.	Category	Description	LogP	Hits
79	KEGG Pathway	Signaling pathways regulating pluripotency of stem cells	−11.46693871	AKT1, MAPK14, JAK2, PIK3CA, PIK3R1, MAPK3, STAT3
80	KEGG Pathway	Breast cancer	−11.3819379	AKT1, EGFR, ESR1, MTOR, PIK3CA, PIK3R1, MAPK3
81	GO Molecular Functions	phosphotransferase activity, alcohol group as acceptor	−11.3713734	AKT1, CDK1, MAPK14, EGFR, MTOR, FYN, JAK2, LYN, PIK3CA, MAPK3
82	KEGG Pathway	Renal cell carcinoma	−11.36358994	AKT1, HIF1A, PIK3CA, PIK3R1, MAPK3, PTPN11
83	KEGG Pathway	Adipocytokine signaling pathway	−11.36358994	AKT1, MTOR, JAK2, NFKB1, PTPN11, STAT3
84	KEGG Pathway	Epithelial cell signaling in Helicobacter pylori infection	−11.32484491	CASP3, MAPK14, EGFR, LYN, NFKB1, PTPN11
85	GO Molecular Functions	nitric-oxide synthase regulator activity	−11.3091372	AKT1, EGFR, ESR1, HSP90AB1
86	GO Biological Processes	positive regulation of protein localization	−11.30101719	AKT1, CDK1, MAPK14, EGFR, FYN, HIF1A, HSP90AB1, JAK2, PIK3R1
87	KEGG Pathway	Non-small cell lung cancer	−11.24905745	AKT1, EGFR, PIK3CA, PIK3R1, MAPK3, STAT3
88	KEGG Pathway	Glioma	−11.13939357	AKT1, EGFR, MTOR, PIK3CA, PIK3R1, MAPK3
89	GO Biological Processes	cellular response to cytokine stimulus	−11.06433556	AKT1, MAPK14, HIF1A, HSP90AB1, JAK2, LYN, NFKB1, MAPK3, PTPN11, STAT3
90	GO Molecular Functions	kinase activity	−11.02897018	AKT1, CDK1, MAPK14, EGFR, MTOR, FYN, JAK2, LYN, PIK3CA, MAPK3
91	GO Biological Processes	cellular response to hormone stimulus	−11.02736862	AKT1, ESR1, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, PTPN11, STAT3
92	GO Biological Processes	response to reactive oxygen species	−10.93516598	AKT1, CASP3, CDK1, EGFR, FYN, HIF1A, MAPK3
93	KEGG Pathway	Influenza A	−10.91717816	AKT1, CASP3, JAK2, NFKB1, PIK3CA, PIK3R1, MAPK3
94	KEGG Pathway	B cell receptor signaling pathway	−10.90030852	AKT1, LYN, NFKB1, PIK3CA, PIK3R1, MAPK3
95	GO Biological Processes	response to growth hormone	−10.8288892	AKT1, JAK2, LYN, PIK3R1, STAT3
96	GO Biological Processes	cellular response to organic cyclic compound	−10.80980539	APP, CASP3, CDK1, EGFR, ESR1, HSP90AB1, JAK2, NFKB1, MAPK3
97	KEGG Pathway	ErbB signaling pathway	−10.8042639	AKT1, EGFR, MTOR, PIK3CA, PIK3R1, MAPK3
98	GO Molecular Functions	kinase binding	−10.72902229	AKT1, MAPK14, EGFR, ESR1, HIF1A, HSP90AB1, JAK2, PIK3R1, PTPN11, STAT3
99	GO Biological Processes	regulation of kinase activity	−10.70181571	AKT1, APP, CASP3, EGFR, MTOR, HSP90AB1, JAK2, LYN, PIK3CA, PIK3R1
100	GO Biological Processes	negative regulation of catabolic process	−10.67450491	AKT1, MAPK14, EGFR, MTOR, FYN, HSP90AB1, PIK3CA, STAT3
101	GO Biological Processes	response to inorganic substance	−10.65450966	AKT1, APP, CASP3, CDK1, EGFR, FYN, HIF1A, PIK3CA, MAPK3
102	GO Biological Processes	protein autophosphorylation	−10.64321417	AKT1, EGFR, MTOR, FYN, JAK2, LYN, MAPK3
103	GO Biological Processes	regulation of cellular catabolic process	−10.6372414	AKT1, APP, CASP3, MAPK14, MTOR, HIF1A, HSP90AB1, PIK3CA, MAPK3, STAT3
104	GO Biological Processes	regulation of intracellular transport	−10.61216349	CDK1, MAPK14, FYN, HSP90AB1, JAK2, PIK3R1, MAPK3, PTPN11
105	KEGG Pathway	Chagas disease	−10.31881764	AKT1, MAPK14, NFKB1, PIK3CA, PIK3R1, MAPK3
106	GO Biological Processes	positive regulation of protein import into nucleus	−10.31610654	CDK1, MAPK14, HSP90AB1, JAK2, PIK3R1
107	KEGG Pathway	Toll-like receptor signaling pathway	−10.2672912	AKT1, MAPK14, NFKB1, PIK3CA, PIK3R1, MAPK3
108	GO Biological Processes	T cell costimulation	−10.2598053	AKT1, FYN, LYN, PIK3CA, PTPN11
109	GO Biological Processes	lymphocyte costimulation	−10.15143311	AKT1, FYN, LYN, PIK3CA, PTPN11
110	KEGG Pathway	Alzheimer disease	−10.15107986	AKT1, APP, CASP3, MTOR, NFKB1, PIK3CA, PIK3R1, MAPK3
111	GO Biological Processes	regulation of nucleocytoplasmic transport	−10.14282183	CDK1, MAPK14, HSP90AB1, JAK2, PIK3R1, PTPN11
112	GO Biological Processes	cellular response to oxidative stress	−10.11953745	AKT1, CDK1, EGFR, FYN, HIF1A, JAK2, MAPK3
113	GO Biological Processes	regulation of intracellular protein transport	−10.07866597	CDK1, MAPK14, FYN, HSP90AB1, JAK2, PIK3R1, PTPN11
114	KEGG Pathway	Cholinergic synapse	−10.04741473	AKT1, FYN, JAK2, PIK3CA, PIK3R1, MAPK3
115	GO Biological Processes	regulation of growth	−10.04724808	AKT1, APP, CDK1, MAPK14, EGFR, MTOR, HIF1A, PIK3CA, STAT3
116	KEGG Pathway	Coronavirus disease — COVID-19	−9.985433669	MAPK14, EGFR, NFKB1, PIK3CA, PIK3R1, MAPK3, STAT3
117	KEGG Pathway	Ras signaling pathway	−9.946357234	AKT1, EGFR, NFKB1, PIK3CA, PIK3R1, MAPK3, PTPN11
118	GO Biological Processes	response to amino acid	−9.932936136	CASP3, EGFR, MTOR, FYN, LYN, PIK3CA
119	GO Biological Processes	cellular response to peptide hormone stimulus	−9.869717035	AKT1, JAK2, LYN, NFKB1, PIK3CA, PIK3R1, STAT3
120	GO Biological Processes	gland development	−9.858986444	AKT1, EGFR, ESR1, HIF1A, JAK2, NFKB1, PIK3CA, MAPK3
121	KEGG Pathway	Salmonella infection	−9.770520972	AKT1, CASP3, MAPK14, HSP90AB1, NFKB1, PIK3CA, MAPK3
122	GO Biological Processes	regulation of protein kinase activity	−9.762743092	AKT1, APP, CASP3, EGFR, MTOR, HSP90AB1, JAK2, LYN, PIK3CA
123	GO Biological Processes	regulation of defense response	−9.717371628	APP, MAPK14, ESR1, FYN, JAK2, LYN, NFKB1, MAPK3, PTPN11
124	KEGG Pathway	Natural killer cell mediated cytotoxicity	−9.6572066	CASP3, FYN, PIK3CA, PIK3R1, MAPK3, PTPN11
125	GO Biological Processes	myeloid cell differentiation	−9.639338898	APP, CASP3, MAPK14, JAK2, LYN, PIK3R1, PTPN11
126	GO Biological Processes	cell activation	−9.633766401	APP, MAPK14, MTOR, FYN, JAK2, LYN, PIK3CA, PIK3R1, STAT3
127	GO Molecular Functions	protein kinase binding	−9.622760047	AKT1, MAPK14, ESR1, HIF1A, HSP90AB1, JAK2, PIK3R1, PTPN11, STAT3
128	GO Biological Processes	response to acid chemical	−9.617301819	CASP3, EGFR, MTOR, FYN, LYN, PIK3CA
129	GO Biological Processes	regulation of peptidyl-tyrosine phosphorylation	−9.570165179	APP, EGFR, MTOR, FYN, JAK2, LYN, PTPN11
130	KEGG Pathway	Apoptosis	−9.55858719	AKT1, CASP3, NFKB1, PIK3CA, PIK3R1, MAPK3
131	KEGG Pathway	Yersinia infection	−9.539311198	AKT1, MAPK14, NFKB1, PIK3CA, PIK3R1, MAPK3
132	KEGG Pathway	Measles	−9.501189451	AKT1, CASP3, NFKB1, PIK3CA, PIK3R1, STAT3
133	KEGG Pathway	Fluid shear stress and atherosclerosis	−9.501189451	AKT1, MAPK14, HSP90AB1, NFKB1, PIK3CA, PIK3R1
134	KEGG Pathway	Endometrial cancer	−9.476514138	AKT1, EGFR, PIK3CA, PIK3R1, MAPK3
135	GO Biological Processes	regulation of cellular response to stress	−9.466736095	AKT1, APP, EGFR, MTOR, FYN, HIF1A, LYN, PIK3R1, MAPK3
136	KEGG Pathway	Autophagy — animal	−9.463627452	AKT1, MTOR, HIF1A, PIK3CA, PIK3R1, MAPK3
137	KEGG Pathway	VEGF signaling pathway	−9.438236053	AKT1, MAPK14, PIK3CA, PIK3R1, MAPK3
138	GO Biological Processes	regulation of protein import into nucleus	−9.438236053	CDK1, MAPK14, HSP90AB1, JAK2, PIK3R1
139	KEGG Pathway	Longevity regulating pathway — multiple species	−9.327329371	AKT1, MTOR, HDAC1, PIK3CA, PIK3R1
140	GO Biological Processes	positive regulation of nucleocytoplasmic transport	−9.327329371	CDK1, MAPK14, HSP90AB1, JAK2, PIK3R1

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141	KEGG Pathway	Gastric cancer	−9.318665766	AKT1, EGFR, MTOR, PIK3CA, PIK3R1, MAPK3
142	GO Biological Processes	regulation of cell-cell adhesion	−9.313692131	AKT1, CASP3, MAPK14, FYN, JAK2, LYN, PIK3CA, PTPN11
143	KEGG Pathway	Herpes simplex virus 1 infection	−9.278943549	AKT1, CASP3, MTOR, JAK2, NFKB1, PIK3CA, PIK3R1, PTPN11
144	GO Biological Processes	positive regulation of protein transport	−9.267204676	CDK1, MAPK14, FYN, HIF1A, HSP90AB1, JAK2, PIK3R1
145	GO Biological Processes	regulation of protein transport	−9.237719413	CDK1, MAPK14, FYN, HIF1A, HSP90AB1, JAK2, PIK3R1, PTPN11
146	KEGG Pathway	Non-alcoholic fatty liver disease	−9.215098795	AKT1, CASP3, MAPK14, NFKB1, PIK3CA, PIK3R1
147	GO Biological Processes	positive regulation of intracellular protein transport	−9.181489447	CDK1, MAPK14, FYN, HSP90AB1, JAK2, PIK3R1
148	GO Biological Processes	growth hormone receptor signaling pathway	−9.170307892	JAK2, LYN, PIK3R1, STAT3
149	GO Biological Processes	cellular response to growth hormone stimulus	−9.170307892	JAK2, LYN, PIK3R1, STAT3
150	GO Biological Processes	regulation of macroautophagy	−9.131891065	AKT1, CASP3, MTOR, HIF1A, PIK3CA, MAPK3
151	GO Biological Processes	positive regulation of establishment of protein localization	−9.107118919	CDK1, MAPK14, FYN, HIF1A, HSP90AB1, JAK2, PIK3R1
152	GO Biological Processes	regulation of establishment of protein localization	−9.071260467	CDK1, MAPK14, FYN, HIF1A, HSP90AB1, JAK2, PIK3R1, PTPN11
153	GO Biological Processes	cellular response to lipid	−9.058297952	AKT1, MAPK14, EGFR, ESR1, JAK2, LYN, NFKB1, MAPK3
154	KEGG Pathway	Hepatocellular carcinoma	−9.004158986	AKT1, EGFR, MTOR, PIK3CA, PIK3R1, MAPK3
155	GO Biological Processes	cellular response to abiotic stimulus	−9.001908371	CASP3, MAPK14, MTOR, NFKB1, PIK3CA, PIK3R1, MAPK3
156	GO Biological Processes	cellular response to environmental stimulus	−9.001908371	CASP3, MAPK14, MTOR, NFKB1, PIK3CA, PIK3R1, MAPK3
157	GO Biological Processes	inflammatory response	−9.000586534	AKT1, APP, MTOR, HIF1A, JAK2, LYN, NFKB1, STAT3
158	KEGG Pathway	Melanoma	−8.994237188	AKT1, EGFR, PIK3CA, PIK3R1, MAPK3
