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Research Paper

Investigating the mechanism of ShuFeng JieDu capsule for the treatment of novel Coronavirus pneumonia (COVID-19) based on network pharmacology

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Abstract

ShuFeng JieDu capsule (SFJDC), a traditional Chinese medicine, has been recommended for the treatment of COVID-19 infections. However, the pharmacological mechanism of SFJDC still remains vague to date. The active ingredients and their target genes of SFJDC were collected from TCMSP. COVID-19 is a type of Novel Coronavirus Pneumonia (NCP). NCP-related target genes were collected from GeneCards database. The ingredients-targets network of SFJDC and PPI networks were constructed. The candidate genes were screened by Venn diagram package for enrichment analysis. The gene-pathway network was structured to obtain key target genes. In total, 124 active ingredients, 120 target genes of SFJDC and 251 NCP-related target genes were collected. The functional annotations cluster 1 of 23 candidate genes (CGs) were related to lung and Virus infection. RELA, MAPK1, MAPK14, CASP3, CASP8 and IL6 were the key target genes. The results suggested that SFJDC cloud be treated COVID-19 by multi-compounds and multi-pathways, and this study showed that the mechanism of traditional Chinese medicine (TCM) in the treatment of disease from the overall perspective.

Key words: ShuFeng JieDu capsule; Novel Coronavirus Pneumonia; network pharmacology, mechanism, pathway; candidate genes

Introduction

Since December 2019, a novel coronavirus pneumonia (NCP) caused by new coronavirus (SARS-COV-2) has been prevalent in China and other countries, such as United States and Korea [1-3]. WHO named this novel coronavirus pneumonia COVID-19 on February 11, 2020 [4] and there was a total of 20 million reported cases of COVID-19 globally and 750,000 deaths as of August 10, 2020 [5].

Its transmission route is mainly through respiratory droplets, but also through contact transmission, which has the characteristics of rapid spread, strong infectivity and general susceptibility of various groups of people. COVID-19 mild patients present with fever, fatigue, dry cough and other symptoms, whereas severe patients can appear with dyspnea, acute respiratory distress syndrome (ARDS) or septic shock and other symptoms. There is no special drug at present [6,7].

The treatment of COVID-19 mainly consisted of bed rest; intensive supportive treatment; oxygen therapy; antiviral therapy; antimicrobial therapy and Chinese medicine treatment. Critical cases need respiratory support (high flow nasal oxygen therapy, non-invasive ventilator or invasive mechanical ventilator); circulatory support for critically ill patients; plasma treatment from recovered patients and immunotherapy [8,9]. Most of the infectious diseases caused by virus belong to the category of "plague" in ancient Chinese traditional medicine, which is caused by many evil spirits invading the body [10]. The traditional medicine, including traditional Chinese medicine (TCM), has a good therapeutic effect on it [11,12]. The Health and Health Commission of China and the State Administration of traditional Chinese Medicine in the "circular on the issuance of a new type of coronavirus infection pneumonia diagnosis and treatment program (version 5)" requested to strengthen the integration of Chinese and western medicine, and recommended a number of proprietary Chinese medicine in the process of diagnosis and treatment [13]. On the basis of the national plan and in accordance with the principle of "three conditions and conditions", local prevention and control projects have also been successively according local issued to conditions [14]. Recommended Chinese medicines include MaXing ShiGan Tang, QingFei PaiDu Tang, HuoXiang ZhengQi Capsules, JinHua QingGan Granules, LianHua QingWen Capsules or ShuFeng JieDu capsule [8]. One clinical study showed that LianHua QingWen could improve the symptoms of COVID-19 patients and shorten the course of disease [15]. A retrospective analysis study showed that the time of disappearance of clinical symptoms, recovery of body temperature, average length of stay in the integrated Chinese and western medicine treatment group (34) was significantly lower than that of the western medicine group (18) among the 52 COVID-19 patients [16].With QingFei PaiDu Tang combined with western medicine to treat the COVID-19 could significantly improve the patient's symptoms and achieved better results [17].

ShuFeng JieDu capsule (SFJDC) is a traditional Chinese medicine used to treat influenza in China [18]. SFJDC is composed of Polygoni Cuspidati Rhizoma Et Radix (PCRR), Forsythiae Fructus (FF), Isatidis Radix (IR), Herba Patriniae (HP), Phragmitis Rhizoma (PR), Verbenae Herb (VH), licorice (I), Radix Bupleuri (RB) (Table 1). SFJDC has antiviral, antiinflammatory, antipyretic and immune regulatory effects [19]. SFJDC was commonly used for upper respiratory tract infection, pulmonary infection, AECOPD and other disease [20]. This drug now is also recommended for the treatment of COVID-19 infections in the latest Diagnosis and Treatment of Pneumonia Caused by COVID-19 (version 5) [13,21]. Currently, SFJDC is recommended in the Diagnosis and Treatment of Pneumonia Caused by COVID-19 in 5 provinces and cities [22].

Network pharmacology is a new discipline based on the theory of system biology, which analyzes the biological systems and selects specific signal nodes for multi-target drug molecular design. Network pharmacology emphasizes the multipathway regulation of signaling pathways and the regulation of multi-component, multi-target, multipathway, linking active components in traditional chinese medicine with target genes from molecular and biological aspects [23]. Network pharmacology will help to understand the relationship among ingredients, genes and diseases and is suitable for the study of complex TCM or TCM compounds. The potential mechanism of preventing COVID-19 by HuoXiang ZhengQi oral solution was realized by network pharmacology and molecular docking [24]. The research group Jing Zhao elucidated the mechanism of QingFei PaiDu Tang in the treatment of COVID-19 using network pharmacology [25]. SFJDC could be efficacious for COVID-19, but active incredients, target genes and putative mechanism are not known.

Table 1. Herb composition of Shu Feng Jie Du Capsule (SFJDC)

English translation	Latin name	Chinese name
Hu-Zhang	Polygoni Cuspidati Rhizoma Et Radix	虎杖
Lian-Qiao	Forsythiae Fructus	连翘
Ban-Lan-Gen	Isatidis Radix	板蓝根
Chai-Hu	Herba Patriniae	柴胡
Bai-Jiang-Cao	Phragmitis Rhizoma	败酱草
Ma-Bian-Cao	Verbenae Herb	马鞭草
Lu-Gen	licorice	芦根
Gan-Cao	Radix Bupleuri	甘草

In the present study, the network pharmacological was used to investigate the possible mechanism and target of SFJDC in the treatment of COVID-19. COVID-19 is a type of Novel Coronavirus Pneumonia (NCP). The active ingredients and their target genes of SFJDC were collected from TCMSP. NCP-related target genes were collected from GeneCards database. The putative mechanism of SFJDC against NCP were analyzed by GO and KEGG pathway. The flowchart of network pharmacology was shown in Figure 1. The study provided possible theoretical reference for SFJDC in the prevention and treatment of COVID-19.

Materials and Methods

Screening of active Ingredients in SFJDC

We identified the active ingredients of SFJDC Traditional Chinese Medicine Systems from Pharmacology Database and Analysis Platform (TCMSP http://tcmspw.com/tcmsp.php) [26]. TCMSP is a unique herbal pharmacology platform that captures the relationship between drugs, target genes and diseases. The database includes the detection of natural compounds such as chemical, target and drug target networks. ADME is pharmacokinetics, which refers to the absorption, distribution, metabolism and excretion of exogenous

chemicals by myosome. The four key parameters of ADME were blood-brain barrier (BBB), oral bioavailability (OB), Caco-2 permeability (Caco-2) and drug-likeness (DL) [27]. In this study select candidate compounds which has OB \geq 30%, DL \geq 0.18, Caco-2 \geq -0.4, BBB \geq -0.3.Then we sorted out each active ingredient for identification of targets.

Identification of SFJDC putative target genes

This study used the TCMSP platform to obtain the putative target genes of active ingredients of SFJDC. The Uniprot (https://www.uniprot.org/) [28] database provides a comprehensive, high quality and freely available source of protein sequence and function information. The putative target information corresponding to the active ingredients were input into UniProt database to obtain the standard name of the action target genes.

Screening of NCP related targets

COVID-19 is a type of Novel Coronavirus Pneumonia (NCP). So We collected NCP related targets from GeneCards (https://www.genecards. org/), which is a searchable, integrative database that provides comprehensive, user-friendly information on all annotated and predicted human genes [29]. The key word "Novel Coronavirus Pneumonia" was used in the GeenCards database.

PPI (Protein-Protein Interaction) network construction of SFJDC putative and NCP related target genes

The PPI network of SFJDC putative and NCP related targets would be obtained from STRING (https://string-db.org/ ver11.0, update Jan 2019) [30]. Active interaction sources were set as follows: Text-

mining, Co-expression, Neighborhood, Experiments, Databases, Gene Fusion and Co-occurrence. The required minimum interaction score was set at 0.4 in PPI network of SFJDC related targets, PPI network of NCP was set at 0.9. The barplot were generated by the R software (https://www.r-project.org/ver 3.6.2) based on counts value.

Construction of SFJDC ingredient-target network

Perl (https://www.perl.org/get.html) is a programming language suitable for writing simple scripts as well as complex applications. We used Strawberry Perl 5.30.1.1 to prepare the ingredienttarget network. Cytoscape is a universal open source software for large-scale integrated development of molecular interaction networks working data. Then the ingredients-targets network of SFJDC was constructed using Cytoscape 3.7.2 software [31].

PPI network construction of SFJDC against NCP

In order to reveal the mechanism of SFIDC against NCP, a PPI network was constructed by the BisoGenet client which is a Cytoscape plugin was used to visualize. In this plugin, Protein-protein interactions information is taken from the DIP, BIOGRID, HPRD, INTACT, MINT, BIND [32]. CytoNCA is a Cytoscape plugin integrating calculation, evaluation and visualization analysis for multiple centrality measure measures including Betweenness Centrality (BC), Degree Centrality (DC), Colseness Centrality (CC), Local average connectivity-based method (LAC), Eigenvector Centrality (EC) and Network Centrality (NC) [33].