159	GO Biological Processes	response to lipopolysaccharide	−8.973856961	AKT1, CASP3, MAPK14, JAK2, LYN, NFKB1, MAPK3
160	GO Biological Processes	regulation of neuron death	−8.964565759	AKT1, CASP3, FYN, HIF1A, HSP90AB1, JAK2, PIK3CA
161	KEGG Pathway	Platinum drug resistance	−8.963603449	AKT1, CASP3, PIK3CA, PIK3R1, MAPK3
162	GO Cellular Components	membrane raft	−8.955303885	APP, CASP3, EGFR, FYN, JAK2, LYN, MAPK3
163	GO Cellular Components	membrane microdomain	−8.946071158	APP, CASP3, EGFR, FYN, JAK2, LYN, MAPK3
164	KEGG Pathway	Tuberculosis	−8.823819654	AKT1, CASP3, MAPK14, JAK2, NFKB1, MAPK3
165	GO Biological Processes	positive regulation of carbohydrate metabolic process	−8.816673471	AKT1, APP, MTOR, HIF1A, NFKB1
166	GO Biological Processes	regulation of autophagy	−8.793406338	AKT1, CASP3, MTOR, HIF1A, PIK3CA, MAPK3, STAT3
167	GO Biological Processes	response to molecule of bacterial origin	−8.78466906	AKT1, CASP3, MAPK14, JAK2, LYN, NFKB1, MAPK3
168	GO Biological Processes	regulation of carbohydrate metabolic process	−8.738226297	AKT1, APP, MTOR, HIF1A, NFKB1, STAT3
169	GO Biological Processes	positive regulation of transferase activity	−8.702923404	AKT1, EGFR, MTOR, HSP90AB1, JAK2, LYN, PIK3CA, MAPK3
170	GO Biological Processes	behavior	−8.65677819	AKT1, APP, CASP3, EGFR, MTOR, FYN, HIF1A, STAT3
171	GO Biological Processes	response to metal ion	−8.656647228	AKT1, APP, CASP3, CDK1, EGFR, HIF1A, MAPK3
172	GO Biological Processes	positive regulation of peptidyl-tyrosine phosphorylation	−8.641878962	EGFR, MTOR, FYN, JAK2, LYN, PTPN11
173	KEGG Pathway	Pathogenic Escherichia coli infection	−8.588420896	CASP3, MAPK14, FYN, NFKB1, MAPK3, PTPN11
174	GO Biological Processes	positive regulation of intracellular transport	−8.562108164	CDK1, MAPK14, FYN, HSP90AB1, JAK2, PIK3R1
175	KEGG Pathway	Focal adhesion	−8.536065464	AKT1, EGFR, FYN, PIK3CA, PIK3R1, MAPK3
176	GO Biological Processes	regulation of T cell activation	−8.526002236	AKT1, CASP3, FYN, JAK2, LYN, PIK3CA, PTPN11
177	KEGG Pathway	Longevity regulating pathway	−8.525038724	AKT1, MTOR, NFKB1, PIK3CA, PIK3R1
178	GO Biological Processes	regulation of leukocyte cell-cell adhesion	−8.518027851	AKT1, CASP3, FYN, JAK2, LYN, PIK3CA, PTPN11
179	KEGG Pathway	Diabetic cardiomyopathy	−8.51028738	AKT1, MAPK14, MTOR, NFKB1, PIK3CA, PIK3R1
180	GO Biological Processes	cellular response to lipopolysaccharide	−8.484768658	AKT1, MAPK14, JAK2, LYN, NFKB1, MAPK3
181	GO Biological Processes	response to tumor necrosis factor	−8.472104958	AKT1, CASP3, MAPK14, JAK2, NFKB1, MAPK3
182	KEGG Pathway	Small cell lung cancer	−8.451944411	AKT1, CASP3, NFKB1, PIK3CA, PIK3R1
183	GO Molecular Functions	phosphoprotein binding	−8.451944411	MTOR, LYN, PIK3R1, MAPK3, PTPN11
184	GO Biological Processes	glucose homeostasis	−8.434489054	AKT1, HIF1A, PIK3CA, PIK3R1, PTPN11, STAT3
185	KEGG Pathway	Rap1 signaling pathway	−8.422073466	AKT1, MAPK14, EGFR, PIK3CA, PIK3R1, MAPK3
186	GO Biological Processes	carbohydrate homeostasis	−8.422073466	AKT1, HIF1A, PIK3CA, PIK3R1, PTPN11, STAT3
187	KEGG Pathway	IL-17 signaling pathway	−8.404566827	CASP3, MAPK14, HSP90AB1, NFKB1, MAPK3
188	GO Biological Processes	response to insulin	−8.373010729	AKT1, MAPK14, MTOR, LYN, PIK3CA, PIK3R1
189	GO Biological Processes	regulation of myeloid cell differentiation	−8.373010729	MAPK14, MTOR, HIF1A, LYN, PIK3R1, STAT3
190	GO Biological Processes	cellular response to molecule of bacterial origin	−8.336827503	AKT1, MAPK14, JAK2, LYN, NFKB1, MAPK3
191	KEGG Pathway	Fc gamma R-mediated phagocytosis	−8.335412816	AKT1, LYN, PIK3CA, PIK3R1, MAPK3
192	GO Biological Processes	regulation of inflammatory response	−8.237345462	APP, MAPK14, ESR1, FYN, JAK2, LYN, NFKB1
193	GO Biological Processes	positive regulation of tumor necrosis factor production	−8.161251129	APP, JAK2, PIK3R1, PTPN11, STAT3
194	GO Biological Processes	regulation of endopeptidase activity	−8.137829153	AKT1, APP, FYN, HDAC1, JAK2, LYN, STAT3
195	GO Biological Processes	cell morphogenesis	−8.128833509	APP, CASP3, MAPK14, EGFR, FYN, HSP90AB1, PIK3R1, PTPN11
196	GO Molecular Functions	protein serine/threonine kinase activity	−8.123887112	AKT1, CDK1, MAPK14, EGFR, MTOR, PIK3CA, MAPK3
197	GO Biological Processes	positive regulation of peptidyl-serine phosphorylation	−8.099437431	AKT1, APP, EGFR, HSP90AB1, PIK3CA
198	GO Biological Processes	positive regulation of tumor necrosis factor superfamily cytokine production	−8.079224588	APP, JAK2, PIK3R1, PTPN11, STAT3
199	GO Biological Processes	positive regulation of glucose import	−8.038895991	AKT1, MAPK14, PIK3R1, PTPN11
200	GO Biological Processes	response to wounding	−8.034862708	CASP3, CDK1, MAPK14, HIF1A, JAK2, LYN, PIK3CA
201	GO Biological Processes	cellular response to biotic stimulus	−8.03255863	AKT1, MAPK14, JAK2, LYN, NFKB1, MAPK3

No.	Category	Description	LogP	Hits
202	GO Biological Processes	negative regulation of cellular catabolic process	−8.021964111	AKT1, MAPK14, MTOR, HSP90AB1, PIK3CA, STAT3
203	GO Biological Processes	response to radiation	−8.014701448	AKT1, APP, CASP3, MAPK14, EGFR, HIF1A, PIK3R1
204	GO Biological Processes	positive regulation of T cell activation	−7.95931519	AKT1, FYN, JAK2, LYN, PIK3CA, PTPN11
205	GO Biological Processes	homeostasis of number of cells	−7.949023446	AKT1, CASP3, HIF1A, JAK2, LYN, PTPN11
206	GO Biological Processes	lipopolysaccharide-mediated signaling pathway	−7.94396352	AKT1, MAPK14, LYN, MAPK3
207	GO Biological Processes	regulation of peptidase activity	−7.928923846	AKT1, APP, FYN, HDAC1, JAK2, LYN, STAT3
208	GO Biological Processes	cellular response to reactive oxygen species	−7.905448208	AKT1, CDK1, EGFR, FYN, MAPK3
209	GO Biological Processes	cellular response to DNA damage stimulus	−7.902844783	CASP3, CDK1, MAPK14, MTOR, LYN, PIK3R1, MAPK3, PTPN11
210	GO Biological Processes	regulation of proteolysis	−7.866662191	AKT1, APP, FYN, HDAC1, HSP90AB1, JAK2, LYN, STAT3
211	GO Biological Processes	positive regulation of cytokine production	−7.758516189	APP, MAPK14, HIF1A, JAK2, PIK3R1, PTPN11, STAT3
212	KEGG Pathway	Prion disease	−7.742082325	CASP3, MAPK14, FYN, PIK3CA, PIK3R1, MAPK3
213	GO Biological Processes	mammary gland development	−7.727664411	AKT1, ESR1, HIF1A, JAK2, NFKB1
214	GO Biological Processes	positive regulation of glucose transmembrane transport	−7.727283629	AKT1, MAPK14, PIK3R1, PTPN11
215	GO Biological Processes	positive regulation of leukocyte cell-cell adhesion	−7.723233682	AKT1, FYN, JAK2, LYN, PIK3CA, PTPN11
216	GO Biological Processes	positive regulation of mitotic cell cycle	−7.71067676	AKT1, APP, CDK1, EGFR, PTPN11
217	GO Biological Processes	positive regulation of kinase activity	−7.70990026	AKT1, EGFR, MTOR, HSP90AB1, JAK2, LYN, PIK3CA
218	KEGG Pathway	Type II diabetes mellitus	−7.647715227	MTOR, PIK3CA, PIK3R1, MAPK3
219	GO Biological Processes	response to epidermal growth factor	−7.609270226	AKT1, EGFR, MAPK3, PTPN11
220	GO Biological Processes	regulation of erythrocyte differentiation	−7.609270226	MAPK14, HIF1A, LYN, STAT3
221	GO Biological Processes	regulation of glycolytic process	−7.609270226	APP, MTOR, HIF1A, STAT3
222	KEGG Pathway	Insulin signaling pathway	−7.579454142	AKT1, MTOR, PIK3CA, PIK3R1, MAPK3
223	KEGG Pathway	MAPK signaling pathway	−7.550897255	AKT1, CASP3, MAPK14, EGFR, NFKB1, MAPK3
224	GO Biological Processes	epidermal growth factor receptor signaling pathway	−7.534866906	AKT1, EGFR, PIK3CA, PTPN11
225	GO Biological Processes	growth hormone receptor signaling pathway via JAK-STAT	−7.525687391	JAK2, LYN, STAT3
226	GO Biological Processes	regulation of peptidyl-serine phosphorylation	−7.486099948	AKT1, APP, EGFR, HSP90AB1, PIK3CA
227	GO Biological Processes	placenta development	−7.396682662	AKT1, MAPK14, EGFR, HIF1A, HSP90AB1
228	GO Biological Processes	response to light stimulus	−7.373274127	AKT1, APP, CASP3, EGFR, HIF1A, PIK3R1
229	GO Biological Processes	negative regulation of intracellular signal transduction	−7.369353052	AKT1, MAPK14, ESR1, MTOR, HDAC1, HIF1A, LYN
230	GO Biological Processes	positive regulation of cell-cell adhesion	−7.316764898	AKT1, FYN, JAK2, LYN, PIK3CA, PTPN11
231	GO Biological Processes	regulation of carbohydrate catabolic process	−7.297230451	APP, MTOR, HIF1A, STAT3
232	KEGG Pathway	mTOR signaling pathway	−7.296919924	AKT1, MTOR, PIK3CA, PIK3R1, MAPK3
233	GO Biological Processes	regulation of lymphocyte activation	−7.269442286	AKT1, CASP3, FYN, JAK2, LYN, PIK3CA, PTPN11
234	GO Biological Processes	regulation of monooxygenase activity	−7.265815884	AKT1, EGFR, HIF1A, NFKB1
235	GO Biological Processes	anoikis	−7.262813148	AKT1, MTOR, PIK3CA
236	GO Biological Processes	leukocyte activation	−7.259125956	APP, MTOR, FYN, JAK2, LYN, PIK3R1, STAT3
237	GO Biological Processes	regulation of developmental growth	−7.238194925	AKT1, APP, CDK1, MAPK14, PIK3CA, STAT3
238	GO Biological Processes	peptidyl-tyrosine phosphorylation	−7.228434555	EGFR, FYN, JAK2, LYN, MAPK3
239	GO Biological Processes	mammary gland epithelium development	−7.204661172	AKT1, ESR1, HIF1A, JAK2
240	GO Biological Processes	regulation of glucose import	−7.204661172	AKT1, MAPK14, PIK3R1, PTPN11
241	GO Biological Processes	peptidyl-tyrosine modification	−7.201649624	EGFR, FYN, JAK2, LYN, MAPK3
242	GO Biological Processes	regulation of small molecule metabolic process	−7.184633513	AKT1, APP, MTOR, HIF1A, NFKB1, STAT3
243	GO Biological Processes	transcription by RNA polymerase II	−7.177075066	MAPK14, ESR1, JAK2, NFKB1, PIK3R1, STAT3
244	GO Biological Processes	response to cadmium ion	−7.174882373	AKT1, CDK1, EGFR, MAPK3
245	GO Biological Processes	astrocyte differentiation	−7.174882373	APP, MAPK3, PTPN11, STAT3
246	GO Biological Processes	DNA-templated transcription	−7.157965956	MAPK14, ESR1, JAK2, NFKB1, PIK3R1, MAPK3, STAT3
247	GO Molecular Functions	insulin receptor substrate binding	−7.149053392	JAK2, PIK3CA, PIK3R1
248	GO Biological Processes	nucleic acid-templated transcription	−7.148044855	MAPK14, ESR1, JAK2, NFKB1, PIK3R1, MAPK3, STAT3
249	GO Biological Processes	ERBB signaling pathway	−7.14561182	AKT1, EGFR, PIK3CA, PTPN11
250	GO Biological Processes	lymphocyte homeostasis	−7.116832552	AKT1, CASP3, HIF1A, LYN
251	GO Biological Processes	RNA biosynthetic process	−7.098951983	MAPK14, ESR1, JAK2, NFKB1, PIK3R1, MAPK3, STAT3
252	KEGG Pathway	GnRH secretion	−7.060684152	AKT1, PIK3CA, PIK3R1, MAPK3
253	GO Biological Processes	regulation of transmembrane transport	−7.045911866	AKT1, APP, MAPK14, FYN, LYN, PIK3R1, PTPN11
254	GO Molecular Functions	protein serine kinase activity	−7.009285065	AKT1, CDK1, MAPK14, MTOR, PIK3CA, MAPK3
255	GO Biological Processes	cytokine-mediated signaling pathway	−6.988211986	AKT1, JAK2, LYN, MAPK3, PTPN11, STAT3
256	KEGG Pathway	Axon guidance	−6.962829317	FYN, PIK3CA, PIK3R1, MAPK3, PTPN11
257	GO Biological Processes	cellular response to tumor necrosis factor	−6.962829317	AKT1, MAPK14, JAK2, NFKB1, MAPK3
258	GO Biological Processes	positive regulation of proteolysis	−6.946595549	AKT1, APP, FYN, JAK2, LYN, STAT3
259	GO Biological Processes	regulation of tumor necrosis factor production	−6.93919451	APP, JAK2, PIK3R1, PTPN11, STAT3

No.	Category	Description	LogP	Hits
260	GO Biological Processes	regulation of tumor necrosis factor superfamily cytokine production	−6.881242688	APP, JAK2, PIK3R1, PTPN11, STAT3
261	GO Biological Processes	forebrain development	−6.878751451	APP, CASP3, EGFR, FYN, HDAC1, HIF1A
262	GO Biological Processes	neuron projection development	−6.847603598	APP, CASP3, FYN, HSP90AB1, JAK2, LYN, PTPN11
263	GO Biological Processes	regulation of ATP metabolic process	−6.828574422	APP, MTOR, HIF1A, STAT3
264	GO Biological Processes	positive regulation of peptidase activity	−6.82484419	APP, FYN, JAK2, LYN, STAT3
265	GO Molecular Functions	phosphatase binding	−6.813743749	MAPK14, EGFR, PIK3R1, MAPK3, STAT3
266	GO Biological Processes	regulation of leukocyte activation	−6.807800895	AKT1, CASP3, FYN, JAK2, LYN, PIK3CA, PTPN11
267	GO Biological Processes	tube morphogenesis	−6.807800895	AKT1, CASP3, MAPK14, EGFR, ESR1, HIF1A, PIK3CA
268	GO Biological Processes	leukocyte differentiation	−6.799720062	APP, MAPK14, MTOR, LYN, PIK3R1, STAT3
269	GO Biological Processes	axon development	−6.78035085	APP, CASP3, FYN, HSP90AB1, JAK2, PTPN11
270	GO Biological Processes	positive regulation of lymphocyte activation	−6.761132373	AKT1, FYN, JAK2, LYN, PIK3CA, PTPN11
271	KEGG Pathway	Pertussis	−6.757710087	CASP3, MAPK14, NFKB1, MAPK3
272	KEGG Pathway	Leishmaniasis	−6.734726677	MAPK14, JAK2, NFKB1, MAPK3
273	GO Biological Processes	regulation of glucose transmembrane transport	−6.734726677	AKT1, MAPK14, PIK3R1, PTPN11
274	GO Molecular Functions	protein domain specific binding	−6.708564952	APP, FYN, HDAC1, HIF1A, HSP90AB1, JAK2, LYN
275	GO Biological Processes	cell population proliferation	−6.687447164	AKT1, CDK1, EGFR, ESR1, FYN, HIF1A, STAT3
276	GO Biological Processes	striated muscle cell differentiation	−6.684921429	AKT1, CASP3, CDK1, MAPK14, MTOR
277	GO Biological Processes	regulation of hemopoiesis	−6.679539858	MAPK14, MTOR, HIF1A, LYN, PIK3R1, STAT3
278	GO Biological Processes	positive regulation of protein kinase activity	−6.648863492	AKT1, EGFR, MTOR, HSP90AB1, JAK2, PIK3CA
279	GO Biological Processes	response to mechanical stimulus	−6.643679794	MAPK14, FYN, NFKB1, PIK3CA, MAPK3
280	GO Biological Processes	MAPK cascade	−6.583299952	CDK1, MAPK14, EGFR, NFKB1, MAPK3
281	GO Biological Processes	regulation of neuron apoptotic process	−6.573403699	CASP3, HIF1A, HSP90AB1, JAK2, PIK3CA
282	GO Biological Processes	negative regulation of neuron death	−6.573403699	AKT1, HIF1A, HSP90AB1, JAK2, PIK3CA
283	GO Biological Processes	regulation of cell activation	−6.567999635	AKT1, CASP3, FYN, JAK2, LYN, PIK3CA, PTPN11
284	GO Cellular Components	perinuclear region of cytoplasm	−6.5599464	APP, EGFR, FYN, HSP90AB1, LYN, PIK3CA, PIK3R1
285	KEGG Pathway	cAMP signaling pathway	−6.543992544	AKT1, NFKB1, PIK3CA, PIK3R1, MAPK3
286	KEGG Pathway	Human T-cell leukemia virus 1 infection	−6.534279953	AKT1, NFKB1, PIK3CA, PIK3R1, MAPK3
287	GO Biological Processes	negative regulation of autophagy	−6.520452713	AKT1, MTOR, PIK3CA, STAT3
288	GO Biological Processes	leukocyte homeostasis	−6.520452713	AKT1, CASP3, HIF1A, LYN
289	GO Biological Processes	positive regulation of glycolytic process	−6.483036536	APP, MTOR, HIF1A
290	GO Biological Processes	cellular response to acid chemical	−6.480647197	EGFR, MTOR, FYN, PIK3CA
291	GO Biological Processes	negative regulation of immune system process	−6.466762437	AKT1, CASP3, MAPK14, FYN, LYN, PIK3R1
292	GO Biological Processes	positive regulation of leukocyte activation	−6.46110729	AKT1, FYN, JAK2, LYN, PIK3CA, PTPN11
293	GO Biological Processes	regulation of leukocyte migration	−6.448838462	AKT1, APP, LYN, PIK3R1, MAPK3
294	GO Biological Processes	response to bacterium	−6.445706502	AKT1, CASP3, MAPK14, JAK2, LYN, NFKB1, MAPK3
295	GO Biological Processes	regulation of cell cycle phase transition	−6.444219713	AKT1, APP, CDK1, MAPK14, EGFR, PTPN11
296	GO Biological Processes	regulation of DNA-binding transcription factor activity	−6.438616284	AKT1, APP, ESR1, JAK2, MAPK3, STAT3
297	GO Biological Processes	brain development	−6.430309537	APP, CASP3, EGFR, FYN, HDAC1, HIF1A, PTPN11
298	KEGG Pathway	Th1 and Th2 cell differentiation	−6.422629285	MAPK14, JAK2, NFKB1, MAPK3
299	GO Biological Processes	positive regulation of phosphoprotein phosphatase activity	−6.419551049	MTOR, HSP90AB1, JAK2
300	GO Biological Processes	cellular response to virus	−6.385019969	MAPK14, HIF1A, JAK2, NFKB1
301	GO Biological Processes	regulation of purine nucleotide metabolic process	−6.385019969	APP, MTOR, HIF1A, STAT3
302	GO Biological Processes	positive regulation of cell activation	−6.366915129	AKT1, FYN, JAK2, LYN, PIK3CA, PTPN11
303	KEGG Pathway	Pathways of neurodegeneration — multiple diseases	−6.318479144	APP, CASP3, MAPK14, MTOR, NFKB1, MAPK3
304	GO Molecular Functions	kinase regulator activity	−6.313772293	CASP3, EGFR, HSP90AB1, PIK3CA, PIK3R1
305	GO Biological Processes	positive regulation of smooth muscle cell proliferation	−6.312205303	AKT1, HDAC1, JAK2, PIK3CA
306	GO Biological Processes	regulation of nucleotide metabolic process	−6.294478208	APP, MTOR, HIF1A, STAT3
307	GO Biological Processes	positive regulation of mitotic cell cycle phase transition	−6.276933938	AKT1, APP, CDK1, EGFR
308	GO Biological Processes	positive regulation of cell adhesion	−6.276216773	AKT1, FYN, JAK2, LYN, PIK3CA, PTPN11
309	GO Biological Processes	positive regulation of protein localization to membrane	−6.259568796	AKT1, EGFR, FYN, PIK3R1
310	KEGG Pathway	Amoebiasis	−6.2423792	CASP3, NFKB1, PIK3CA, PIK3R1
311	GO Biological Processes	response to heat	−6.2423792	AKT1, MTOR, HSP90AB1, LYN
312	GO Biological Processes	response to muscle stretch	−6.192832789	MAPK14, NFKB1, PIK3CA
313	GO Biological Processes	regulation of miRNA maturation	−6.192832789	EGFR, ESR1, STAT3
314	GO Biological Processes	positive regulation of growth	−6.186929648	AKT1, CDK1, MAPK14, EGFR, MTOR
315	GO Biological Processes	biological process involved in symbiotic interaction	−6.186929648	CDK1, EGFR, HDAC1, HSP90AB1, JAK2
316	GO Biological Processes	positive regulation of DNA-binding transcription factor activity	−6.146311481	AKT1, APP, ESR1, JAK2, STAT3
317	GO Biological Processes	regulation of oxidoreductase activity	−6.14274028	AKT1, EGFR, HIF1A, NFKB1

No.	Category	Description	LogP	Hits
318	GO Biological Processes	rhythmic process	−6.114379365	CASP3, CDK1, ESR1, MTOR, HDAC1
319	GO Biological Processes	regulation of hormone levels	−6.10924127	ESR1, HIF1A, JAK2, LYN, NFKB1, PTPN11
320	GO Biological Processes	regulation of production of small RNA involved in gene silencing by RNA	−6.092829425	EGFR, ESR1, STAT3
321	GO Biological Processes	learning or memory	−6.090748602	APP, CASP3, EGFR, FYN, HIF1A
322	GO Biological Processes	muscle cell differentiation	−6.082931121	AKT1, CASP3, CDK1, MAPK14, MTOR
323	KEGG Pathway	Leukocyte transendothelial migration	−6.048625783	MAPK14, PIK3CA, PIK3R1, PTPN11
324	GO Biological Processes	positive regulation of lamellipodium assembly	−6.045588366	MTOR, PIK3CA, PIK3R1
325	GO Biological Processes	B cell homeostasis	−6.000014465	CASP3, HIF1A, LYN
326	GO Biological Processes	regulation of DNA metabolic process	−5.999299105	AKT1, CDK1, EGFR, HSP90AB1, PIK3CA, MAPK3
327	GO Biological Processes	cell morphogenesis involved in differentiation	−5.980677858	APP, CASP3, FYN, HSP90AB1, PIK3R1, PTPN11