Table 2. The active ingredients of each herb contained in SFJDC

Mol ID	Molecule Name	OB (%)	Caco-2	BBB	DL	Source
MOL000173	wogonin	30.68	0.79	0.04	0.23	FF
MOL000211	Mairin	55.38	0.73	0.22	0.78	FF: RB
MOL000239	Jaranol	50.83	0.61	-0.22	0.29	RB
MOL000358	beta-sitosterol	36.91	1.32	0.99	0.75	PR: PCRR: IR: FF:
						VH
MOL000359	sitosterol	36.91	1.32	0.87	0.75	PR; IR; RB
MOL000392	formononetin	69.67	0.78	0.02	0.21	RB
MOL000449	Stigmasterol	43.83	1.44	1	0.76	PR; IR; HP; I; VH
MOL000497	licochalcone a	40.79	0.82	-0.21	0.29	RB
MOL000791	bicuculline	69.67	0.72	0.02	0.88	FF
MOL000953	CLR	37.87	1.43	1.13	0.68	IR
MOL001484	Inermine	75.18	0.89	0.4	0.54	RB
MOL001645	Linoleyl acetate	42.1	1.36	1.08	0.2	HP
MOL001663	(4aS 6aR 6aS 6bR 8aR 10R 12aR 14bS)-10-hvdroxy-2.2 6a 6b 9.9.12a-heptamethyl-1.3.4.5.	32.03	0.61	0.39	0.76	VH
1102001000	6,6a,7,8,8a,10,11,12,13,14b-tetradecahydropicene-4a-carboxylic acid	02.00	0.01	0.05	00	
MOL001676	Vilmorrianine C	33.96	0.59	0.14	0.22	PR
MOL001677	asperglaucide	58.02	0.28	-0.22	0.52	PR
MOL001689	acacetin	34.97	0.67	-0.05	0.24	PR: IR
MOI 001697	Sinoacutine	63 39	0.72	0.36	0.53	PR
MOI 001749	ZINC03860434	43 59	1.04	0.6	0.35	IR
MOL 001755	24 Ethylcholest 4 on 3 one	36.08	1.01	1.22	0.76	IR
MOL001755	quindeline	33.17	1.40	0.00	0.70	IR IP
MOL001750	heta aitastaral dadacantata	24.57	1.5	0.55	0.22	IN ID
MOL001769	beta-snosterol dodecantate	34.37	1.20	0.57	0.57	IK
MOL001771	portferast-5-en-5beta-of	36.91	1.45	1.14	0.75	IK
MOL001774	Ineketone	37.14	0.39	0.1	0.3	IK
MOL001779	Sinoacutine	49.11	0.7	0.39	0.46	IR
MOL001781	Indigo	38.2	0.83	0.02	0.26	IR
MOL001782	(2Z)-2-(2-oxoindolin-3-ylidene)indolin-3-one	48.4	0.85	-0.06	0.26	IR
MOL001783	2-(9-((3-methyl-2-oxopent-3-en-1-yl)oxy)-2-oxo-1,2,8,9-tetrahydrofuro[2,3-h]quinolin-8-	64	0.39	-0.09	0.57	IR
	yl)propan-2-yl acetate					
MOL001792	DFV	32.76	0.51	-0.29	0.18	IR; RB
MOL001793	(E)-2-[(3-indole)cyanomethylene-]-3-indolinone	54.59	1.06	0.22	0.32	IR
MOL001800	rosasterol	35.87	1.28	0.89	0.75	IR
MOL001803	Sinensetin	50.56	1.12	0.04	0.45	IR
MOL001804	Stigmasta-5,22-diene-3beta,7alpha-diol	43.04	1.35	0.84	0.82	IR
MOL001806	Stigmasta-5,22-diene-3beta,7beta-diol	42.56	1.37	0.81	0.83	IR
MOL001810	6-(3-oxoindolin-2-ylidene)indolo[2,1-b]quinazolin-12-one	45.28	1.19	0.48	0.89	IR
MOL001814	(E)-3-(3,5-dimethoxy-4-hydroxy-benzylidene)-2-indolinone	57.18	0.69	0.16	0.25	IR
MOL001820	(E)-3-(3,5-dimethoxy-4-hydroxyb-enzylidene)-2-indolinone	65.17	0.28	-0.17	0.25	IR
MOL001828	3-[(3.5-dimethoxy-4-oxo-1-cyclohexa-2.5-dienylidene)methyl]-2.4-dihydro-1H-pyrrolo	51.84	0.81	0.03	0.56	IR
	[2,1-b]quinazolin-9-one					
MOL002311	Glycyrol	90.78	0.71	-0.2	0.67	RB
MOL002565	Medicarpin	49.22	1	0.53	0.34	RB
MOL002773	beta-carotene	37.18	2.25	1.52	0.58	VH
MOL003281	20(S)-dammar-24-ene-36.20-diol-3-acetate	40.23	0.93	0.28	0.82	FF
MOL003290	(3R 4R)-3 4-bis[(3 4-dimethoxyphenyl)methyl]oxolan-2-one	52.3	0.78	0.17	0.48	FF
MOL003295	(+)-ninoresinol monomethyl ether	53.08	0.69	0	0.57	FF
MOI 003306	ACon1_001697	85.12	0.76	0	0.57	FF
MOI 003308	(+)-ninoresinal monomethyl ether-A-D-beta-glucoside at	61.2	0.7	012	0.57	FF
MOL003315	3beta Acetul 20.25 enovudammerane 24alnha el	33.07	0.75	0.12	0.37	EE
MOL003322	EORSVTHINOI	81.25	0.59	0.24	0.57	EE
MOL003322		05.04	0.59	-0.00	0.57	EE EE
MOL003330	e-muin e-e-te-te	95.04 43.06	1.20	0.07	0.37	FF
MOL003344	p-anyrin acetate	42.06	1.30	1.1	0.74	FF
MOL003347	nyperform	44.03	0.87	0.4	0.6	FF
MOL003348	adhyperform	44.03	0.93	0.58	0.61	FF
MOL003365	Lactucasterol	40.99	0.88	0.5	0.85	FF
MOL003370	Onjixanthone I	79.16	0.84	0.04	0.3	FF
MOL003656	Lupiwighteone	51.64	0.68	-0.23	0.37	RB
MOL003896	7-Methoxy-2-methyl isoflavone	42.56	1.16	0.56	0.2	RB
MOL004598	3,5,6,7-tetramethoxy-2-(3,4,5-trimethoxyphenyl)chromone	31.97	0.75	0.08	0.59	HP
MOL004609	Areapillin	48.96	0.6	-0.29	0.41	HP
MOL004624	Longikaurin A	47.72	0.08	0.09	0.53	HP
MOL004628	Octalupine	47.82	0.48	0.3	0.28	HP
MOL004644	Sainfuran	79.91	0.9	0.23	0.23	HP
MOL004653	(+)-Anomalin	46.06	0.46	0	0.66	HP
MOL004718	α-spinasterol	42.98	1.28	0.79	0.76	HP
MOL004805	(25)-2-[4-hydroxy-3-(3-methylbut-2-envl)phenyl]-8,8-dimethyl-2.3-dihydropyrano[2.3-f	31.79	1	0.25	0.72	RB
]chromen-4-one					
MOL004806	euchrenone	30.29	1.09	0.39	0.57	RB
MOL004808	glyasperin B	65.22	0.47	-0.09	0.44	RB
MOL004810	glyasperin F	75.84	0.43	-0.15	0.54	RB

MOI 004811	Glyasperin C	45 56	0.71	0.07	0.4	RB
MOI 004814	Isotrifoliol	31.94	0.53	-0.25	0.12	RB
MOI 004815	(F) 1 (24 dihydroxynhonyl) 3 (22 dimethylchromen 6 yl)nron 2 en 1 one	30.62	0.55	0.12	0.35	RB
MOL004015	(E)-1-(2,4-uniyuroxyphenyi)-5-(2,2-uniterryterromen-6-yi)prop-2-en-1-one	59.02	0.00	-0.12	0.55	RD DD
MOL004820	Classidation A	50.46 44.72	0.65	0.04	0.52	KD DD
MOL004828		44.72	0.79	0.06	0.35	RB
MOL004829	Glepidotin B	64.46	0.46	-0.09	0.34	RB
MOL004833	Phaseolinisoflavan	32.01	1.01	0.46	0.45	RB
MOL004835	Glypallichalcone	61.6	0.76	0.23	0.19	RB
MOL004838	8-(6-hydroxy-2-benzofuranyl)-2,2-dimethyl-5-chromenol	58.44	1	0.34	0.38	RB
MOL004848	licochalcone G	49.25	0.64	-0.04	0.32	RB
MOL004849	3-(2,4-dihydroxyphenyl)-8-(1,1-dimethylprop-2-enyl)-7-hydroxy-5-methoxy-coumarin	59.62	0.4	-0.23	0.43	RB
MOL004855	Licoricone	63.58	0.53	-0.14	0.47	RB
MOL004856	RBnin A	51.08	0.8	0.13	0.4	RB
MOL004857	RBnin B	48.79	0.58	-0.1	0.45	RB
MOL004863	3-(3,4-dihydroxyphenyl)-5,7-dihydroxy-8-(3-methylbut-2-enyl)chromone	66.37	0.52	-0.13	0.41	RB
MOL004866	2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-6-(3-methylbut-2-enyl)chromone	44.15	0.48	-0.28	0.41	RB
MOL004879	Glycyrin	52.61	0.59	-0.13	0.47	RB
MOL004882	Licocoumarone	33.21	0.84	0.06	0.36	RB
MOL004883	Licoisoflavone	41.61	0.37	-0.27	0.42	RB
MOI.004884	Licoisoflavone B	38.93	0.46	-0.18	0.55	RB
MOI 004885	licoisoflavanone	52 47	0.39	-0.22	0.54	RB
MOI 004891	shippterocarpin	80.3	11	0.68	0.73	RB
MOI 004907	Clyzaglabrin	61.07	0.34	-0.2	0.35	RB
MOL004907	Clabridin	53.25	0.04	-0.2	0.35	RD
MOL004900	Clabracia	53.25	0.97	0.30	0.47	RD DD
MOL004910	Glabranin	52.9 46.07	0.97	0.51	0.51	KD DD
MOL004911	Glabrene	40.27	0.99	0.04	0.44	KD DD
MOL004912		52.51	0.59	-0.11	0.5	RB
MOL004913	1,3-dihydroxy-9-methoxy-6-benzofurano[3,2-c]chromenone	48.14	0.48	-0.19	0.43	KB
MOL004915	Eurycarpin A	43.28	0.43	-0.06	0.37	RB
MOL004941	(2R)-7-hydroxy-2-(4-hydroxyphenyl)chroman-4-one	71.12	0.41	-0.25	0.18	RB
MOL004945	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-8-(3-methylbut-2-enyl)chroman-4-one	36.57	0.72	-0.04	0.32	RB
MOL004948	Isoglycyrol	44.7	0.91	0.05	0.84	RB
MOL004957	HMO	38.37	0.79	0.25	0.21	RB
MOL004959	1-Methoxyphaseollidin	69.98	1.01	0.48	0.64	RB
MOL004966	3'-Hydroxy-4'-O-Methylglabridin	43.71	1	0.73	0.57	RB
MOL004974	3'-Methoxyglabridin	46.16	0.94	0.47	0.57	RB
MOL004978	2-[(3R)-8,8-dimethyl-3,4-dihydro-2H-pyrano[6,5-f]chromen-3-yl]-5-methoxyphenol	36.21	1.12	0.61	0.52	RB
MOL004980	Inflacoumarin A	39.71	0.73	-0.24	0.33	RB
MOL004985	icos-5-enoic acid	30.7	1.22	1.09	0.2	RB
MOL004988	Kanzonol F	32.47	1.18	0.56	0.89	RB
MOL004989	6-prenylated eriodictyol	39.22	0.4	-0.29	0.41	RB
MOL004991	7-Acetoxy-2-methylisoflavone	38.92	0.74	0.16	0.26	RB
MOL004996	gadelaidic acid	30.7	1.2	0.94	0.2	RB
MOL005000	RBnin G	60.44	0.78	0.23	0.39	RB
MOL005001	RBnin H	50.1	0.6	-0.14	0.78	RB
MOL005003	Licoagrocarpin	58.81	1 23	0.61	0.58	RB
MOL005007	Glyasperins M	72.67	0.49	-0.04	0.59	RB
MOI 005012	Licoagraisoflavone	57.28	0.71	0.09	0.49	RB
MOL005012	Odoratin	49.95	0.71	-0.24	0.42	RB
MOL005017	Phaseal	49.93	0.42	-0.24	0.5	RD DB
MOL005017	Vambiogra	70.77 E4.9E	1.00	-0.00	0.56	RD DB
MOL005018		54.65	1.09	0.52	0.07	KD DD
MOL005020	denyarogiyasperins C	53.82 40.55	0.68	-0.12	0.37	KĎ
MOL005229	Artemetin	49.55	0.81	-0.09	0.48	vн
MOL005503	Cornudentanone	39.66	0.47	0.09	0.33	VH
MOL008752	Dihydroverticillatine	42.69	0.56	0.11	0.84	VH
MOL013281	6,8-Dihydroxy-7-methoxyxanthone	35.83	0.68	0.1	0.21	PCRR
MOL013287	Physovenine	106.21	0.51	0.2	0.19	PCRR
MOL013288	Picralinal	58.01	0.23	-0.21	0.75	PCRR

Identification of candidate genes (CGs) and enrichment analysis of CGs

The CGs were filtered with R software using the Venn Diagram package (https://cran.r-project.org/ web/packages/VennDiagram/index.html). The CGs would be used for Gene Ontology (GO) analysis (including biological processes (BP), molecular functions (MF), and cellular components (CC)) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways. GO and KEGG pathway analyses results were processed by the "enrichplot" (http://www.bioconductor.org/packages/release/bioc/html/enric hplot.html) "clusterProfiler" (http://www.bioconductor.org/packages/release/bioc/html/clust erProfiler.html) and "ggplot2" packages by R software. A *P* value of less than 0.05 was used regarded as statistically significant. At the same time, we input CGs into DAVID (https://david.ncifcrf.

gov/) for functional enrichment analysis to obtain disease clustering.

Construction of gene-pathway network

KEGG pathways that had significant changes of P<0.05 were further analyzed. The genes that significantly regulated pathways for gene-pathway network construction. The key target genes of SFJDC against NCP were screened by gene-pathway network.

Results

The active ingredients of each herb contained in SFJDC

One hundred and thirty-seven active ingredients were screened out of TCMSP based on ADME, 4 in PCRR, 17 in FF, 25 in IR, 9 in HP, 7 in PR, 7 in VH, 1 in I, 67 in RB and 13 of which were repeated. Finally, 124 candidate active components of each herb contained in SFJDC were screened for further analysis after removing duplation (**Table 2**).

Putative target genes of each herb in SFJDC and NCP related target genes

The 124 candidate active components were imported into TCMSP database and Uniport database to identify the Putative target genes of each herb in SFJDC. One hundred and ten components were finally selected after removing 14 ingredients which did not link to any target genes. The target genes of 110 compounds were collected. 1705 genes were identified, 103 in PR, 209 in IR, 65 in HP, 1052 in RB, 75 in PCRR, 173 in FF and 27 in I. There were 1585 genes of the eight herbs overlapped, which was suggestive of potential interaction between the compounds of SFJDCA in the course of treatment. A total of 120 genes were identified after removing duplation (Table 3). And 251 NCP related target genes were identified from Gene Cards database (Table 4).

PPI network of SFJDC putative and NCP related target genes

In this study, we constructed the PPI network of SFJDC putative and NCP related target genes separately. The network of SFJDC putative target genes which minimum interaction score was set at 0.4 contained 119 nodes and 1108 edges which indicated the target genes interactions after removing the discrete points (**Figure 2A**). According the PPI network, the top thirty genes were listed in **Figure 2B**. After hiding the discrete points, NCP-related target genes PPI network contained 248 nodes and 1235 edges (**Figure 2C**). Similarly, the first 30 related genes were shown in **Figure 2D**.

SFJDC ingredient-target network analysis

The ingredient-target network of SFJDC was constructed using the screened ingredients and their targets as shown in **Figure 3**. The network contained 117 nodes and 419 edges which indicated the compound-target genes interaction. A median of 110 candidate compouds was 5 degrees which indicating that most compounds of SFJDC were affected by multiple target genes. The top three effective ingredient according were Wogonin, licochalcone a and acacetin. Wogonin, licochalcone a and acacetin have 42, 30 and 23 target genes, respectively. And the OB of Wogonin, licochalcone a and acacetin were 30.68, 40.79 and 34.97%, respectively. Hence, they might be the crucial effective compounds of SFJDC according the network.

PPI network analysis of SFJDC against NCP

PPI network of SFJDC against NCP were visualized using Cytoscape software. The network contained 2407 nodes and 53639 edges was shown in **Figure 4A**. The average degree of all nodes was 44.5692 and we selected the nodes with more than 44.5692 degrees as significant genes. A subnetwork of significant genes for SFJDC against NCP was constructed which consisted of 766 nodes and 28872 edges (**Figure 4B**). The average value of BC was 711.9504. The significant genes were further screened and a new network was constructed with 169 nodes and 4238 edges (**Figure 4C**). 169 genes were eventually identified for SFJDC against NCP including 156 other human genes and 13 target genes.

Identification of candidate genes (CGs) and Enrichment analysis of CGs

Twenty-three candidate genes (CGs) were identified by using the VennDiagram package (**Figure 5**). Then R software was used to perform GO and KEGG pathway analysis of the CGs. GO of CGs was analyzed based on BP, CC, MF. 1215 GO terms were significantly enriched (P<0.05), 1148 in BP, 28 in CC, 39 in MF. Top 20 terms were shown in **Figure 6**. The data of top 20 GO analysis were listed in **Table 5**. Based on these GO terms data, we found that most significantly terms were response to lipopolysaccharide, response to molecule of bacterial origin, membrane raft, membrane microdomain, BH domain binding and death domain binding, suggested that SFJDC could treat NCP with multiple synergies.

The pathways that were significantly affected by SFJDC in the process of treating NCP were identified by KEGG pathway. 110 KEGG pathways were significantly enriched (P<0.05). Top twenty pathways were shown in **Figure 7**, color represented *P* value and size of the spot represented count of genes. Based

on the analysis of KEGG pathway data (**Table 6**), the top five pathways such as Kaposi sarcoma-associated herpesvirus infection, AGE-RAGE signaling pathway in diabetic complications, Human cytomegalovirus infection, IL-17 signaling pathway and Hepatitis B, might be the core pharmacological mechanism of SFJDC for NCP.

In this study, we chose the functional annotation

clustering and set the classification stringency as high in DAVID. A total of 20 functional annotation clusters were obtained (**Table 7**). Annotation Cluster 1 (enrichment score 6.04) contains three categories: Asthma, Bronchiolitis Viral, Respiratory Syncytial Virus Infections, respiratory syncytial virus bronchiolitis, and all of them were lung related diseases and Virus infection disease.



Figure 2. PPI network of SFJDC putative and NCP related target genes and the Barplot of PPI. (A) PPI network of SFJDC putative target genes. (B) PPI network of NCP related target genes. (C) Barplot showing the significant genes in PPI network of SFJDC. (D) Barplot showing the significant genes in PPI network of NCP. PPI, protein-protein interaction; SFJDC: ShuFeng JieDu capsule; NCP: Novel Coronavirus Pneumonia.

Herb	Mol ID	Molname	Target genes
FF	MOL000173	wogonin	ADRB2 AHSA1 AKT1 AR BAX BBC3 BCL2 CALM1 CASP3 CASP9 CCL2 CCND1 CDK2 CDKN1A CHEK1 DPP4 EIF6 ESR1 FSD1 GABRA1 GSK3B HSP90AA1 IL6 IL8RA JUN KDR MAPK14 MCL1 MMP1 NOS2 PPARG PRKCD PRSS1 PTGER3 PTGS1 PTGS2 RELA RXRA SCN5A TEP1 TNF515 TP63
RB FF	MOL000211	Mairin	PGR
RB	MOL000239	Iaranol	AR CALM1 CDK2 CHEK1 DPP4 ESR2 HSP90AA1 NCOA2 NOS2 PRSS1 PTGS1 PTGS2 SCN5A
PR IR; PCRR;	MOL000358	beta-sitosterol	ADRA1A ADRA1B ADRB2 BAX BCL2 CASP3 CASP8 CASP9 CHRM1 CHRM2 CHRM3 CHRM4 CHRNA2 DRD1 GABRA1 HSP90AA1 JUN KCNH2 MAP2 NCOA2 OPRM1 PGR
FF DD ID DD	MOI 000250	aitaataral	PONTPRKCA PIGSI PIGS2 SCN5A SLC6A4
	MOL000359	formononatin	ACUE ADDA1A ADDD2 AD ATDEE1B CALM1 CONA2 CDV2 CHEV1 CHDM1 DD04 ECD1
KD	WICE000392	Tormononeum	ESR2 GSK3B HSD3B1 HSD3B2 HSP90AA1 HTR IL4 JUN MAOB MAPK14 ND6 NOS2 PKIA PPARG PPARG PRSS1 PTGS2 PKRA SLC6A3 SLC6A4
PR IR HP I	MOL000449	Stigmasterol	ADHIC ADRA1A ADRA1B ADRA2A ADRB1 ADRB2 AKR1B1 CHRM1 CHRM2 CHRM3 CTRB1 GABRA1 IGHG1 LTA4H MAOA MAOB NCOA1 NCOA2 NR3C2 PGR PLAU PTGS1 PTGS2 RXRA SCN5A SLC6A2 SLC6A3
RB	MOL000497	licochalcone a	ADRA1B ADRB2 AR BCL2 CA2 CALM1 CCNA2 CCND1 CDK2 CDK4 CHEK1 CHRM1 EIF6 ESR1 ESR2 FOSL2 GSK3B HSP90AA1 MAPK1 MAPK14 NCOA2 NOS2 PPARG PTGS1 PTGS2 RB1 RELA SCN5A SLC6A3 STAT3
FF	MOL000791	bicuculline	ACHE ALDH3A1 AR BMPR2 CRH FOS GABBR1 GJA1 GJB1 GNRH1 GNRHR GRIN2D GRM1 GRM5 HSP90AA1 HTR KCNH2 KDR PTGS1 PTGS2 SCN5A SLC6A2 VCP
IR	MOL000953	CLR	NCOA2 NR3C2 PGR
RB	MOL001484	Inermine	ADRA1B ADRA1D ADRB2 CALM1 CHRM1 CHRM3 HSP90AA1 HTR3A IGHG1 OPRM1 PRSS1 PTGS1 PTGS2 RXRA SCN5A
HP	MOL001645	Linoleyl acetate	NCOA2 PTGS1 PTGS2 RXRA
PR	MOL001677	asperglaucide	HTR KCNH2 PRSS1 PTGS2
PR; IR	MOL001689	acacetin	ADRB2 AR BAX BCL2 CALM1 CASP3 CASP8 CDK2 CDKN1A CHEK1 CYP19A1 DPP4 FASLG FASN HSP90AA1 NCOA1 NCOA2 NOS2 PRSS1 PTGS1 PTGS2 RELA TP63
PR	MOL001697	Sinoacutine	ACHE ADRA1A ADRA1B AR CHRM1 CHRM2 CHRM3 CHRM4 CHRM5 ESR1 ESR2 GABRA1 HTR OPRD1 OPRM1 PTGS1 PTGS2 SCN5A
IR	MOL001749	ZINC03860434	ADRB2 CHRM1 CHRM3 SCN5A
IR	MOL001755	24-Ethylcholest-4-en-3-one	NR3C2 PGR
IR	MOL001756	quindoline	MAOB NCOA2 PKIA PTGS1 PTGS2
IR	MOL001771	poriferast-5-en-3beta-ol	NCOA2 PGR
IR	MOL001774	Ineketone	NR3C2
IK	MOL001779	Sinoacutine	ACHE ADRATI DAR CALINI CHKMI CHKM3 CHKM3 DP74 ESKI ESK2 H5P90AAT HTK NOS2 OPRDT DPRMT PTGS1 PTGS2 RXRA SCN5A
IR IR	MOL001781 MOL001782	Indigo (2Z)-2-(2-oxoindolin-3-ylidene)indolin-3-one	AR CCNA2 CDK2 PIGS1 PIGS2 KXKA AR CCNA2 CDK2 CHEK1 ESR1 GABRA1 GSK3B HSP90AA1 MAPK14 NOS2 PTGS1 PTGS2 RXRA
IR	MOL001783	2-(9-((3-methyl-2-oxopent-3-en-1-yl)oxy)-2-oxo- 1,2,8,9-tetrahydrofuro[2,3-h]quinolin-8-yl) propan-2-yl acetate	HSP90AA1 KCNH2 NCONA2 PR5S1 PTGS2
IR RB	MOL001792	DFV	ADRB2 ESR1 HSP90AA1 MAOB PKIA PTGS1 PTGS2 RXRA SLC6A4
IR	MOL001793	(E)-2-[(3-indole)cyanomethylene-]-3-indolinone	AR CCNA2 CDK2 CHEK1 ESR1 GSK3B HSP90AA1 MAPK14 NOS2 PTGS1 PTGS2 RXRA
IR	MOL001800	rosasterol	PGR
IR	MOL001803	Sinensetin	ACHE ADRA1B ADRB2 AR CALM1 CHEK1 DPP4 ESR2 F7 HSP90AA1 HTR KCNH2 NCOA1 NCOA2 NOS2 PRSS1 PTGS1 PTGS2 SCN5A
IR	MOL001804	Stigmasta-5,22-diene-3beta,7alpha-diol	NCOA2 PGR
IR	MOL001810	6-(3-oxoindolin-2-ylidene)indolo[2,1-b]quinazolin- 12-one	ESR1 KDR PRSS1 PTGS1 PTGS2
IR	MOL001814	(E)-3-(3,5-dimethoxy-4-hydroxy-benzylidene)-2- indolinone	GABRA1 HSP90AA1 PTGS1 PTGS2 RXRA SCN5A
IR	MOL001820	(E)-3-(3,5-dimethoxy-4-hydroxyb-enzylidene)-2- indolinone	ADRB2 CHRM1 GABRA1 HSP90AA1 PTGS1 PTGS2 RXRA SCN5A
IR	MOL001828	3-[(3,5-dimethoxy-4-oxo-1-cyclohexa-2,5- dienylidene)methyl]-2,4-dihydro-1H-pyrrolo [2,1-b]quinazolin-9-one	F7 HSP90AA1 KCNH2 PRSS1 PTGS1 PTGS2 SCN5A
RB	MOL002311	Glycyrol	CCNA2 CHEK1 ESR1 GSK3B HTR KDR MAPK14 NOS2 PPARG PTGS2
RB	MOL002565	Medicarpin	ADRA1A ADRA1B ADRA1D ADRB2 CALM1 CCNA2 CDK2 CHRM1 CHRM2 CHRM3 CHRM4 CHRM5 DPP4 DRD1 ESR1 ESR2 HSP90AA1 MAPK10 NOS2 OPRD1 OPRM1 PRSS1 PTGS1 PTGS2 RXRA SCN5A SLC6A3 SLC6A4
FF	MOL003290	(3R,4R)-3,4-bis[(3,4-dimethoxyphenyl)methyl] oxolan-2-one	ADRA1B ADRA1D ADRB2 CALM1 CHRM3 ESR1 F7 HSP90AA1 KCNH2 NCOA2 PTGS2 SCN5A SLC6A3
FF	MOL003295	(+)-pinoresinol monomethyl ether	ADRA1B ADRB2 CALM1 HSP90AA1 KCNH2 NCOA1 NCOA2 PTGS1 PTGS2 RXRA RXRB SCN5A
FF	MOL003306	ACon1_001697	ADRA1B ADRB2 CALM1 HSP90AA1 KCNH2 NCOA1 NCOA2 PTGS1 PTGS2 SCN5A
FF	MOL003308	(+)-pinoresinol monomethyl ether-4-D-beta-glucoside_qt	ADRB2 CALM1 HSP90AA1 KCNH2 NCOA1 NCOA2 PTGS2 SCN5A
FF	MOL003315	3beta-Acetyl-20,25-epoxydammarane-24alpha-ol	NR3C1
FF	MOL003322	FORSYTHINOL	ADRA1B ADRB2 CALM1 HSP90AA1 KCNH2 NCOA1 NCOA2 PTGS2 SCN5A
FF	MOL003330	(-)-Phillygenin	ADRA1B ADRB2 CALM1 CHRM1 CHRM3 CHRM5 HSP90AA1 IGHG1 KCNH2 NCOA2 PTGS2 SCN5A
FF	MOL003347	hyperforin	CYP3A4 ICAM1 IL8RA NR1I2
FF	MOL003370	Onjixanthone I	CALM1 CHEK1 DPP4 ESR2 HSP90AA1 NOS2 PTGS1 PTGS2 RXRA SCN5A