328	GO Biological Processes	regulation of cyclin-dependent protein kinase activity	−5.959461169	AKT1, CASP3, EGFR, HSP90AB1
329	GO Biological Processes	cellular response to interleukin-6	−5.955994392	JAK2, NFKB1, STAT3
330	KEGG Pathway	AMPK signaling pathway	−5.945046194	AKT1, MTOR, PIK3CA, PIK3R1
331	GO Biological Processes	response to estradiol	−5.945046194	CASP3, EGFR, ESR1, STAT3
332	GO Biological Processes	positive regulation of cell cycle phase transition	−5.930752906	AKT1, APP, CDK1, EGFR
333	GO Biological Processes	regulation of ossification	−5.930752906	MAPK14, HIF1A, MAPK3, PTPN11
334	GO Biological Processes	heart development	−5.92565936	CASP3, CDK1, MTOR, HIF1A, MAPK3, PTPN11
335	GO Biological Processes	regulation of mononuclear cell migration	−5.916579293	AKT1, APP, LYN, MAPK3
336	GO Biological Processes	negative regulation of inflammatory response to antigenic stimulus	−5.913426001	MAPK14, FYN, LYN
337	GO Biological Processes	sensory organ development	−5.894134614	EGFR, HDAC1, HIF1A, MAPK3, PTPN11, STAT3
338	GO Biological Processes	positive regulation of DNA metabolic process	−5.882297389	AKT1, CDK1, EGFR, HSP90AB1, MAPK3
339	GO Biological Processes	positive regulation of defense response	−5.840238532	APP, FYN, JAK2, LYN, MAPK3
340	GO Biological Processes	negative regulation of cell adhesion	−5.833311345	AKT1, CASP3, JAK2, PIK3R1, PTPN11
341	GO Biological Processes	response to interleukin-6	−5.83228327	JAK2, NFKB1, STAT3
342	GO Biological Processes	positive regulation of erythrocyte differentiation	−5.83228327	MAPK14, HIF1A, STAT3
343	GO Biological Processes	response to interleukin-1	−5.794093479	APP, HIF1A, NFKB1, MAPK3
344	GO Biological Processes	negative regulation of macroautophagy	−5.793548793	AKT1, MTOR, PIK3CA
345	GO Biological Processes	cognition	−5.792230092	APP, CASP3, EGFR, FYN, HIF1A
346	GO Biological Processes	regulation of ERK1 and ERK2 cascade	−5.785462154	APP, EGFR, LYN, MAPK3, PTPN11
347	GO Cellular Components	extrinsic component of membrane	−5.778716384	AKT1, FYN, LYN, PIK3CA, PIK3R1
348	GO Biological Processes	positive regulation of ATP metabolic process	−5.75594382	APP, MTOR, HIF1A
349	GO Biological Processes	positive regulation of phosphatase activity	−5.75594382	MTOR, HSP90AB1, JAK2
350	GO Molecular Functions	chromatin binding	−5.746621067	CDK1, EGFR, ESR1, HDAC1, NFKB1, STAT3
351	GO Molecular Functions	transcription factor binding	−5.746621067	MAPK14, ESR1, MTOR, HDAC1, HIF1A, STAT3
352	GO Biological Processes	positive regulation of lamellipodium organization	−5.7194046	MTOR, PIK3CA, PIK3R1
353	KEGG Pathway	Aldosterone-regulated sodium reabsorption	−5.7194046	PIK3CA, PIK3R1, MAPK3
354	GO Biological Processes	cellular response to cadmium ion	−5.7194046	AKT1, EGFR, MAPK3
355	GO Biological Processes	TOR signaling	−5.7194046	AKT1, MTOR, HIF1A
356	GO Molecular Functions	protein tyrosine kinase activity	−5.717106795	EGFR, FYN, JAK2, LYN
357	GO Cellular Components	vesicle lumen	−5.705936715	APP, MAPK14, EGFR, HSP90AB1, NFKB1
358	GO Biological Processes	epithelial cell differentiation	−5.704903422	AKT1, CASP3, CDK1, ESR1, HDAC1, HIF1A
359	GO Biological Processes	activation of protein kinase activity	−5.704610329	EGFR, MTOR, JAK2, PIK3CA
360	GO Molecular Functions	growth factor receptor binding	−5.692205769	APP, FYN, JAK2, LYN
361	KEGG Pathway	Alcoholic liver disease	−5.667667106	AKT1, CASP3, MAPK14, NFKB1
362	KEGG Pathway	Spinocerebellar ataxia	−5.655530442	AKT1, MTOR, PIK3CA, PIK3R1
363	GO Biological Processes	regulation of Wnt signaling pathway	−5.648248833	APP, MAPK14, EGFR, HDAC1, NFKB1
364	GO Molecular Functions	protein phosphatase binding	−5.584491271	MAPK14, EGFR, PIK3R1, STAT3
365	GO Biological Processes	response to UV	−5.584491271	AKT1, CASP3, EGFR, PIK3R1
366	GO Biological Processes	regulation of plasma membrane bounded cell projection organization	−5.564362497	AKT1, MTOR, FYN, LYN, PIK3CA, PIK3R1
367	GO Molecular Functions	RNA polymerase II-specific DNA-binding transcription factor binding	−5.561617477	MAPK14, ESR1, HDAC1, HIF1A, STAT3
368	GO Biological Processes	regulation of lamellipodium assembly	−5.550801664	MTOR, PIK3CA, PIK3R1
369	GO Biological Processes	regulation of nitric-oxide synthase activity	−5.550801664	AKT1, EGFR, HIF1A
370	GO Biological Processes	positive regulation of nitric oxide biosynthetic process	−5.550801664	AKT1, HSP90AB1, JAK2
371	GO Biological Processes	positive regulation of small molecule metabolic process	−5.550065144	AKT1, APP, MTOR, HIF1A
372	GO Biological Processes	positive regulation of cell projection organization	−5.549535326	MTOR, FYN, LYN, PIK3CA, PIK3R1
373	GO Biological Processes	negative regulation of neuron apoptotic process	−5.527499702	HIF1A, HSP90AB1, JAK2, PIK3CA
374	GO Biological Processes	cellular response to epidermal growth factor stimulus	−5.519576786	AKT1, EGFR, PTPN11

No.	Category	Description	LogP	Hits
375	GO Biological Processes	regulation of cell projection organization	−5.498973816	AKT1, MTOR, FYN, LYN, PIK3CA, PIK3R1
376	GO Biological Processes	positive regulation of cell cycle	−5.490172526	AKT1, APP, CDK1, EGFR, PTPN11
377	GO Biological Processes	phosphatidylinositol 3-kinase signaling	−5.489091551	AKT1, PIK3CA, PIK3R1
378	GO Biological Processes	positive regulation of nitric oxide metabolic process	−5.489091551	AKT1, HSP90AB1, JAK2
379	GO Molecular Functions	non-membrane spanning protein tyrosine kinase activity	−5.459311913	FYN, JAK2, LYN
380	GO Molecular Functions	protein serine/threonine/tyrosine kinase activity	−5.459311913	AKT1, MAPK14, MAPK3
381	GO Biological Processes	regulation of miRNA-mediated gene silencing	−5.459311913	EGFR, ESR1, STAT3
382	GO Biological Processes	regulation of binding	−5.43248626	AKT1, APP, HSP90AB1, JAK2, MAPK3
383	GO Molecular Functions	phosphotyrosine residue binding	−5.430206121	PIK3R1, MAPK3, PTPN11
384	GO Biological Processes	positive regulation of signaling receptor activity	−5.430206121	HDAC1, HIF1A, JAK2
385	KEGG Pathway	Carbohydrate digestion and absorption	−5.401744524	AKT1, PIK3CA, PIK3R1
386	GO Biological Processes	regulation of inflammatory response to antigenic stimulus	−5.401744524	MAPK14, FYN, LYN
387	GO Biological Processes	regulation of post-transcriptional gene silencing by RNA	−5.401744524	EGFR, ESR1, STAT3
388	GO Biological Processes	negative regulation of lipid transport	−5.401744524	AKT1, NFKB1, PTPN11
389	GO Biological Processes	positive regulation of nucleotide metabolic process	−5.373899384	APP, MTOR, HIF1A
390	GO Biological Processes	positive regulation of purine nucleotide metabolic process	−5.373899384	APP, MTOR, HIF1A
391	GO Biological Processes	regulation of post-transcriptional gene silencing	−5.373899384	EGFR, ESR1, STAT3
392	GO Biological Processes	regulation of MAPK cascade	−5.369760328	APP, EGFR, JAK2, LYN, MAPK3, PTPN11
393	GO Biological Processes	cellular response to vascular endothelial growth factor stimulus	−5.34664472	AKT1, MAPK14, PIK3CA
394	GO Biological Processes	positive regulation of protein dephosphorylation	−5.34664472	MTOR, HSP90AB1, JAK2
395	GO Biological Processes	regulation of protein localization to membrane	−5.336995166	AKT1, EGFR, FYN, PIK3R1
396	GO Biological Processes	ephrin receptor signaling pathway	−5.319956156	FYN, LYN, PTPN11
397	GO Biological Processes	regulation of gene silencing by RNA	−5.319956156	EGFR, ESR1, STAT3
398	GO Biological Processes	positive regulation of endopeptidase activity	−5.317104693	FYN, JAK2, LYN, STAT3
399	GO Biological Processes	pallium development	−5.317104693	CASP3, EGFR, HDAC1, HIF1A
400	GO Biological Processes	response to temperature stimulus	−5.317104693	AKT1, MTOR, HSP90AB1, LYN
401	GO Biological Processes	regulation of smooth muscle cell proliferation	−5.307247384	AKT1, HDAC1, JAK2, PIK3CA
402	GO Biological Processes	regulation of signaling receptor activity	−5.307247384	APP, HDAC1, HIF1A, JAK2
403	GO Biological Processes	regulation of protein serine/threonine kinase activity	−5.30569614	AKT1, CASP3, EGFR, HSP90AB1, LYN
404	GO Biological Processes	negative regulation of cell differentiation	−5.285062466	APP, EGFR, LYN, PIK3R1, PTPN11, STAT3
405	GO Biological Processes	positive regulation of organ growth	−5.268187119	AKT1, CDK1, MAPK14
406	GO Biological Processes	growth	−5.242557031	APP, ESR1, MTOR, HSP90AB1, PTPN11
407	GO Biological Processes	developmental growth	−5.242557031	APP, ESR1, MTOR, HSP90AB1, PTPN11
408	GO Biological Processes	regulation of cell cycle process	−5.226855647	AKT1, APP, CDK1, MAPK14, EGFR, PTPN11
409	GO Biological Processes	negative regulation of inflammatory response	−5.221052096	MAPK14, FYN, LYN, NFKB1
410	KEGG Pathway	NOD-like receptor signaling pathway	−5.221052096	MAPK14, HSP90AB1, NFKB1, MAPK3
411	GO Biological Processes	stem cell differentiation	−5.221052096	MAPK14, ESR1, HIF1A, MAPK3
412	GO Biological Processes	regulation of lamellipodium organization	−5.218424834	MTOR, PIK3CA, PIK3R1
413	GO Biological Processes	positive regulation of cyclin-dependent protein kinase activity	−5.218424834	AKT1, EGFR, HSP90AB1
414	GO Biological Processes	peptidyl-serine phosphorylation	−5.211743589	AKT1, CDK1, MAPK14, MTOR
415	GO Biological Processes	negative regulation of oxidative stress-induced cell death	−5.19424907	AKT1, FYN, HIF1A