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RB	MOI 003656	Luniwighteone	AR CALM1 CCNA2 CDK2 CHFK1 DPP4 FSR1 FSR2 GSK3B HSP90A A1 HTR MAPK14
КD	MOLOUSUSU	Euphwightcolic	NCOA2 NOS2 PPARG PRSS1 PTGS2 SCN5A
RB	MOL003896	7-Methoxy-2-methyl isoflavone	ACHE ADRA1B ADRA1D ADRB1 ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 CHRM1 CHRM3 CHRM5 DPP4 DRD1 ESR1 ESR2 GABRA1 GSK3B HSP90AA1 HTR IGHG1 LTA4H MAOB MAPK14 NCOA1 NCOA2 NOS2 OPRM1 PK1A PPARC PRS1 PTCS1 PTCS2 RXRA
			SCN5A SLC6A3 SLC6A4
HP	MOL004598	3,5,6,7-tetramethoxy-2-(3,4,5-trimethoxyphenyl)ch romone	ACHE AR CALM1 ESR1 ESR2 F7 HTR NCOA2 PRSS1 PTGS2
HP	MOL004609	Areapillin	AR CALM1 DPP4 ESR2 F7 HSP90AA1 HTR IGHG1 NCOA1 NCOA2 NOS2 PRSS1 PTGS2 SCN5A
HP	MOL004624	Longikaurin A	CHRM1 CHRM2 PRSS1
HP	MOL004653	(+)-Anomalin	DPP4 HTR KCNH2 PTGS2
HP	MOL004718	α-spinasterol	NCOA2 NR3C2 PGR
RB	MOL004805	(2S)-2-[4-hydroxy-3-(3-methylbut-2-enyl)phenyl]- 8,8-dimethyl-2,3-dihydropyrano[2,3-f]chromen-4- one	AR CALM1 ESR1 ESR2 GSK3B KCNH2 MAPK14 NOS2 PPARG PTGS2
RB	MOL004806	euchrenone	BACE1 CALM1 ESR1 ESR2 KCNH2 NOS2 PTGS2 SCN5A
RB	MOL004808	glyasperin B	ACHE AR CALM1 CCNA2 CDK2 DPP4 ESR1 ESR2 F7 GSK3B HSP90AA1 HTR KDR NCOA2 NOS2 PPARG PRSS1 PTGS2
RB	MOL004810	glyasperin F	AR CALM1 CCNA2 CDK2 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NOS2 PPARG PRSS1 PTGS1 PTGS2 SCN5A
RB	MOL004811	Glyasperin C	ACHE AR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 HTR KCNH2 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2 RXRA SCN5A
RB	MOL004814	Isotrifoliol	AR CCNA2 CDK2 CHEK1 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NOS2 PTGS2
RB	MOL004815	(E)-1-(2,4-dihydroxyphenyl)-3-(2,2-dimethyl- chromen-6-yl)prop-2-en-1-one	ADRA1B AR CA2 CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 GSK3B MAPK14 NCOA2 NOS2 PPARG PTGS1 PTGS2 RXRA SCN5A
RB	MOL004820	kanzonols W	AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 GSK3B MAPK14 NCOA1 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5A
RB	MOL004828	Glepidotin A	AR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 F7 GSK3B HSP90AA1 HTR IGHG1 KDR MAPK14 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5A
RB	MOL004829	Glepidotin B	ADRA1B CALM1 ESR1 F7 HSP90AA1 IGHG1 NCOA1 PTGS1 PTGS2 RXRA SCN5A
RB	MOL004833	Phaseolinisoflavan	ACHE ADRA1B ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 CHRM1 ESR1 ESR2 GSK3B
DD	101004005		MAPK14 NCOA1 NOS2 PPARG PRSS1 PTGS2 RXRA SCN5A
KD	MOL004835	Giypanichaicone	HSP90AA1 LTA4H MAOB MAPK14 NCOA1 NOS2 PKIA PPARG PTGS1 PTGS2 SCN5A SL C6A3 SL C6A4
RB	MOL004838	8-(6-hydroxy-2-benzofuranyl)-2,2-dimethyl-5- chromenol	ESR1 HSP90AA1 NOS2 PTGS2 RXRA
RB	MOL004848	licochalcone G	AR CALM1 CCNA2 CDK2 ESR1 ESR2 GSK3B HSP90AA1 IGHG1 KDR MAPK14 NCOA2 NOS2 PPARG PTGS2
RB	MOL004849	3-(2,4-dihydroxyphenyl)-8-(1,1-dimethylprop-2- enyl)-7-hydroxy-5-methoxy-coumarin	AR CALMI CDK2 CHEKI DPP4 ESRI ESR2 F7 GSK3B HSP90AA1 HTR KCNH2 KDR MAPK14 NCOA1 NCOA2 NOS2 PPARG PRS51 PTG52
RB	MOL004855	Licoricone	AR CALM1 CHEK1 ESR1 HTR KCNH2 KDR NCOA2 NOS2 PPARG PRSS1 PTGS2
RB	MOL004856	RBnin A	ACHE AR CALM1 CCNA2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 HTR NCOA2 NOS2
			PPARG PRSS1 PTGS2 SCN5A
RB	MOL004857	RBnin B	ADRA1B ADRB2 AR CALM1 CCNA2 CHEK1 DPP4 ESR1 ESR2 F7 GSK3B HSP90AA1 HTR
RB	MOL004863	3-(3,4-dihydroxyphenyl)-5,7-dihydroxy-8-(3- methylhyt 2 anyl)chromono	AR CALMI CON2 FLAKE FK551 F1G52 AR CALMI CONA2 CDEKI ESRI GSK3B HSP90AA1 HTR MAPK14 NCOA2 NOS2
RB	MOL004866	2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-6-(3- methylbut-2-enyl)chromone	ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 DPP4 F7 HSP90AA1 HTR PPARG PRSS1 PTGS2
RB	MOL004879	Glycyrin	AR CALM1 CHEK1 DPP4 ESR1 ESR2 HTR KCNH2 KDR NCOA2 NOS2 PPARG PRSS1 PTGS2
RB	MOL004882	Licocoumarone	AR CCNA2 CDK2 ESR1 ESR2 GSK3B HSP90AA1
RB	MOL004883	Licoisoflavone	AR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 HSP90AA1 HTR KDR MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2
RB	MOL004884	Licoisoflavone B	ACHE AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 GSK3B HTR NOS2 PPARG PRSS1 PTGS2
RB	MOL004885	licoisoflavanone	ACHE AR CALM1 CCNA2 CDK2 ESR1 ESR2 F7 GSK3B HSP90AA1 NCOA1 NOS2 PPARG PRSS1 PTGS1 PTGS2 SCN5A
RB	MOL004891	shinpterocarpin	ADRA1B ADRA1D ADRB2 AR CALM1 CCNA2 CDK2 CHRM1 CHRM3 ESR1 ESR2 GSK3B HTR3A KCNH2 MAPK14 NCOA1 NOS2 OPRD1 OPRM1 PPARG PRSS1 PTGS1 PTGS2 RXRA
RB	MOL004907	Glyzaglabrin	AR CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NOS2 PPARG PRSS1 PTG51 PTG52
RB	MOL004908	Glabridin	ACHE ADRA1B ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 CHRM1 ESR1 ESR2 GSK3B IGHG1 MAPK14 NCOA1 NCOA2 NOS2 PPARC PRS1 PTCS2 RXRA RXRB SCN5A
RB	MOL004910	Glabranin	CALM1 ESR1 HSP90AA1 NOS2 PTGS1 PTGS2 SCN5A
RB	MOL004911	Glabrene	ADRB2 AR CALM1 CDK2 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRS51 PTG51 PTG52 RXRA SCN5A
RB	MOL004912	Glabrone	ACHE AR CALMI CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HTR MAPK14 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5A
RB	MOL004913	1,3-dihydroxy-9-methoxy-6-benzofurano[3,2-c] chromenone	CCNA2 CDK2 CHEK1 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 PPARG
RB	MOL004915	Eurycarpin A	AR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 HTR MAPK14 NOS2 PPARG PRSS1 PTGS2 SCN5A
RB	MOL004941	(2R)-7-hydroxy-2-(4-hydroxyphenyl)chroman-4- one	PTGS1 ESR1 PTGS2 RXRA ADRB2 HSP90AA1 MAOB PKIA CALM1 GABRA1 SLC6A4
RB	MOL004945	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-8-(3- methylbut-2-enyl)chroman-4-one	NOS2