416	GO Biological Processes	positive regulation of cellular catabolic process	−5.176305649	AKT1, APP, MTOR, HIF1A, MAPK3
417	GO Biological Processes	regulation of protein kinase B signaling	−5.175020017	EGFR, MTOR, HSP90AB1, PIK3CA
418	GO Biological Processes	positive regulation of miRNA metabolic process	−5.170520494	HIF1A, NFKB1, STAT3
419	GO Biological Processes	response to carbohydrate	−5.156956912	CASP3, HIF1A, LYN, PIK3CA
420	KEGG Pathway	Regulation of lipolysis in adipocytes	−5.147222978	AKT1, PIK3CA, PIK3R1
421	GO Biological Processes	cell activation involved in immune response	−5.13022388	APP, MTOR, LYN, STAT3
422	GO Molecular Functions	protein phosphorylated amino acid binding	−5.124341255	PIK3R1, MAPK3, PTPN11
423	GO Biological Processes	cellular response to metal ion	−5.103912874	AKT1, APP, EGFR, MAPK3
424	GO Biological Processes	ameboidal-type cell migration	−5.103912874	AKT1, HIF1A, PIK3CA, PTPN11
425	GO Biological Processes	positive regulation of protein localization to plasma membrane	−5.10186085	AKT1, EGFR, PIK3R1
426	GO Biological Processes	regulation of phosphoprotein phosphatase activity	−5.10186085	MTOR, HSP90AB1, JAK2
427	GO Biological Processes	regulation of stress-activated protein kinase signaling cascade	−5.095234082	APP, EGFR, LYN, MAPK3
428	GO Biological Processes	response to axon injury	−5.079768035	CDK1, JAK2, LYN
429	GO Cellular Components	euchromatin	−5.079768035	ESR1, HIF1A, JAK2
430	GO Biological Processes	regulation of protein binding	−5.078011037	AKT1, APP, HSP90AB1, MAPK3
431	GO Biological Processes	peptidyl-serine modification	−5.044090601	AKT1, CDK1, MAPK14, MTOR
432	GO Biological Processes	insulin receptor signaling pathway	−5.036693674	AKT1, PIK3CA, PIK3R1

No.	Category	Description	LogP	Hits
433	GO Biological Processes	regulation of nitric oxide biosynthetic process	−5.036693674	AKT1, HSP90AB1, JAK2
434	GO Biological Processes	immune effector process	−5.021923564	APP, MTOR, FYN, LYN, STAT3
435	GO Biological Processes	positive regulation of interleukin-1 beta production	−5.015687954	APP, JAK2, STAT3
436	GO Biological Processes	regulation of nervous system development	−5.003431986	AKT1, MTOR, HDAC1, HIF1A, LYN
437	GO Biological Processes	positive regulation of dephosphorylation	−4.995021393	MTOR, HSP90AB1, JAK2
438	GO Biological Processes	regulation of multicellular organism growth	−4.974683304	APP, PIK3CA, STAT3
439	GO Biological Processes	regulation of nitric oxide metabolic process	−4.974683304	AKT1, HSP90AB1, JAK2
440	GO Biological Processes	negative regulation of lipid localization	−4.974683304	AKT1, NFKB1, PTPN11
441	GO Biological Processes	positive regulation of response to external stimulus	−4.966951761	APP, FYN, JAK2, LYN, MAPK3
442	GO Biological Processes	positive regulation of tyrosine phosphorylation of STAT protein	−4.934952243	FYN, JAK2, LYN
443	GO Biological Processes	positive regulation of protein localization to cell periphery	−4.934952243	AKT1, EGFR, PIK3R1
444	KEGG Pathway	Regulation of actin cytoskeleton	−4.930541491	EGFR, PIK3CA, PIK3R1, MAPK3
445	GO Molecular Functions	protein kinase regulator activity	−4.930541491	CASP3, EGFR, HSP90AB1, PIK3CA
446	GO Biological Processes	connective tissue development	−4.914936319	MAPK14, HIF1A, PIK3CA, MAPK3
447	GO Molecular Functions	DNA-binding transcription factor binding	−4.913445892	MAPK14, ESR1, HDAC1, HIF1A, STAT3
448	GO Biological Processes	peptidyl-threonine phosphorylation	−4.896418685	AKT1, CDK1, MTOR
449	GO Biological Processes	positive regulation of gliogenesis	−4.896418685	MTOR, HDAC1, LYN
450	GO Biological Processes	positive regulation of ERK1 and ERK2 cascade	−4.891800683	APP, EGFR, MAPK3, PTPN11
451	GO Biological Processes	positive regulation of epithelial cell proliferation	−4.884160059	AKT1, EGFR, HIF1A, STAT3
452	GO Biological Processes	response to activity	−4.877579024	CDK1, HIF1A, PIK3CA
453	KEGG Pathway	Adherens junction	−4.859013164	EGFR, FYN, MAPK3
454	GO Biological Processes	cellular response to inorganic substance	−4.853945402	AKT1, APP, EGFR, MAPK3
455	GO Biological Processes	response to extracellular stimulus	−4.835776875	AKT1, MAPK14, MTOR, LYN, MAPK3
456	GO Biological Processes	positive regulation of neurogenesis	−4.831641092	MTOR, HDAC1, HIF1A, LYN
457	GO Biological Processes	positive regulation of MAPK cascade	−4.827330461	APP, EGFR, JAK2, MAPK3, PTPN11
458	GO Biological Processes	stress-activated MAPK cascade	−4.804882292	MAPK14, NFKB1, MAPK3
459	GO Biological Processes	regulation of miRNA metabolic process	−4.804882292	HIF1A, NFKB1, STAT3
460	GO Biological Processes	positive regulation of interleukin-1 production	−4.804882292	APP, JAK2, STAT3
461	GO Biological Processes	muscle structure development	−4.798046532	AKT1, CASP3, CDK1, MAPK14, MTOR
462	GO Cellular Components	cell-cell junction	−4.789758108	AKT1, APP, LYN, PIK3CA, PIK3R1
463	GO Biological Processes	positive regulation of transmembrane transport	−4.787915562	AKT1, MAPK14, PIK3R1, PTPN11
464	GO Biological Processes	regulation of glial cell differentiation	−4.770029941	CDK1, MTOR, HDAC1
465	GO Biological Processes	regulation of cytokine production involved in inflammatory response	−4.752954509	MAPK14, HIF1A, STAT3
466	GO Biological Processes	regulation of cell development	−4.744778454	AKT1, MTOR, HDAC1, HIF1A, LYN
467	GO Biological Processes	regulation of mitotic cell cycle	−4.740739379	AKT1, APP, CDK1, EGFR, PTPN11
468	GO Biological Processes	stress-activated protein kinase signaling cascade	−4.736104742	MAPK14, NFKB1, MAPK3
469	GO Biological Processes	peptidyl-threonine modification	−4.736104742	AKT1, CDK1, MTOR
470	GO Biological Processes	oligodendrocyte differentiation	−4.736104742	MTOR, HDAC1, LYN
471	GO Biological Processes	response to osmotic stress	−4.736104742	CASP3, MTOR, HSP90AB1
472	GO Biological Processes	positive regulation of catabolic process	−4.732685766	AKT1, APP, MTOR, HIF1A, MAPK3
473	GO Biological Processes	phosphatidylinositol-mediated signaling	−4.703059127	AKT1, PIK3CA, PIK3R1
474	GO Biological Processes	cellular response to amino acid stimulus	−4.703059127	EGFR, MTOR, FYN
475	GO Biological Processes	regulation of oxidative stress-induced cell death	−4.703059127	AKT1, FYN, HIF1A
476	GO Biological Processes	regulation of protein modification by small protein conjugation or removal	−4.683417268	AKT1, FYN, HIF1A, HSP90AB1
477	GO Biological Processes	regulation of tyrosine phosphorylation of STAT protein	−4.670849093	FYN, JAK2, LYN
478	GO Biological Processes	telencephalon development	−4.663290224	CASP3, EGFR, HDAC1, HIF1A
479	GO Biological Processes	cellular chemical homeostasis	−4.661636742	APP, HIF1A, PIK3CA, PIK3R1, MAPK3
480	GO Biological Processes	inositol lipid-mediated signaling	−4.639433862	AKT1, PIK3CA, PIK3R1
481	GO Biological Processes	regulation of phosphatase activity	−4.639433862	MTOR, HSP90AB1, JAK2
482	GO Cellular Components	receptor complex	−4.63468005	APP, EGFR, HSP90AB1, JAK2, LYN
483	GO Biological Processes	positive regulation of cell cycle process	−4.630283105	AKT1, APP, CDK1, EGFR
484	GO Biological Processes	regulation of canonical Wnt signaling pathway	−4.630283105	MAPK14, EGFR, HDAC1, NFKB1
485	GO Molecular Functions	signaling adaptor activity	−4.608775571	PIK3R1, PTPN11, STAT3
486	GO Biological Processes	embryonic placenta development	−4.608775571	AKT1, EGFR, HIF1A
487	KEGG Pathway	Gap junction	−4.578838997	CDK1, EGFR, MAPK3
488	GO Biological Processes	regulation of leukocyte proliferation	−4.572492135	CASP3, JAK2, LYN, MAPK3
489	GO Biological Processes	sensory organ morphogenesis	−4.566194801	HDAC1, HIF1A, MAPK3, STAT3
490	GO Molecular Functions	enzyme activator activity	−4.555947887	APP, CASP3, EGFR, FYN, PIK3CA
491	GO Cellular Components	cell body	−4.555947887	APP, CASP3, FYN, HDAC1, HSP90AB1
492	GO Biological Processes	negative regulation of defense response	−4.553672253	MAPK14, FYN, LYN, NFKB1
493	GO Biological Processes	feeding behavior	−4.53521617	APP, FYN, STAT3
494	GO Biological Processes	neuron apoptotic process	−4.521001917	APP, CASP3, HIF1A
495	GO Biological Processes	positive regulation of nervous system development	−4.510582264	MTOR, HDAC1, HIF1A, LYN
496	KEGG Pathway	GnRH signaling pathway	−4.506945045	MAPK14, EGFR, MAPK3
497	GO Biological Processes	erythrocyte differentiation	−4.493042151	CASP3, JAK2, LYN
498	GO Biological Processes	regulation of protein dephosphorylation	−4.493042151	MTOR, HSP90AB1, JAK2
499	GO Biological Processes	ossification	−4.48645947	AKT1, MAPK14, EGFR, HIF1A
500	GO Biological Processes	response to steroid hormone	−4.48645947	CASP3, ESR1, JAK2, PIK3CA

No.	Category	Description	LogP	Hits
501	GO Biological Processes	regulation of cellular response to oxidative stress	−4.47928994	AKT1, FYN, HIF1A
502	KEGG Pathway	Inflammatory mediator regulation of TRP channels	−4.438906001	MAPK14, PIK3CA, PIK3R1
503	GO Cellular Components	extrinsic component of cytoplasmic side of plasma membrane	−4.425725605	AKT1, FYN, LYN
504	GO Biological Processes	epithelial cell migration	−4.425725605	AKT1, PIK3CA, PTPN11
505	GO Biological Processes	positive regulation of interleukin-6 production	−4.425725605	APP, PTPN11, STAT3
506	GO Biological Processes	response to decreased oxygen levels	−4.404729449	AKT1, CASP3, MTOR, HIF1A
507	GO Biological Processes	negative regulation of intrinsic apoptotic signaling pathway	−4.39976917	AKT1, HDAC1, HIF1A