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RB MOL004948 logbycycol ARD DPV ESRI CSK3B NOS2 PTCS2 RB MOL004957 IMO ARREAR CALMIC CCNA2 CDK2 CHERL CHEMI DPV ESRI ESR2 CSK3B IGTGI MADB MAPKIA NOS2 PKIA PPAGE PRESI PTCS1 PTCS2 RXRA SCN5A SLC6A4 RB MOL004959 I-Methoxyphaseolidin ADRAIn DANRB AR CALMI CCNA2 CDK2 ESRI SERS CSK3B ESPIGAIL HTR KCNTE KDR MAPKIA NCOA1 NCOA2 NOS2 PPAKE PRESI PTCS1 PTCS2 RXRA SCN5A RB MOL004969 3'-Hidroxy-4'-O-Methylglabridin ACHE IA DARB AR CALMI CCNA2 CDK2 EFAKE PTCSSI PTCS1 PTCS2 SCN5A RB MOL004970 3'-Methoxyglabridin ACHE IA DARB AR CALMI CCNA2 CDK2 CHERI ESRI ESR2 FC SCR8 HEP90A.11 KCNTE MAPKIA NCOA1 NCOA2 NOS2 PPAKE PRES PTCS5I PTCS1 PTCS2 SCN5A RB MOL004978 2-((R)-8-A-dimethyl-3-4-dihydro-2H-pyrano)(5-4) ACHE ADRAIB ADR2 AR CALMI CCNA2 CDK2 CHERI CHEMI (HERM SERI ESR2 CKDRB KCN12 MAPKIA NCOA1 NCOA2 NOS2 PPAKE PRES PTCSI PTCSI PTCSI PTCSI PTCSI PTCSI PTCSI PTCSI PTCSI SCN5A SCN5A RB MOL004980 Inflacoumarin A ADRE2 AR CALMI DPV ESRI HSP00A1 HTR NCOA2 PPARE PRESI PTCSI PTCSI PTCSI SCN5A RB MOL004985 icos-s-enoic acid NCOA2 RB MOL004986 Ferry related exidityol CALMI ESRI FSR NAAIL DPME SRI HSP00A1 HTR NCOA2 PPARE PRESI PTCSI PTC					
RB MOL004957 HMO ADRR2 AR CALMI CCN2 CUESC CHERI CHRMI DPP4 ESRI ESR2 GSK3B IGHCI MA0B MP4K14 NOSE PKIA DPRAG PKSSI PTCS2 INCR3 SUSAS SLCA4 RB MOL004969 I-Methoxyphaeoliidin ADRAIB ADRAID ADRR2 AR CALMI CCN2 CDK2 ESRI ESR2 GSK3B IFSP0AA1 HTR KCNH2 KDR MP4K14 NCOA1 NCOA2 CDK2 ESRI ESR2 FGSK3B IFSP0AA1 RB MOL00497 3'-Methoxyglabridin ADRAIB ADRR2 AR CALMI CCN2 CDK2 CHEKI ESRI ESR2 FGSK3B IFSP0AA1 KCNH2 KDR MAPK14 NCOA1 NCOA2 NCS2 PTAGE PSSI PTCSI PTCS2 KXRA SCN5A KCNH2 KDR MAPK14 NCOA1 NCOA2 NCS2 PTAGE PSSI PTCSI PTCS2 KXRA SCN5A CKNB2 KDR MAPK14 NCOA1 NCOA2 NCS2 PTAGE PSSI PTCSI PTCS2 KXRA SCN5A KCNH2 MAPK14 NCOA1 NCOA2 NCS2 PTAGE PSSI PTCSI PTCS2 KXRA SCN5A CKNB2 KCNL2 MAPK14 NCOA1 NCOA2 NCS2 PTAGE PSSI PTCSI PTCS2 KXRA SCN5A CKNB KCNL2 MAPK14 NCOA1 NCOA2 NCS2 PTAGE PSSI PTCSI PTCS2 KXRA SCN5A CKNB KCNL2 MAPK14 NCOA1 NCOA2 NCS2 PTAGE PSSI PTCSI PTCS2 KXRA SCN5A CKNB KCNL2 MAPK14 NCOA1 NCOA2 NCS2 PTAGE PSSI PTCSI PTCS2 KXRA KXRB SCNSA RB MOL00498 Inflacoumarin A ADR82 AR CALMI DPP4 ESRI ESR2 TCS2 SCN5A CKNB KCNL2 MAPK14 NCOA1 NCOA2 NCS2 PTAGE PSSI PTCSI PTCS2 KB MOL00498 CALMI ESRI ESR2 NCOA2 PTCS2 CSNSA RB MOL00498 inflacoumarin A ADR82 AR CALMI DPP4 ESRI ESR2 CSCN5A CKNB KCNL2 MAPK14 NCOA2 NCO2 PTCS2 CSNSA RB MOL00498 inflacoumarin A CALMI ESRI ESR2 CNSA RB MOL00498 inflacoumarin A CALMI ESRI ESR2 CSCN3A RB MOL00498 inflacoumarin A CALMI ESRI ESR2 CSCN3A RB MOL00498 inflacoumarin A CALMI ESRI ESR2 CSCN3A	1	RB	MOL004948	Isoglycyrol	AR DPP4 ESR1 GSK3B NOS2 PTGS2
RBMOL0049991-MethoxyphaseollidinADRAID ADRR2D ACILMI CCNA2 CDK2 ESRI ESR2 GSK3B H5F90AA1 HTRRBMOL004963'Hydroxy-4'-O-MethylglabridinADRAIB ADR82 AR CALMI CCNA2 CDK2 CHEKI ESR1 ESR2 F7 GSK3B H5F90AA1 KCN12 KDR MAPK14 NCOA1 NCOA2 NOS2 PPARC PRS5I PTGSI PTGS2 PKASRBMOL004973'MethoxyglabridinCHE ADRAIB ADR82 AR CALMI CCNA2 CDK2 CHEKI ESRI ESR2 F7 GSK7B H5F90AA1 KCN12 KDR MAPK14 NCOA1 NCOA2 NOS2 PPARC PRS5I PTGSI PTGS2 FXRA SCNSARBMOL004982/GR3-8.4-dimethyl-3.4-dihydro-2H-pyrano[65-4] chromen-3-yl]-5-methoxyphenolACHE ADRAIB ADR82 AR CALMI CCNA2 CDX2 CHEKI CH		RB	MOL004957	НМО	ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 CHRM1 DPP4 ESR1 ESR2 GSK3B IGHG1 MAOB MAPK14 NOS2 PKIA PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5A SLC6A3 SLC6A4
RBMOL004963'Hydroxy-4'-O-MethylglabridinADRA1B ADR82 AR CALMI CCNA2 CDK2 CHEKI ESRI ESR2 I7 GSK3B HSF90AA1 KCNH2 KDR MAPK14 NCOA1 NCOA2 NOS2 PPARG PRSSI PTGSI PTGS2 PCSAS NCOA2 NOS2 PPARG PRSSI PTGSI PTGS2 PCSAS HSF90AA1 KCNH2 MAPK14 NCOA1 NCOA2 NOS2 PPARG PRSSI PTGSI PTGS2 RXRA SCNSARBMOL004972-[(3R)-8,8-dimethyl-3,4-dihydro-2H-pyrano[6; 4] Chromen-3-yl]-5-methoxyphenolACHE ADRA1B ADR82 AR CALMI CCNA2 CDK2 CHEKI ESRI PTGSI PTGS2 RXRA SCNSA CRSAB KCNH2 MAPK14 NCOA1 NCOA2 NOS2 PPARG PRSSI PTGSI PTGS2 RXRA RXRB SCNSA SLCGA3RBMOL00498Inflacoumarin AADR82 AR CALMI DPP4 ESRI HSF90AA1 HTR NCOA2 PPARG PRSSI PTGSI PTGS2 SCNSARBMOL00498icos-5-enoic acidNCOA2RBMOL00498Kanzonol FACHE ADRA1B ADR82 AR CALMI DPP4 ESRI GSR SI PTGSI PTGS2 SCNSARBMOL00498f-Acetoxy-2-methylisoflaroneACHE ADRA1B ADR812 NCOA2 PTGS2 SCNSARBMOL00499gadelaidic acidNCOA2RBMOL00499gadelaidic acidNCOA2RBMOL00500Rmin GACCHALI CCNA2 CCH2 ESRI ESR2 CSK3B HSP90AA1 HTR MAPK14 NCOA2 NCOA2RBMOL005007Rinin HAR CALMI CCNA2 CDK2 PERSI PTGS2RBMOL005007Gayaperins MACHE ADRA1B ADR82 AR CALMI CCNA2 CDK2 CHRMI CHRM GHRM5 ESRI ESR2 GSK3B HSP90AA1 HTR KCNH2 MAPK14 NCOA2 NOS2 PPARG PRSSI PTGS1 PTGS2 RXRA SCNSARBMOL005007Rinin HAR CALMI CCNA2 CDK2 CHRMI CHRM GHRM5 ESRI ESR2 GSK3B HSP90AA1 HTR MAPK14 NCOA2 NOS2 PPARG PRSSI PTGS1 PTGS2 RXRA SCNSARBMOL005007Gayaperins MACHE ADRA1B ADR82 AR CALMI CCNA2 CDK2 CHRMI CHRM GHRM5 ESRI ESR2 SCNSA<		RB	MOL004959	1-Methoxyphaseollidin	ADRA1B ADRA1D ADRB2 AR CALM1 CCNA2 CDK2 ESR1 ESR2 GSK3B HSP90AA1 HTR KCNH2 KDR MAPK14 NCOA1 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5A
FRBMOL00497MoltonysplashidinACHE ADRAH B ADR8 AR CALMIT CCNA2 CDK2 CHEKI ESRI ESR2H ST90AA1 KCNHE ADRAH B ADR82 AR CALMIT CCNA2 CDK2 CHEKI ESRI ESR2H ST90AA1 KCNHE ADRAH B ADR82 AR CALMIT CCNA2 CDK2 CHEKI CHRMIT CHRMB ESRI ESR2 CSKB B KCNHE J ADR82 AR CALMIT DPV4 ESRI HSP0AA1 HTT NCOA2 PPARG PRSSI PTGS1 PTGS2 RXRA RXRB SCNAS ALCGA3RBMOL00498infacoumarin AADR82 AR CALMIT DPV4 ESRI HSP0AA1 HTT NCOA2 PPARG PRSSI PTGS1 PTGS2 SCNAS ALCGA3RBMOL00498icos-5enoic acidACHE ADRAH B ADR82 AR CALMIT DPV4 ESRI HSP0AA1 HTT NCOA2 PPARG PRSSI PTGS1 PTGS2 SCNASRBMOL00498icos-5enoic acidCALMIT ESRI ESR2 NCOA2 PTGS2RBMOL00499icos-5enoic acidCALMIT ESRI FT HSP0AA1 NCS2 PTGS2 SCN5ARBMOL00499icos-5enoic acidNCOA2RBMOL00499icos-5enoic acidNCOA2RBMOL00499icos-5enoic acidNCOA2RBMOL00599icos-5enoic acidNCOA2RBMOL00599icos-5enoic acidNCOA2RBMOL00499icos-5enoic acidNCOA2RBMOL00599icos-5enoic acidNCOA2RBMOL00599icos-5enoic acidNCOA2RBMOL00599icos-5enoic acidAC CALMI CCNA2 CDK2 CHEKI DPV4 ESRI ESR2 FG SCN3B HSP0AA1 HTR MAPK14 NCOA2RBMOL00509ic		RB	MOL004966	3'-Hydroxy-4'-O-Methylglabridin	ADRA1B ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 F7 GSK3B HSP90AA1 KCNH2 KDR MAPK14 NCOA1 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 SCN5A
RBMOL00497824 (3R)-8.8-dimethyl-3.4-dihydro-2H-pyrano[6.5-1]CAFLE ADRAIB ADR2 AR CALMI CCNA2 CDX2 CHEK1 CHEM1 CHRM1 ESR1 ESR2 CGK88 KCNH2 MAPK14 NCOA1 NCOA2 DXS2 PPARG PRSS1 PTGS1 PTGS2 RXRA RXRB SCN5A SLC6A3RBMOL004980Inflacoumarin AADR82 AR CALMI DPP4 ESR1 H5P90AA1 HTR NCOA2 PPARG PRSS1 PTGS1 PTGS2 SCN5ARBMOL004985icos-5-enoic acidNCOA2RBMOL004980Formylated eriodictyolCALMI ESR1 FSR2 NCOA2 PTGS2RBMOL004996Formylated eriodictyolCALMI ESR1 FSR2 NCOA2 PTGS2RBMOL004997Foremylated eriodictyolCALMI ESR1 FSR2 NCOA2 PTGS2RBMOL004998Foremylated eriodictyolCALMI ESR1 FSR2 NCOA2 PTGS2RBMOL004999gadelaidic acidNCOA2RBMOL004990gadelaidic acidNCOA2RBMOL005000RBnin GAC ALMI CCNA2 ESR1 H5P90AA1 HTR MAPK14 NCOA2NOS2 PPARG PRSS1 PTGS1 PTGS2RKRA GRAS5CGK38 H5P90AA1 HTR MAPK14 NCOA2RBMOL005007GyasperinsCGK38 H5P90AA1 HTR KAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2RBMOL00507Gyasperins MCGK38 H5P90AA1 HTR KAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA RXRB SCN5ARBMOL00507Gyasperins MACHE AR AC ALMI CCNA2 CDK2 CHEK1 DPP4 ESR1 FSR2 GSK38 H5P90AA1 HTR MAPK14 NCOA2 NCO2 POS2 PPARG PRSS1 PTGS1 PTGS2 RXRA RXRB SCN5ARBMOL00507Gyasperins MACHE AR AC ALMI CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK38 H5P90AA1 MAPK14 NCOA2 NCO2 PPARG PRSS1 PTGS1 PTGS2 RXRA RXRB SCN5ARBMOL00507HaseolACCALMI CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GS		RB	MOL004974	3'-Methoxyglabridin	ACHE ADRA1B ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 F7 GSK3B HSP90AA1 KCNH2 MAPK14 NCOA1 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5A
RBMOL004980Inflacoumarin AADR82 AR CALM1 DPP4 ESR1 HSP90AA1 HTR NCOA2 PPARG PRSS1 PTGS1 PTGS2 SCN5ARBMOL004988icos-5-enoic acidNCOA2RBMOL004980Kanzonol FAR CALM1 ESR1 ESR2 NCOA2 PTGS2RBMOL0049906-prenylated eriodictyolCALM1 ESR1 F7 H5P90AA1 NOS2 PTGS2 SCN5ARBMOL004990r-Acetoxy-2-methylisoflavoneACHE ADRA1B ADRA1D ADR82 AR CALM1 CDK2 CHEK1 DPP4 ESR1 GABRA1 GSK38 HSP90AA1 HTR MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5ARBMOL00490gadelaidic acidNCOA2RBMOL005000RBnin HAR CALM1 CCNA2 CHEK1 DPP4 ESR1 ESR2 GSK38 H5P90AA1 HTR MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1RBMOL005000RBnin HAR CALM1 CCNA2 ESR1 H5P90AA1 KDR NCOA2 PRSS1 PTGS2RBMOL005000RBnin HAR CALM1 CCNA2 ESR1 HSP90AA1 HTR KCNH2 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA RXRB SCN5ARBMOL005000IcicoagroicarpinACHE ADRA1B ADR82 AR CALM1 CCNA2 CDK2 CHRM1 CHRM3 CHRM5 ESR1 ESR2 SCR53RBMOL005012IcicoagroisoflavoneACHE AC CALM1 CCNA2 CDK2 ESR1 ESR2 F7 GSK3B H5P90AA1 KCNH2 KDR NCOA1 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 SCN5ARBMOL005012IcicoagroisoflavoneAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B H5P90AA1 MAPK14 NCOA2 NCO2A PRSS1 PTGS1 PTGS2 SCN5ARBMOL005012IcicoagroisoflavoneAR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 GSK3B H5P90AA1 MAPK14 NCOA2 NCO2A PRSS1 PTGS1 PTGS2 SCN5ARBMOL005012IcicoagroisoflavoneAR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 GSK3B H5P90AA1 MAPK14 NCOA2 NCS2 PPARG PRSS1 PTGS1 PTGS2 SCN5A <td< td=""><td></td><td>RB</td><td>MOL004978</td><td>2-[(3R)-8,8-dimethyl-3,4-dihydro-2H-pyrano[6,5-f] chromen-3-yl]-5-methoxyphenol</td><td>ACHE ADRA1B ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 CHRM1 CHRM3 ESR1 ESR2 GSK3B KCNH2 MAPK14 NCOA1 NCOA2 NOS2 PPARG PRS51 PTG51 PTG52 RXRA RXRB SCN5A SLC6A3</td></td<>		RB	MOL004978	2-[(3R)-8,8-dimethyl-3,4-dihydro-2H-pyrano[6,5-f] chromen-3-yl]-5-methoxyphenol	ACHE ADRA1B ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 CHRM1 CHRM3 ESR1 ESR2 GSK3B KCNH2 MAPK14 NCOA1 NCOA2 NOS2 PPARG PRS51 PTG51 PTG52 RXRA RXRB SCN5A SLC6A3
RBMOL004985icos-5-enoic acidNCOA2RBMOL04986Kanzono JFAR CALMI ESRI ESR2 NCOA2 PTGS2RBMOL049896-prenylated eriodictyolCALMI ESRI F7 HSP0AA1 NOS2 PTGS2 SCN5ARBMOL049997-Acetoxy-2-methylisoflavoneACHE ADRA1B ADRA1D ADRB2 AR CALMI CDK2 CHEKI DPP4 ESRI GABRA1 GSK3B HSP0AA1 HTM MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 EXRA SCN5ARBMOL004999gadelaidic acidNCOA2RBMOL005000RBnin GAR CALMI CCNA2 CHEKI DPP4 ESRI ESR2 GSK3B HSP90AA1 HTT MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1RBMOL005001RBnin HAR CALMI CCNA2 ESRI HSP90AA1 KDR NCOA2 PRSS1 PTGS2 RKB SCN5ARBMOL005000RJaine GACHE ADRA1B ADRB2 AR CALMI CCNA2 CDK2 CHRMI CHRM3 CHRM5 ESRI ESR2 GSK3B HSP90AA1 HTR KONH2 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA RXRB SCN5ARBMOL005007Glyasperins MACHE ADRA1B ADRB2 AR CALMI CCNA2 CDK2 CHRMI CHRM3 CHRM5 ESRI ESR2 GSK3B HSP90AA1 HCNH2 KDR NCOA1 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 SCN5ARBMOL005012LicoagroisoflavoneACHE ACALMI CCNA2 CDK2 CHEKI DPP4 ESRI ESR2 GSK3B HSP90AA1 KON2 PPARG PRSS1 PTGS2 PTARG PRSS1 PTGS1 PTGS2 SCN5ARBMOL005017PhaeolAR CALMI CCNA2 CDK2 CHEKI DPP4 ESRI ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5ARBMOL005010doratinARCCMA2 COK2 CHEKI ESRI GSK3B HSP90AA1 MAPK14 NCOA2 		RB	MOL004980	Inflacoumarin A	ADRB2 AR CALM1 DPP4 ESR1 HSP90AA1 HTR NCOA2 PPARG PRSS1 PTGS1 PTGS2 SCN5A
RBMOL00498Kanzonol FAR CALM1 ESR1 ESR2 NCOA2 PTGS2RBMOL004996-prenylated eriodictyolCALM1 ESR1 F7 H5P30AA1 NOS2 PTGS2 SCN5ARBMOL004997-Acetoxy-2-methylisoflavoneHSP50AA1 HTR MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5ARBMOL00500gadelaidic acidNCOA2RBMOL00500RBnin GNCOA2RBMOL00500RBnin HAR CALM1 CCNA2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 HTR MAPK14 NCOA2RBMOL00500RJnin HAR CALM1 CCNA2 ESR1 HSP90AA1 KDR NCOA2 PRS51 PTGS2RBMOL00500RJanin HAR CALM1 CCNA2 ESR1 HSP90AA1 KDR NCOA2 PRS51 PTGS2RBMOL00500RJanin HAR CALM1 CCNA2 ESR1 HSP90AA1 KDR NCOA2 PRS51 PTGS2RBMOL00500RJaperins MACHE AR CALM1 CCNA2 CDK2 ESR1 ESR2 GSK3B HSP90AA1 KCNH2 KDR NCOA1RBMOL005002Glyasperins MACHE AR CALM1 CCNA2 CDK2 ESR1 ESR2 F7 GSK3B HSP90AA1 KCNH2 KDR NCOA1RBMOL005002LicoagroisoflavoneAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HTR MAPK14 NCOA2RBMOL005012LicoagroisoflavoneAR CALM1 CCNA2 CDK2 CHEK1 DP74 ESR1 ESR2 GSK3B HTR MAPK14 NCOA2RBMOL005003dehydroglyasperins CAR CALM1 ECNA2 CDK2 CHEK1 DP74 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2RBMOL005004dehydroglyasperins CAR CALM1 ECNA2 CDK2 CHEK1 DP74 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2RBMOL005005dehydroglyasperins CAD RC2 AC CDK2 CHEK1 ESR1 ESR3 HSP90AA1 MAPK14 NCOA2 NOS2RBMOL005005dehydroglyasperins CAD RC2 AC CDK2 CHEK1 ESR1 ESR2 HSP90AA1		RB	MOL004985	icos-5-enoic acid	NCOA2
RBMOL0049996-prenylated eriodictyolCALM1 ESR1 F7 HSP90AA1 NOS2 PTGS2 SCN5ARBMOL0049917-Acetoxy-2-methylisoflavoneACTEE ADRA1B ADRA1D ADR82 AR CALM1 CDK2 CHEK1 DPP4 ESR1 GABRA1 GSK3B HSP90AA1 HTR MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5ARBMOL005000RBnin GAR CALM1 CCNA2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 HTR MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2RBMOL005001RBnin HAR CALM1 CCNA2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 HTR MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2RBMOL005001RBnin HAR CALM1 CCNA2 ESR1 HSP90AA1 KDR NCOA2 PRSS1 PTGS1 SCS7B HSP90AA1 HTR KCNH2 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA RXRB SCN5ARBMOL005007Glyasperins MACHE ADRA1B ADR82 AR CALM1 CCNA2 CDK2 CHRM1 CHRM3 CHRM5 ESR1 ESR2 GSK3B HSP90AA1 HTR KCNH2 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA RXRB SCN5ARBMOL005007Glyasperins MACHE AR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 KCNH2 KDR NCOA1 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 SCN5ARBMOL005017PhaseolAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NCO32 PTGS2 RXRA SCN5ARBMOL005017PhaseolAR CALM1 CCNA2 CDK2 CHEK1 DP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5ARBMOL005010PhaseolAR CALM1 CCNA2 CDK2 CHEK1 DP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5ARBMOL005017PhaseolAR CALM1 CCNA2 CDK2 CHEK1 DP4 ESR1 ESR2 HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 SCN5ARBMOL005010dehydroglyasperins CADRB2 AR CALM1 CCNA2 CDK2 CHE		RB	MOL004988	Kanzonol F	AR CALM1 ESR1 ESR2 NCOA2 PTGS2
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RBMOL004999gadelaidic acidNCOA2RBMOL005000RBnin GAR CALMI CCNA2 CHEK1 DP4 ESRI ESR2 GSK3B HSP90AA1 HTR MAPK14 NCOA2 NOS2 PPARG PRS51 PTG52RBMOL005001RBnin HAR CALMI CCNA2 ESRI HSP90AA1 KDR NCOA2 PRS51 PTG52RBMOL005003LicoagrocarpinACHE ADRA1B ADR82 AR CALMI CCNA2 CDK2 CHRMI CHRM3 CHRM5 ESRI ESR2 GSK3B HSP90AA1 HTR KCNH2 MAPK14 NCOA2 NOS2 PPARG PRS51 PTG51 PTG52 PXRA RXRB SCN5ARBMOL005007Glyasperins MACHE AR CALMI CCNA2 CDK2 ESRI ESR2 F7 GSK3B HSP90AA1 KCNH2 KDR NCOA1 NCOA2 NOS2 PPARD PPARG PRS51 PTG51 PTG52 SCN5ARBMOL005012LicoagroisoflavoneAR CALMI CCNA2 CDK2 CHEK1 DPP4 ESRI ESR2 GSK3B HTR MAPK14 NOS2 PPARG PRS51 PTGS1 PTGS2 SCN5ARBMOL005017PhaseolAR CALMI CCNA2 CDK2 CHEK1 DP74 ESRI ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRS51 PTGS1 PTGS2 PXRA SCN5ARBMOL005018AambioonaAR CCNA2 CALMI CCNA2 CDK2 CHEK1 DP74 ESRI ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRS51 PTGS1 PTGS2 PTGS2 NOS2 PPARG PRS51 PTGS1 PTGS2 RXRA SCN5ARBMOL005018AambioonaAR CALMI CCNA2 CDK2 CHEK1 ESRI ESR2 GSK3B HSP90AA1 MAPK14 PCA2 RDS2 NOS2 PPARG PRS51 PTGS1 PTGS2 RXRA SCN5ARBMOL005018AambioonaAR CALMI CCNA2 CDK2 CHEK1 ESRI ESR2 HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRS51 PTGS2 PTGS2 PTARG PRS51 PTGS2 SCN5APCRRMOL013287PhysovenineADRB2 AC CALMI CCNA2 CDK2 CHEK1 ESR1 ESR2 HSP90AA1 MAPK14 NCOA2 CNS2 PPARG PRS51 PTGS1 PTGS2 FXRA SCN5A SLC6A3 SLC6A4PCRRMOL013288PrainfalADRB2 AC CALM1 CNA2 CDK2 CHEK1 DP74 GSK3B HSP90AA1 MAPK14 PKIA PTGS1 PTGS2 PFARG PRS51 PTGS1 PTGS2		RB	MOL004991	7-Acetoxy-2-methylisoflavone	ACHE ADRA1B ADRA1D ADRB2 AR CALM1 CDK2 CHEK1 DPP4 ESR1 GABRA1 GSK3B HSP90AA1 HTR MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5A