508	GO Biological Processes	T cell activation	−4.399045356	MTOR, FYN, PIK3R1, STAT3
509	GO Molecular Functions	ubiquitin protein ligase binding	−4.393381025	EGFR, HIF1A, HSP90AB1, LYN
510	GO Biological Processes	DNA damage checkpoint signaling	−4.386987757	CDK1, MAPK14, PTPN11
511	GO Biological Processes	epithelium migration	−4.386987757	AKT1, PIK3CA, PTPN11
512	GO Biological Processes	neuron death	−4.386987757	APP, CASP3, HIF1A
513	GO Biological Processes	cellular response to interleukin-1	−4.386987757	HIF1A, NFKB1, MAPK3
514	GO Biological Processes	erythrocyte homeostasis	−4.374334095	CASP3, JAK2, LYN
515	GO Biological Processes	regulation of organ growth	−4.374334095	AKT1, CDK1, MAPK14
516	GO Biological Processes	positive regulation of myeloid cell differentiation	−4.374334095	MAPK14, HIF1A, STAT3
517	GO Biological Processes	regulation of protein localization to plasma membrane	−4.374334095	AKT1, EGFR, PIK3R1
518	GO Biological Processes	gland morphogenesis	−4.374334095	EGFR, ESR1, NFKB1
519	GO Cellular Components	postsynapse	−4.366875902	AKT1, APP, FYN, JAK2, LYN
520	GO Biological Processes	regulation of response to oxidative stress	−4.361805693	AKT1, FYN, HIF1A
521	GO Biological Processes	positive regulation of cell development	−4.348762212	MTOR, HDAC1, HIF1A, LYN
522	GO Biological Processes	response to hydrogen peroxide	−4.33711505	CASP3, CDK1, FYN
523	GO Biological Processes	regulation of gliogenesis	−4.324948173	MTOR, HDAC1, LYN
524	GO Biological Processes	adaptive immune response	−4.317443373	MTOR, FYN, JAK2, LYN, STAT3
525	GO Biological Processes	tissue migration	−4.312897278	AKT1, PIK3CA, PTPN11
526	GO Biological Processes	negative regulation of small molecule metabolic process	−4.312897278	AKT1, NFKB1, STAT3
527	GO Molecular Functions	transcription coregulator binding	−4.300960207	ESR1, HDAC1, HIF1A
528	GO Biological Processes	cellular homeostasis	−4.294797319	APP, HIF1A, PIK3CA, PIK3R1, MAPK3
529	GO Molecular Functions	ubiquitin-like protein ligase binding	−4.289344942	EGFR, HIF1A, HSP90AB1, LYN
530	GO Biological Processes	glial cell development	−4.28913486	AKT1, APP, LYN
531	GO Biological Processes	DNA integrity checkpoint signaling	−4.28913486	CDK1, MAPK14, PTPN11
532	GO Biological Processes	heart process	−4.28913486	MTOR, FYN, PIK3CA
533	GO Biological Processes	cellular response to external stimulus	−4.278771671	MTOR, LYN, NFKB1, MAPK3
534	GO Biological Processes	positive regulation of plasma membrane bounded cell projection assembly	−4.277419197	MTOR, PIK3CA, PIK3R1
535	GO Biological Processes	negative regulation of protein catabolic process	−4.277419197	EGFR, FYN, HSP90AB1
536	GO Biological Processes	regulation of interleukin-1 beta production	−4.277419197	APP, JAK2, STAT3
537	GO Biological Processes	mononuclear cell differentiation	−4.27351078	MTOR, LYN, PIK3R1, STAT3
538	GO Cellular Components	secretory granule lumen	−4.268266909	APP, MAPK14, HSP90AB1, NFKB1
539	GO Biological Processes	cellular glucose homeostasis	−4.265811232	HIF1A, PIK3CA, PIK3R1
540	GO Biological Processes	glucose metabolic process	−4.254309033	AKT1, MAPK14, PIK3CA
541	GO Biological Processes	angiogenesis	−4.252636362	AKT1, MAPK14, HIF1A, PIK3CA
542	GO Cellular Components	cytoplasmic vesicle lumen	−4.252636362	APP, MAPK14, HSP90AB1, NFKB1
543	GO Biological Processes	response to oxygen levels	−4.252636362	AKT1, CASP3, MTOR, HIF1A
544	GO Biological Processes	camera-type eye development	−4.232027594	EGFR, HDAC1, HIF1A, STAT3
545	GO Biological Processes	positive regulation of endothelial cell proliferation	−4.231614461	AKT1, HIF1A, STAT3
546	KEGG Pathway	Serotonergic synapse	−4.231614461	APP, CASP3, MAPK3
547	GO Biological Processes	protein import into nucleus	−4.231614461	AKT1, PIK3R1, STAT3
548	GO Biological Processes	regulation of cyclin-dependent protein serine/threonine kinase activity	−4.20932102	AKT1, CASP3, EGFR
549	GO Biological Processes	wound healing	−4.206630399	CASP3, MAPK14, HIF1A, PIK3CA
550	GO Biological Processes	cardiocyte differentiation	−4.198320411	CDK1, MTOR, MAPK3
551	GO Biological Processes	import into nucleus	−4.187414996	AKT1, PIK3R1, STAT3
552	GO Biological Processes	positive regulation of protein kinase B signaling	−4.176603168	EGFR, HSP90AB1, PIK3CA
553	GO Biological Processes	regulation of myeloid leukocyte differentiation	−4.155254047	MTOR, LYN, PIK3R1
554	GO Biological Processes	negative regulation of protein serine/threonine kinase activity	−4.155254047	AKT1, CASP3, LYN
555	GO Biological Processes	positive regulation of hormone secretion	−4.144713737	HIF1A, JAK2, PTPN11
556	GO Biological Processes	regulation of lipid metabolic process	−4.14240793	AKT1, MTOR, LYN, NFKB1
557	GO Molecular Functions	heat shock protein binding	−4.134260977	CDK1, HIF1A, HSP90AB1
558	GO Biological Processes	regulation of protein localization to cell periphery	−4.12389435	AKT1, EGFR, PIK3R1
559	GO Biological Processes	regulation of mitotic cell cycle phase transition	−4.108857799	AKT1, APP, CDK1, EGFR

No.	Category	Description	LogP	Hits
560	GO Biological Processes	developmental growth involved in morphogenesis	−4.103413988	APP, ESR1, HSP90AB1
561	GO Biological Processes	axonogenesis	−4.09469053	APP, FYN, HSP90AB1, PTPN11
562	GO Molecular Functions	transmembrane transporter binding	−4.093297584	FYN, HSP90AB1, LYN
563	GO Biological Processes	hormone-mediated signaling pathway	−4.093297584	ESR1, JAK2, PTPN11
564	GO Molecular Functions	histone deacetylase binding	−4.093297584	HDAC1, HIF1A, HSP90AB1
565	GO Biological Processes	protein localization to organelle	−4.087576727	AKT1, CDK1, ESR1, PIK3R1, STAT3
566	GO Biological Processes	regulation of response to biotic stimulus	−4.075992955	FYN, LYN, MAPK3, PTPN11
567	GO Biological Processes	regulation of protein catabolic process	−4.075992955	AKT1, EGFR, FYN, HSP90AB1
568	GO Biological Processes	myeloid cell homeostasis	−4.073305893	CASP3, JAK2, LYN
569	GO Biological Processes	regulation of interleukin-1 production	−4.073305893	APP, JAK2, STAT3
570	GO Biological Processes	response to virus	−4.071352359	MAPK14, HIF1A, JAK2, NFKB1
571	KEGG Pathway	Oocyte meiosis	−4.063428119	CDK1, MAPK14, MAPK3
572	GO Biological Processes	myeloid leukocyte differentiation	−4.063428119	APP, MAPK14, PIK3R1
573	GO Biological Processes	signal transduction in response to DNA damage	−4.05362745	CDK1, MAPK14, PTPN11
574	GO Biological Processes	regulation of dephosphorylation	−4.043902712	MTOR, HSP90AB1, JAK2
575	GO Biological Processes	regulation of apoptotic signaling pathway	−4.016687297	AKT1, HDAC1, HIF1A, JAK2
576	GO Biological Processes	negative regulation of cell cycle	−4.007754974	CASP3, CDK1, MAPK14, PTPN11
577	GO Biological Processes	regulation of neurogenesis	−4.003307428	MTOR, HDAC1, HIF1A, LYN
578	GO Biological Processes	eye development	−4.003307428	EGFR, HDAC1, HIF1A, STAT3
579	KEGG Pathway	Apelin signaling pathway	−3.987086424	AKT1, MTOR, MAPK3
580	GO Biological Processes	negative regulation of phosphorylation	−3.985639816	AKT1, CASP3, LYN, STAT3
581	GO Biological Processes	visual system development	−3.985639816	EGFR, HDAC1, HIF1A, STAT3
582	GO Biological Processes	regulation of supramolecular fiber organization	−3.972516008	APP, MTOR, PIK3CA, PIK3R1
583	GO Biological Processes	response to glucocorticoid	−3.959616028	CASP3, JAK2, PIK3CA
584	GO Biological Processes	sensory system development	−3.959499083	EGFR, HDAC1, HIF1A, STAT3
585	GO Biological Processes	cellular response to decreased oxygen levels	−3.932735628	AKT1, MTOR, HIF1A
586	GO Biological Processes	intracellular receptor signaling pathway	−3.923902355	ESR1, JAK2, STAT3
587	GO Biological Processes	myeloid leukocyte activation	−3.923902355	APP, JAK2, LYN
588	GO Biological Processes	cellular response to insulin stimulus	−3.906420889	AKT1, PIK3CA, PIK3R1
589	GO Biological Processes	positive regulation of leukocyte migration	−3.906420889	APP, PIK3R1, MAPK3
590	GO Biological Processes	regulation of insulin secretion	−3.897771021	HIF1A, JAK2, PTPN11
591	GO Biological Processes	regulation of reactive oxygen species metabolic process	−3.897771021	MAPK14, FYN, HIF1A
592	KEGG Pathway	Adrenergic signaling in cardiomyocytes	−3.88918064	AKT1, MAPK14, MAPK3
593	GO Biological Processes	learning	−3.88918064	APP, FYN, HIF1A
594	GO Biological Processes	response to glucose	−3.880648952	CASP3, HIF1A, PIK3CA
595	GO Biological Processes	negative regulation of cell population proliferation	−3.866797508	APP, CASP3, JAK2, LYN, STAT3
596	GO Biological Processes	cell cycle checkpoint signaling	−3.863758546	CDK1, MAPK14, PTPN11
597	GO Biological Processes	hexose metabolic process	−3.855398314	AKT1, MAPK14, PIK3CA
598	GO Biological Processes	positive regulation of lipid metabolic process	−3.855398314	AKT1, MTOR, LYN
599	GO Biological Processes	negative regulation of catalytic activity	−3.851419774	AKT1, APP, CASP3, LYN, NFKB1
600	GO Biological Processes	regulation of cellular carbohydrate metabolic process	−3.847093746	AKT1, MTOR, STAT3
601	GO Biological Processes	biological process involved in interaction with host	−3.847093746	CDK1, EGFR, HSP90AB1
602	GO Biological Processes	regulation of lipid transport	−3.847093746	AKT1, NFKB1, PTPN11
603	GO Biological Processes	regulation of epithelial cell proliferation	−3.846895193	AKT1, EGFR, HIF1A, STAT3
604	GO Biological Processes	response to hexose	−3.838844119	CASP3, HIF1A, PIK3CA
605	GO Biological Processes	response to xenobiotic stimulus	−3.830871007	CASP3, CDK1, HSP90AB1, LYN
606	GO Biological Processes	blood vessel morphogenesis	−3.818958209	AKT1, MAPK14, HIF1A, PIK3CA
607	GO Cellular Components	cell leading edge	−3.818958209	AKT1, APP, EGFR, PIK3CA
608	KEGG Pathway	Necroptosis	−3.814417894	HSP90AB1, JAK2, STAT3
609	GO Biological Processes	intrinsic apoptotic signaling pathway	−3.814417894	CASP3, JAK2, PIK3R1
610	GO Cellular Components	spindle	−3.799300393	AKT1, APP, CDK1, MAPK14
611	GO Biological Processes	cellular response to oxygen levels	−3.798395852	AKT1, MTOR, HIF1A
612	GO Biological Processes	cell morphogenesis involved in neuron differentiation	−3.791505082	APP, FYN, HSP90AB1, PTPN11
613	GO Biological Processes	response to monosaccharide	−3.774742982	CASP3, HIF1A, PIK3CA
614	GO Biological Processes	negative regulation of binding	−3.774742982	AKT1, JAK2, MAPK3
615	GO Biological Processes	negative regulation of response to external stimulus	−3.772183189	MAPK14, FYN, LYN, NFKB1
616	GO Biological Processes	cartilage development	−3.76695759	MAPK14, HIF1A, MAPK3
617	GO Biological Processes	response to corticosteroid	−3.76695759	CASP3, JAK2, PIK3CA
618	GO Biological Processes	positive regulation of leukocyte proliferation	−3.751531556	JAK2, LYN, MAPK3

No.	Category	Description	LogP	Hits
619	GO Biological Processes	positive regulation of cell growth	−3.751531556	AKT1, EGFR, MTOR
620	GO Biological Processes	negative regulation of phosphate metabolic process	−3.745523306	AKT1, CASP3, LYN, STAT3
621	GO Biological Processes	positive regulation of developmental growth	−3.743889754	AKT1, CDK1, MAPK14
622	GO Biological Processes	T cell differentiation	−3.743889754	MTOR, PIK3R1, STAT3
623	GO Biological Processes	negative regulation of phosphorus metabolic process	−3.74175123	AKT1, CASP3, LYN, STAT3
624	GO Biological Processes	embryonic organ development	−3.723024969	AKT1, EGFR, HIF1A, MAPK3
625	GO Cellular Components	extrinsic component of plasma membrane	−3.713784254	AKT1, FYN, LYN
626	GO Biological Processes	regulation of intrinsic apoptotic signaling pathway	−3.713784254	AKT1, HDAC1, HIF1A
627	GO Cellular Components	cytoplasmic side of plasma membrane	−3.706370606	AKT1, FYN, LYN
628	GO Biological Processes	monosaccharide metabolic process	−3.699001001	AKT1, MAPK14, PIK3CA
629	GO Biological Processes	morphogenesis of an epithelium	−3.697176481	CASP3, EGFR, ESR1, HIF1A
630	GO Biological Processes	positive regulation of epithelial cell migration	−3.684391899	AKT1, MTOR, HIF1A
631	GO Biological Processes	regulation of interleukin-6 production	−3.684391899	APP, PTPN11, STAT3
632	GO Biological Processes	viral life cycle	−3.677151412	CDK1, EGFR, HSP90AB1
633	GO Biological Processes	positive regulation of binding	−3.677151412	APP, HSP90AB1, JAK2
634	GO Biological Processes	lymphocyte activation	−3.675353577	MTOR, FYN, PIK3R1, STAT3
635	GO Biological Processes	regulation of peptide hormone secretion	−3.662796157	HIF1A, JAK2, PTPN11
636	GO Biological Processes	response to nutrient levels	−3.657396464	AKT1, MAPK14, MTOR, MAPK3
637	GO Molecular Functions	DNA-binding transcription activator activity, RNA polymerase II-specific	−3.643177204	ESR1, HIF1A, NFKB1, STAT3
638	GO Biological Processes	regulation of peptide secretion	−3.641570578	HIF1A, JAK2, PTPN11
639	GO Biological Processes	regulation of lipid biosynthetic process	−3.641570578	AKT1, MTOR, NFKB1
640	GO Biological Processes	neuron projection morphogenesis	−3.639642436	APP, FYN, HSP90AB1, PTPN11
641	GO Biological Processes	regulation of endothelial cell proliferation	−3.634575522	AKT1, HIF1A, STAT3
642	GO Molecular Functions	DNA-binding transcription activator activity	−3.629085697	ESR1, HIF1A, NFKB1, STAT3
643	GO Biological Processes	regulation of peptide transport	−3.627619802	HIF1A, JAK2, PTPN11
644	GO Biological Processes	plasma membrane bounded cell projection morphogenesis	−3.622087173	APP, FYN, HSP90AB1, PTPN11
645	GO Biological Processes	regulation of lipid localization	−3.62070299	AKT1, NFKB1, PTPN11
646	GO Biological Processes	cell projection morphogenesis	−3.604726492	APP, FYN, HSP90AB1, PTPN11
647	GO Biological Processes	negative regulation of immune response	−3.586688008	MAPK14, FYN, LYN
648	GO Biological Processes	leukocyte activation involved in immune response	−3.586688008	MTOR, LYN, STAT3
649	GO Cellular Components	nuclear envelope	−3.573954754	APP, EGFR, MTOR, MAPK3
650	GO Biological Processes	protein localization to nucleus	−3.573340115	AKT1, PIK3R1, STAT3
651	GO Biological Processes	regulation of stress-activated MAPK cascade	−3.553585232	APP, EGFR, MAPK3
652	GO Cellular Components	neuronal cell body	−3.543777771	APP, CASP3, HDAC1, HSP90AB1
653	GO Biological Processes	positive regulation of cellular component biogenesis	−3.540460545	ESR1, MTOR, PIK3CA, PIK3R1
654	GO Biological Processes	cell part morphogenesis	−3.540460545	APP, FYN, HSP90AB1, PTPN11
655	GO Biological Processes	regulation of plasma membrane bounded cell projection assembly	−3.527728477	MTOR, PIK3CA, PIK3R1
656	GO Biological Processes	regulation of cell projection assembly	−3.515000881	MTOR, PIK3CA, PIK3R1
657	GO Biological Processes	blood vessel development	−3.510919344	AKT1, MAPK14, HIF1A, PIK3CA
658	GO Biological Processes	negative regulation of cell-cell adhesion	−3.508686107	AKT1, CASP3, JAK2
659	GO Cellular Components	transcription regulator complex	−3.504430133	ESR1, HDAC1, HIF1A, STAT3
660	GO Cellular Components	lamellipodium	−3.502403584	AKT1, APP, PIK3CA
661	GO Biological Processes	skeletal system development	−3.497967908	MAPK14, HIF1A, MAPK3, PTPN11
662	GO Cellular Components	cytoplasmic side of membrane	−3.496152993	AKT1, FYN, LYN
663	GO Biological Processes	response to ketone	−3.496152993	AKT1, JAK2, PIK3CA
664	GO Biological Processes	antigen receptor-mediated signaling pathway	−3.483746354	FYN, LYN, PIK3CA
665	GO Biological Processes	transmembrane receptor protein serine/threonine kinase signaling pathway	−3.477589694	MAPK14, MAPK3, STAT3
666	GO Biological Processes	negative regulation of protein modification process	−3.472384681	AKT1, CASP3, FYN, LYN
667	GO Biological Processes	regulation of synapse organization	−3.465368187	APP, MAPK14, FYN
668	GO Biological Processes	regulation of protein ubiquitination	−3.459302753	AKT1, FYN, HSP90AB1
669	GO Biological Processes	vasculature development	−3.444099337	AKT1, MAPK14, HIF1A, PIK3CA
670	GO Biological Processes	regulation of synapse structure or activity	−3.429417403	APP, MAPK14, FYN
671	GO Biological Processes	negative regulation of protein kinase activity	−3.423526768	AKT1, CASP3, LYN
672	GO Biological Processes	regulation of cytoskeleton organization	−3.410216277	MTOR, PIK3CA, PIK3R1, MAPK3
673	GO Biological Processes	regulation of cellular amide metabolic process	−3.374082112	AKT1, APP, CASP3, MTOR
674	GO Molecular Functions	cell adhesion molecule binding	−3.353388935	EGFR, HSP90AB1, LYN, PTPN11
675	GO Biological Processes	positive regulation of protein serine/threonine kinase activity	−3.349422184	AKT1, EGFR, HSP90AB1
676	GO Biological Processes	tissue morphogenesis	−3.332970719	CASP3, EGFR, ESR1, HIF1A
677	GO Biological Processes	regulation of secretion by cell	−3.330075877	HIF1A, JAK2, LYN, PTPN11
678	GO Biological Processes	negative regulation of apoptotic signaling pathway	−3.327496504	AKT1, HDAC1, HIF1A

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679	GO Biological Processes	regulation of hormone secretion	−3.32207613	HIF1A, JAK2, PTPN11
680	GO Biological Processes	regulation of cysteine-type endopeptidase activity	−3.316679756	AKT1, FYN, JAK2
681	GO Biological Processes	phagocytosis	−3.311307176	FYN, LYN, PIK3CA
682	GO Biological Processes	positive regulation of immune response	−3.307111854	FYN, JAK2, LYN, PIK3CA
683	GO Biological Processes	regulation of lymphocyte proliferation	−3.295330199	CASP3, JAK2, LYN
684	GO Biological Processes	negative regulation of cell cycle phase transition	−3.295330199	CDK1, MAPK14, PTPN11
685	GO Biological Processes	regulation of innate immune response	−3.290050804	FYN, LYN, PTPN11
686	GO Biological Processes	negative regulation of kinase activity	−3.290050804	AKT1, CASP3, LYN
687	GO Biological Processes	embryonic morphogenesis	−3.28448718	CASP3, HDAC1, HIF1A, MAPK3
688	GO Biological Processes	viral process	−3.279560252	CDK1, EGFR, HSP90AB1
689	GO Biological Processes	regulation of mononuclear cell proliferation	−3.274348719	CASP3, JAK2, LYN
690	GO Biological Processes	nucleocytoplasmic transport	−3.258846876	AKT1, PIK3R1, STAT3
691	GO Biological Processes	nuclear transport	−3.258846876	AKT1, PIK3R1, STAT3
692	GO Biological Processes	leukocyte migration	−3.253723246	FYN, LYN, PIK3R1
693	GO Biological Processes	cellular component morphogenesis	−3.251166236	APP, FYN, HSP90AB1, PTPN11
694	GO Biological Processes	cell fate commitment	−3.238480841	CASP3, MTOR, STAT3
695	GO Biological Processes	response to alcohol	−3.228424595	AKT1, CDK1, FYN
696	GO Biological Processes	cellular response to extracellular stimulus	−3.218451074	MTOR, LYN, MAPK3
697	GO Biological Processes	regulation of I-kappaB kinase/NF-kappaB signaling	−3.213494927	ESR1, FYN, HDAC1