RBMOL005000RBnin GAR CALM1 CCNA2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 HTR MAPK14 NCOA2 NO52 PPARG PRSS1 PTG52RBMOL005001RBnin HAR CALM1 CCNA2 ESR1 HSP90AA1 KDR NCOA2 PRS51 PTG52RBMOL005003LicoagrocarpinACHE ADRA1B ADR82 AR CALM1 CCNA2 CDK2 CHRM1 CHRM3 CHRM5 ESR1 ESR2 GSK3B HSP90AA1 HTR KCNH2 MAPK14 NCOA2 NOS2 PPARG PRS51 PTG51 PTG52 RXRA RXRB SCN5ARBMOL005007Glyasperins MACHE ADRA1B ADR82 AR CALM1 CCNA2 CDK2 ESR1 ESR2 F7 GSK3B HSP90AA1 KCNH2 KDR NCOA1 		RB	MOL004996	gadelaidic acid	NCOA2
RBMOL005001RBnin HAR CALM1 CCNA2 ESR1 HSP90AA1 KDR NCOA2 PRS51 PTG52RBMOL005003LicoagrocarpinACHE ADRA1B ADRB2 AR CALM1 CCNA2 CDK2 CHRM1 CHRM3 CHRM5 ESR1 ESR2 GSK3B HSP90AA1 HTR KCNH2 MAPK14 NCOA2 NOS2 PPARG PRS51 PTG52 RXRA RXRB SCN5ARBMOL005007Glyasperins MACHE AR CALM1 CCNA2 CDK2 ESR1 ESR2 F7 GSK3B HSP90AA1 KCNH2 KDR NCOA1 NCOA2 NOS2 PPARG PRS51 PTG52 SCN5ARBMOL005012LicoagroisoflavoneACHE AR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 KCNH2 KDR NCOA1 NCOA2 NOS2 PPARG PRS51 PTG52 SCN5ARBMOL005016OdoratinAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRS51 PTG52 SCN5ARBMOL005017PhaseolAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRS51 PTG52 NCN5ARBMOL005017AmbioonaAR CCNA2 CDK2 CHEK1 ESR1 GSK3B HSP90AA1 HTR KDR MAPK14 PPARG PTG52 NOS2 PPARG PRS51 PTG52 NCOA2 NOS2 PTG52RBMOL005018AambioonaCALM1 ESR1 ESR2 NCOA2 NOS2 PTG52RBMOL005020dehydroglyasperins C PARG PRS51 PTG52 SCN5AADRB2 AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRS51 PTG52 SCN5APCRRMOL013287PhysovenineADRB2 CA2 CDK2 CHEK1 DPP4 GSK3B HSP90AA1 MAPK14 PTG51 PTG52 PTG51 PTG52 SCN5APCRRMOL013287PhysovenineADRB2 CA2 CDK2 CHEK1 DPP4 GSK3B HSP90AA1 MAPK14 PTG51 PTG52 PTG51 PTG52 PTG52 RXRA SCN53 LC6A3 SLC6A3 SLC6A4PCRRMOL013288PicalinalACHE ADRA1A ADRA1B ADRA2B ADRB2 AR CA2 CCNA2 CDK2 CHRM1 CHRM2 CHRM3 CHRNA2 DRD1 ESR1 ESR2 GABRA1 GRIA2 GSK3B HSP90AA1 HTR NOS2 OPRD1 OPRM1 PRS51		RB	MOL005000	RBnin G	AR CALM1 CCNA2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 HTR MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2
RBMOL005003LicoagrocarpinACHE ADRA1B ADRB2 AR CALM1 CCNA2 CDK2 CHRM1 CHRM3 CHRM5 ESR1 ESR2 GSK3B H5P90AA1 HTR KCNH2 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA RXRB SCN5ARBMOL005007Glyasperins MACHE AR CALM1 CCNA2 CDK2 CSR1 ESR2 F7 GSK3B H5P90AA1 KCNH2 KDR NCOA1 NCOA2 NOS2 PPARD PPARG PRSS1 PTGS1 PTGS2 SCN5ARBMOL005012LicoagroisoflavoneAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HTR MAPK14 NOS2 PPARG 		RB	MOL005001	RBnin H	AR CALM1 CCNA2 ESR1 HSP90AA1 KDR NCOA2 PRSS1 PTGS2
RBMOL005007Glyasperins MACHE AR CALM1 CCNA2 CDK2 ESR1 ESR2 F7 GSK3B HSP90AA1 KCNH2 KDR NCOA1 NCOA2 NOS2 PPARD PPARG PRS51 PTG51 PTG52 SCN5ARBMOL005012LicoagroisoflavoneAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HTR MAPK14 NOS2 PPARG PRS51 PTG52 SCN5ARBMOL005016OdoratinAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRS51 PTG52 PTG52 RXRA SCN5ARBMOL005017PhaseolAR CCNA2CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 PPARG PTG52RBMOL005018XambioonaCALM1 ESR1 ESR2 NCOA2 NOS2 PTGS2RBMOL005020dehydroglyasperins CADRB2 AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRS51 PTG52 SCN5APCRRMOL0132816,8-Dihydroxy-7-methoxyxanthoneADRB2 CA2 CDK2 CHEK1 DPP4 GSK3B HSP90AA1 MAPK14 PKIA PTG51 PTG52 PCRRPCRRMOL013288PicralinalATOADRPAT CALMA ADRA1B ADRA2B ADRB2 AR CA2 CNA2 CDK2 CHRM1 CHRM2 CHRM3 PRS51 PTG51 PTG52 RXRA SCN5A SLC6A2 SLC6A3 SLC6A4PCRRMOL013288PicralinalAR OPRD1 OPRM1 SCN5A		RB	MOL005003	Licoagrocarpin	ACHE ADRA1B ADRB2 AR CALM1 CCNA2 CDK2 CHRM1 CHRM3 CHRM5 ESR1 ESR2 GSK3B HSP90AA1 HTR KCNH2 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA RXRB SCN5A
RBMOL005012LicoagroisoflavoneAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HTR MAPK14 NOS2 PPARG PRSS1 PTGS2 SCN5ARBMOL005016OdoratinAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5ARBMOL005017PhaseolAR CCNA2 CDK2 CHEK1 ESR1 GSK3B HSP90AA1 HTR KDR MAPK14 PPARG PTGS2RBMOL005018XambioonaCALM1 ESR1 ESR2 NCOA2 NOS2 PTGS2RBMOL005002dehydroglyasperins CADRB2 AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2 SCN5APCRRMOL0132816,8-Dihydroxy-7-methoxyxanthoneADRB2 CA2 CDK2 CHEK1 DPP4 GSK3B HSP90AA1 MAPK14 PKIA PTGS1 PTGS2 PARG PRSS1 PTGS2 SCN5APCRRMOL013287PhysovenineACHE ADRA1A ADRA1B ADRA2B ADRB2 AR CA2 CCNA2 CDK2 CHEM1 CHRM2 CHRM3 CHRNA2 DRD1 ESR1 ESR2 GABRA1 GRIA2 GSK3B HSP90AA1 HTR NOS2 OPRD1 OPRM1 PRSS1 PTGS1 PTGS2 RXRA SCN5A SLC6A2 SLC6A3 SLC6A4PCRRMOL013288PicralinalAR OPRD1 OPRM1 SCN5A		RB	MOL005007	Glyasperins M	ACHE AR CALM1 CCNA2 CDK2 ESR1 ESR2 F7 GSK3B HSP90AA1 KCNH2 KDR NCOA1 NCOA2 NOS2 PPARD PPARG PRSS1 PTGS1 PTGS2 SCN5A
RBMOL005016OdoratinAR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5ARBMOL005017PhaseolAR CCNA2 CDK2 CHEK1 ESR1 GSK3B HSP90AA1 HTR KDR MAPK14 PPARG PTGS2RBMOL005018XambioonaCALM1 ESR1 ESR2 NCOA2 NOS2 PTGS2RBMOL005020dehydroglyasperins C PPARG PRSS1 PTGS2 SCN5AADRB2 AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2 SCN5APCRRMOL0132816,8-Dihydroxy-7-methoxyxanthone 		RB	MOL005012	Licoagroisoflavone	AR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HTR MAPK14 NOS2 PPARG PRSS1 PTGS2 SCN5A
RBMOL005017PhaseolAR CCNA2 CDK2 CHEK1 ESR1 GSK3B HSP90AA1 HTR KDR MAPK14 PPARG PTGS2RBMOL005018XambioonaCALM1 ESR1 ESR2 NCOA2 NOS2 PTGS2RBMOL005020dehydroglyasperins CADRB2 AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2 SCN5APCRRMOL0132816,8-Dihydroxy-7-methoxyxanthoneADRB2 CA2 CDK2 CHEK1 DP4 GSK3B HSP90AA1 MAPK14 PKIA PTGS1 PTGS2 ACHE ADRA1A ADRA1B ADRA2B ADRB2 AR CA2 CCNA2 CDK2 CHEM1 CHRM1 CHRM2 CHRM3 CHRNA2 DRD1 ESR1 ESR2 GABRA1 GRIA2 GSK3B HSP90AA1 HTR NOS2 OPRD1 OPRM1 PRSS1 PTGS1 PTGS2 RXRA SCN5A SLC6A2 SLC6A3 SLC6A4PCRRMOL013288PicralinalAR OPRD1 OPRM1 SCN5A		RB	MOL005016	Odoratin	AR CALM1 CCNA2 CDK2 CHEK1 DPP4 ESR1 ESR2 GSK3B HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS1 PTGS2 RXRA SCN5A
RB MOL005018 Xambioona CALM1 ESR1 ESR2 NCOA2 NOS2 PTGS2 RB MOL005020 dehydroglyasperins C ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2 SCN5A PCRR MOL013281 6,8-Dihydroxy-7-methoxyxanthone ADRB2 CA2 CDK2 CHEK1 DP4 GSK3B HSP90AA1 MAPK14 PKIA PTGS1 PTGS2 PCRR MOL013287 Physovenine ADRB2 CA2 CDK2 CHEK1 DP4 GSK3B HSP90AA1 MAPK14 PKIA PTGS1 PTGS2 PCRR MOL013288 Picralinal AR OPRD1 OPRM1 SCN5A		RB	MOL005017	Phaseol	AR CCNA2 CDK2 CHEK1 ESR1 GSK3B HSP90AA1 HTR KDR MAPK14 PPARG PTGS2
RB MOL005020 dehydroglyasperins C ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2 SCN5A PCRR MOL013281 6,8-Dihydroxy-7-methoxyxanthone ADRB2 CA2 CDK2 CHEK1 DPP4 GSK3B HSP90AA1 MAPK14 PKIA PTGS1 PTGS2 PCRR MOL013287 Physovenine ADRB2 CA2 CDK2 CHEK1 DPP4 GSK3B HSP90AA1 MAPK14 PKIA PTGS1 PTGS2 PCRR MOL013288 Picralinal ACHE ADRA1A ADRA1B ADRA2B ADRB2 AR CA2 CCNA2 CDK2 CHRM1 CHRM2 CHRM3 CHRNA2 DRD1 ESR1 ESR2 GABRA1 GRIA2 GSK3B HSP90AA1 HTR NOS2 OPRD1 OPRM1 PRSS1 PTGS1 PTGS2 RXRA SCN5A SLC6A2 SLC6A3 SLC6A4 PCRR MOL013288 Picralinal AR OPRD1 OPRM1 SCN5A		RB	MOL005018	Xambioona	CALM1 ESR1 ESR2 NCOA2 NOS2 PTGS2
PCRR MOL013281 6,8-Dihydroxy-7-methoxyxanthone ADRB2 CA2 CDK2 CHEK1 DPP4 GSK3B HSP90AA1 MAPK14 PKIA PTGS1 PTGS2 PCRR MOL013287 Physovenine ACHE ADRA1A ADRA1B ADRA2B ADRB2 AR CA2 CCNA2 CDK2 CHRM1 CHRM3 CHRNA2 DRD1 ESR1 ESR2 GABRA1 GRIA2 GSK3B HSP90AA1 HTR NOS2 OPRD1 OPRM1 PRSS1 PTGS1 PTGS2 RXRA SCN5A SLC6A2 SLC6A3 SLC6A4 PCRR MOL013288 Picralinal AR OPRD1 OPRM1 SCN5A		RB	MOL005020	dehydroglyasperins C	ADRB2 AR CALM1 CCNA2 CDK2 CHEK1 ESR1 ESR2 HSP90AA1 MAPK14 NCOA2 NOS2 PPARG PRSS1 PTGS2 SCN5A
PCRR MOL013287 Physovenine ACHE ADRA1A ADRA1B ADRA2B ADRB2 AR CA2 CCNA2 CDK2 CHRM1 CHRM2 CHRM3 CHRNA2 DRD1 ESR1 ESR2 GABRA1 GRIA2 GSK3B HSP90AA1 HTR NOS2 OPRD1 OPRM1 PRSS1 PTGS1 PTGS2 RXRA SCN5A SLC6A2 SLC6A3 SLC6A4 PCRR MOL013288 Picralinal AR OPRD1 OPRM1 SCN5A		PCRR	MOL013281	6,8-Dihydroxy-7-methoxyxanthone	ADRB2 CA2 CDK2 CHEK1 DPP4 GSK3B HSP90AA1 MAPK14 PKIA PTGS1 PTGS2
PCRR MOL013288 Picralinal CHRNA2 DRD1 ESR1 ESR2 GABRA1 GRIA2 GSK3B HSP90AA1 HTR NOS2 OPRD1 OPRM1 PCRR MOL013288 Picralinal AR OPRD1 OPRM1 SCN5A SCN5A		PCRR	MOL013287	Physovenine	ACHE ADRA1A ADRA1B ADRA2B ADRB2 AR CA2 CCNA2 CDK2 CHRM1 CHRM2 CHRM3
PCRR MOL013288 Picralinal AR OPRD1 OPRM1 SCN5A					CHRNA2 DRD1 ESR1 ESR2 GABRA1 GRIA2 GSK3B HSP90AA1 HTR NOS2 OPRD1 OPRM1 PRSS1 PTGS1 PTGS2 RXRA SCN5A SLC6A2 SLC6A3 SLC6A4
		PCRR	MOL013288	Picralinal	AR OPRD1 OPRM1 SCN5A