698	GO Biological Processes	regulation of protein secretion	−3.203643059	HIF1A, JAK2, PTPN11
699	GO Biological Processes	positive regulation of cell death	−3.197201754	CASP3, FYN, JAK2, LYN
700	GO Biological Processes	immune response-activating cell surface receptor signaling pathway	−3.179358629	FYN, LYN, PIK3CA
701	GO Biological Processes	immune response-activating signal transduction	−3.179358629	FYN, LYN, PIK3CA
702	GO Cellular Components	dendrite	−3.178758296	APP, MTOR, FYN, HSP90AB1
703	GO Biological Processes	skin development	−3.174559717	CASP3, EGFR, HDAC1
704	GO Biological Processes	regulation of secretion	−3.173529711	HIF1A, JAK2, LYN, PTPN11
705	GO Cellular Components	dendritic tree	−3.173529711	APP, MTOR, FYN, HSP90AB1
706	GO Molecular Functions	cytokine receptor binding	−3.127591272	CASP3, JAK2, PIK3R1
707	GO Biological Processes	chordate embryonic development	−3.122214977	AKT1, CASP3, EGFR, HIF1A
708	GO Biological Processes	lymphocyte differentiation	−3.113850219	MTOR, PIK3R1, STAT3
709	GO Biological Processes	negative regulation of transferase activity	−3.113850219	AKT1, CASP3, LYN
710	GO Biological Processes	regulation of actin filament organization	−3.104775871	MTOR, PIK3CA, PIK3R1
711	GO Biological Processes	positive regulation of secretion by cell	−3.104775871	HIF1A, JAK2, PTPN11
712	GO Biological Processes	sex differentiation	−3.091291399	CASP3, ESR1, PTPN11
713	GO Biological Processes	response to hypoxia	−3.077956501	CASP3, MTOR, HIF1A
714	GO Biological Processes	embryo development ending in birth or egg hatching	−3.067716739	AKT1, CASP3, EGFR, HIF1A
715	GO Biological Processes	negative regulation of cell cycle process	−3.060403867	CDK1, MAPK14, PTPN11
716	GO Biological Processes	regulation of transmembrane receptor protein serine/threonine kinase signaling pathway	−3.051722902	HDAC1, HSP90AB1, JAK2
717	GO Biological Processes	immune response-regulating cell surface receptor signaling pathway	−3.043104336	FYN, LYN, PIK3CA
718	GO Biological Processes	regulation of epithelial cell migration	−3.043104336	AKT1, MTOR, HIF1A
719	GO Cellular Components	transferase complex, transferring phosphorus-containing groups	−3.03029162	CDK1, PIK3CA, PIK3R1
720	GO Biological Processes	anatomical structure homeostasis	−3.026050998	APP, HIF1A, PTPN11
721	GO Biological Processes	reproductive structure development	−3.026050998	CASP3, ESR1, PTPN11
722	GO Biological Processes	reproductive system development	−3.009237221	CASP3, ESR1, PTPN11
723	GO Biological Processes	positive regulation of secretion	−2.992656636	HIF1A, JAK2, PTPN11
724	KEGG Pathway	Huntington disease	−2.984451869	CASP3, MTOR, HDAC1
725	GO Biological Processes	negative regulation of cellular component organization	−2.982605606	AKT1, FYN, PIK3CA, PIK3R1
726	GO Biological Processes	epidermis development	−2.968209677	CASP3, EGFR, HDAC1
727	GO Biological Processes	apoptotic signaling pathway	−2.960170811	CASP3, JAK2, PIK3R1
728	GO Cellular Components	plasma membrane protein complex	−2.955282642	CASP3, EGFR, JAK2, LYN
729	GO Biological Processes	epithelial tube morphogenesis	−2.952185827	CASP3, ESR1, HIF1A
730	GO Biological Processes	regulation of ion transport	−2.944044952	AKT1, APP, FYN, LYN
731	GO Biological Processes	regulation of leukocyte differentiation	−2.940307881	MTOR, LYN, PIK3R1
732	GO Cellular Components	glutamatergic synapse	−2.913045558	MAPK14, JAK2, LYN
733	GO Biological Processes	regulation of protein stability	−2.909201521	CASP3, HSP90AB1, PIK3R1
734	GO Biological Processes	muscle tissue development	−2.893948723	CDK1, MAPK14, MTOR
735	GO Molecular Functions	cadherin binding	−2.8788897	EGFR, HSP90AB1, PTPN11
736	GO Biological Processes	protein catabolic process	−2.878356085	AKT1, CASP3, MTOR, FYN
737	GO Biological Processes	activation of immune response	−2.864019809	FYN, LYN, PIK3CA
738	GO Biological Processes	negative regulation of protein phosphorylation	−2.86033136	AKT1, CASP3, LYN

No.	Category	Description	LogP	Hits
739	GO Biological Processes	regulation of cellular response to growth factor stimulus	−2.86033136	HDAC1, HIF1A, HSP90AB1
740	GO Biological Processes	establishment of protein localization to organelle	−2.849334574	AKT1, PIK3R1, STAT3
741	GO Cellular Components	endocytic vesicle	−2.842059846	EGFR, MTOR, LYN
742	GO Biological Processes	negative regulation of organelle organization	−2.834829674	AKT1, PIK3CA, PIK3R1
743	GO Molecular Functions	protein-macromolecule adaptor activity	−2.827643541	PIK3R1, PTPN11, STAT3
744	GO Biological Processes	negative regulation of proteolysis	−2.809867569	AKT1, APP, HSP90AB1
745	GO Biological Processes	glycerolipid metabolic process	−2.785423734	PIK3CA, PIK3R1, PTPN11
746	KEGG Pathway	Amyotrophic lateral sclerosis	−2.768269992	CASP3, MAPK14, MTOR
747	GO Biological Processes	regulation of actin cytoskeleton organization	−2.764869125	MTOR, PIK3CA, PIK3R1
748	GO Biological Processes	regulation of cellular component size	−2.758096837	MTOR, HSP90AB1, PIK3CA
749	GO Biological Processes	negative regulation of cell migration	−2.754725308	AKT1, HDAC1, STAT3
750	GO Biological Processes	multicellular organismal homeostasis	−2.741335398	PIK3CA, PTPN11, STAT3
751	GO Biological Processes	regulation of body fluid levels	−2.738011712	MAPK14, HIF1A, PIK3CA
752	GO Biological Processes	immune response-regulating signaling pathway	−2.734697441	FYN, LYN, PIK3CA
753	GO Biological Processes	negative regulation of cell motility	−2.705284465	AKT1, HDAC1, STAT3
754	GO Biological Processes	in utero embryonic development	−2.692446234	AKT1, EGFR, HIF1A
755	GO Biological Processes	regulation of cation transmembrane transport	−2.670314265	APP, FYN, LYN
756	GO Biological Processes	cellular cation homeostasis	−2.642464276	APP, HIF1A, MAPK3
757	GO Biological Processes	regulation of actin filament-based process	−2.633327528	MTOR, PIK3CA, PIK3R1
758	GO Biological Processes	regulation of protein-containing complex assembly	−2.621256215	ESR1, MTOR, PTPN11
759	GO Cellular Components	early endosome	−2.609309517	APP, EGFR, MAPK3
760	GO Cellular Components	lysosomal membrane	−2.597485029	MTOR, HSP90AB1, LYN
761	GO Cellular Components	lytic vacuole membrane	−2.597485029	MTOR, HSP90AB1, LYN
762	GO Biological Processes	negative regulation of locomotion	−2.594547728	AKT1, HDAC1, STAT3
763	GO Biological Processes	cellular ion homeostasis	−2.591617883	APP, HIF1A, MAPK3
764	GO Cellular Components	focal adhesion	−2.58578042	EGFR, JAK2, MAPK3
765	GO Biological Processes	regulation of cell growth	−2.58578042	AKT1, EGFR, MTOR
766	GO Biological Processes	regulation of metal ion transport	−2.582872731	AKT1, FYN, LYN
767	GO Biological Processes	regulation of membrane potential	−2.559871708	AKT1, APP, MTOR
768	GO Cellular Components	cell-substrate junction	−2.557028635	EGFR, JAK2, MAPK3
769	GO Biological Processes	regulation of neuron projection development	−2.517947539	AKT1, FYN, LYN
770	GO Biological Processes	modulation of chemical synaptic transmission	−2.512471725	APP, FYN, JAK2
771	GO Biological Processes	regulation of trans-synaptic signaling	−2.509743612	APP, FYN, JAK2
772	GO Cellular Components	vacuolar membrane	−2.477504427	MTOR, HSP90AB1, LYN
773	GO Biological Processes	carbohydrate metabolic process	−2.464335813	AKT1, MAPK14, PIK3CA
774	GO Biological Processes	negative regulation of transport	−2.43079445	AKT1, NFKB1, PTPN11
775	GO Biological Processes	regulation of translation	−2.41313628	AKT1, APP, MTOR
776	GO Molecular Functions	molecular adaptor activity	−2.398217012	PIK3R1, PTPN11, STAT3
777	GO Biological Processes	cation homeostasis	−2.385933099	APP, HIF1A, MAPK3
778	GO Biological Processes	circulatory system process	−2.373781572	MTOR, FYN, PIK3CA
779	GO Biological Processes	positive regulation of organelle organization	−2.359370794	MTOR, HIF1A, MAPK3
780	GO Biological Processes	regulation of anatomical structure size	−2.356986852	MTOR, HSP90AB1, PIK3CA
781	GO Biological Processes	organelle localization	−2.356986852	MTOR, HIF1A, LYN
782	GO Biological Processes	chemotaxis	−2.354607959	APP, MAPK14, FYN
783	GO Biological Processes	taxis	−2.349865237	APP, MAPK14, FYN
784	GO Biological Processes	inorganic ion homeostasis	−2.349865237	APP, HIF1A, MAPK3
785	GO Biological Processes	regulation of ion transmembrane transport	−2.331092361	APP, FYN, LYN
786	GO Biological Processes	ion homeostasis	−2.319517109	APP, HIF1A, MAPK3
787	GO Biological Processes	locomotion	−2.30806047	APP, MAPK14, FYN
788	GO Biological Processes	positive regulation of apoptotic process	−2.303510524	CASP3, JAK2, LYN
789	GO Biological Processes	positive regulation of programmed cell death	−2.269965568	CASP3, JAK2, LYN
790	GO Biological Processes	supramolecular fiber organization	−2.226759802	APP, HSP90AB1, JAK2
791	GO Biological Processes	regulation of cellular macromolecule biosynthetic process	−2.212028112	AKT1, APP, MTOR
792	GO Biological Processes	regulation of system process	−2.179078245	APP, JAK2, PTPN11
793	GO Biological Processes	chromatin organization	−2.143156466	ESR1, HDAC1, JAK2
794	GO Biological Processes	mitotic cell cycle	−2.116012976	APP, CDK1, PTPN11
795	GO Cellular Components	axon	−2.078378011	APP, HIF1A, HSP90AB1
796	GO Cellular Components	side of membrane	−2.001660852	AKT1, FYN, LYN