Gene-pathway network analysis

The construction of gene-pathway network is based on significant enrichment pathway and regulated these ways, which was shown in **Figure 8**. The V shapes represented pathway and the squares represent target genes in the network. The network showed that RELA was the core target gene which had largest degree. Other five genes also had larger degree such as MAPK1, MAPK14, CASP3, CASP8 and IL6. They might be the key target genes using SFJDC in the process of treating NCP. All of the above analysis could reveal a new strategy for drug development on NCP.

Discussion

The theory of TCM has been formed and developed for thousands of years in China. In China, TCM has a good therapeutic effect on COVID-19, which has been written into the diagnosis and treatment guidelines. The guideline points out that the combination of traditional Chinese and western medicine should be strengthened in the treatment process [34]. SFJDC is a traditional Chinese medicine, mainly used to treat upper respiratory tract infections, such as influenza, sore throat, mumps, streptococcus, etc. [21]. Now, SFJDC has become an effective drug for the treatment of COVID-19 [35]. In recent years, the research on Chinese medicine prescriptions has developed to the level of effective parts, components, components. Network pharmacology can better understand and demonstrate the interaction between multi-component multi-target and disease [36]. This study aims to analyze the active components and potential mechanism of SFJDC in the treatment of COVID-19 through network pharmacology.

In the present study, the ingredients-targets network of SFJDC was constructed using 110 ingredients and 120 targets. The network contained 117 nodes and 419 edges which indicated the compound-target genes interaction. The results showed that most compounds of SFJDC were affected by multiple target genes, such as Wogonin, licochalcone a and acacetin acted on 42, 30 and 23 target genes, respectively. Various compounds of SFJDC may have the same targets to achieve synergy. Wogonin, a naturally occurring flavonoid, has been shown to multi-activity, such as anti-inflammatory, anti-fibrosis, anti-cancer and chondroprotective properties [37]. Study showed that wogonin had an anti-infulenza activity by modulation of AMPK pathway [38]. Licochalcone a, a flavonoid extracted from licorice toot, was known for its anti-inflammatory, anti-cancer, anti-oxidative and anti-bacterial bioactivity [39]. Acacetin, a flavone compound, played an important role in antiinflammatory and anti-peroxidative [40].

Table 4.	Known	therapeutic	target genes	for	COVID-	19
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Gene	GC Id	Score	Gene	GC Id	Score
TNF	GC06P033397	33.08	ITGAL	GC16P030472	4.07
IL6	GC07P022765	31.28	STAT6	GC12M057095	4.04
CXCL8	GC04P073740	31.05	BAK1	GC06M033572	4.03
CD40LG	GC0XP136649	30.56	PIK3CG	GC07P106865	4.02
IL10	GC01M206767	30.33	FOS	GC14P075278	4.01
IFNG	GC12M068064	27.48	HELLS	GC10P094501	4
CRP	GC01M159715	25.76	CP	GC03M149162	3.96
STAT1	GC02M190964	22.73	APOA1	GC11M116835	3.95
MBI 2	GC10M052760	22.70	RPS27A	GC02P055231	3.91
TP53	CC17M007661	10	CREBBD	CC16M003726	3.87
CCL2	CC17P034255	19 12	TERC	GC1010005720	3.83
	GC1/1 054255	17.69	I MANI	GC05W1190027	2.05
	GC04W1122451	16 71	DI ADCAA	GC10101059527	3.02 2.91
UCL5 IENIA1	GC1710055671	16.71	FLAZG4A	GC01P166796	3.61 2.6E
IFNAI	GC09F021478	16.00	DBKCA	GC19F041709	3.65
EGFK	GC0/P055019	16.29	PKKCA	GC1/P066302	3.65
CXCLI0	GC04M076021	15.3	EIF2SI	GC14P067359	3.65
TGFB1	GC19M041301	14.98	CLEC12A	GC12P009951	3.61
IL1B	GC02M112829	13.78	SUMOI	GC02M202206	3.59
ACE2	GC0XM015494	12.32	CCR3	GC03P046227	3.56
CSF2	GC05P132073	11.95	UBB	GC17P016380	3.53
PPARG	GC03P012287	11.93	MAPKAPK2	GC01P206684	3.48
CCR5	GC03P046384	11.37	CD3D	GC11M118338	3.47
CXCL9	GC04M076001	11.3	СНКВ	GC22M050578	3.43
GPT	GC08P144502	11.12	PPIA	GC07P044808	3.43
MAPK1	GC22M021754	11.09	RUNX1	GC21M034787	3.42
CASP3	GC04M184627	10.88	BCL2L1	GC20M031664	3.4
IFNB1	GC09M021077	10.77	GZMA	GC05P055102	3.38
ALB	GC04P073397	10.68	IRF1	GC05M132481	3.35
FGF2	GC04P122826	10.53	CD81	GC11P002377	3.35
SFTPD	GC10M079937	10.47	CST3	GC20M023608	3.29
CXCR3	GC0XM071615	10.18	PTGS1	GC09P122370	3.24
IL4	GC05P132673	10.12	F10	GC13P113122	3.22
HLA-B	GC06M031289	9.84	CBL	GC11P119206	3.18
CD79A	GC19P041877	9.73	CXCL11	GC04M076033	3.13
CXCL2	GC04M074097	9.61	MAVS	GC20P003827	3.12
ACE	GC17P063477	9.6	KPNB1	GC17P047649	3.1
TMPRSS2	GC21M041464	9.59	SLC17A5	GC06M073593	3.07
IRF3	GC19M049659	9.51	ITGA5	GC12M054396	3
MAPK3	GC16M030117	9.37	ARF1	GC01P228082	2.99
IL17A	GC06P052186	9.29	IFNL1	GC19P039296	2.97
IL5	GC05M132541	9.27	GRB2	GC17M075318	2.86
ICAM1	GC19P010270	9.22	CD3E	GC11P118304	2.84
CCL3	GC17M036088	92	ATF2	GC02M175072	2.78
П 13	GC05P132656	9.19	CFACAM3	GC19P041796	2.70
MAPK ⁸	GC10P048306	9.19	HAVCR2	GC05M157062	2.72
TTR	CC18P021557	9.00	IAK1	CC01M064832	2.0
т 18	CC11M112142	9.04 8.59	NPM1	CC05P171287	2.09
ANDED	CC15M090794	0.00 8 E0	TRI/1	CC12P04451	2.07
AINFEF DIV2D1	GC151V1069/84	0.30	IDNI E11	GC12F004431	2.04
CTCI	GC00P002725	0.57	Г11 VЛП	GC04F100205	2.00
CISL	GC09P087725	8.52	VHL U 16	GC03P010205	2.63
CD209	GC19M007739	8.45	IL16	GC15P081159	2.59
DDX58	GC09M032455	8.2	KPNA2	GC17P068035	2.57
FURIN	GC15P090868	8.08	RELB	GC19P045002	2.57
ADA	GC20M044620	7.97	FCER2	GC19M007689	2.56
APOE	GC19P044906	7.97	PIK3CB	GC03M138652	2.55
MAPK14	GC06P046047	7.77	PRSS2	GC07P144731	2.54
DPP4	GC02M161992	7.64	RAPGEF3	GC12M047736	2.52

NFKB1	GC04P102501	7.61	BECN1	GC17M042810	2.51
HLA-A	GC06P033211	7.44	HAVCR1	GC05M157007	2.48
SERPINE1	GC07P101127	7.43	ISG15	GC01P001001	2.41
PIK3CA	GC03P179148	7.27	PML	GC15P073994	2.41
PTGS2	GC01M186640	7.24	PRKCE	GC02P045651	2.39
CD14	GC05M140631	7.16	CEACAM1	GC19M042507	2.38
MX1	GC21P041420	7.07	PIK3CD	GC01P009629	2.37
IFIH1	GC02M162267	6.99	ERN1	GC17M064039	2.37
BCI 2	GC18M063123	6.96	IFITM1	GC11P000313	2.36
ECCR2A	CC01P161505	6.67	IPAK3	CC12P066188	2.35
CDK4	GC011 101505	6.64	NPTY1	GC121 000100	2.35
LICDAE	GC12W057745	0.04	LIEE	GC1710000400	2.35
D5PA5	GC09IVI125254	6.59	TI D10	GC06F026087	2.34
BAX	GC19P048954	6.53	ILKI0	GC04M038773	2.33
CCL11	GC17P034285	6.47	SLC40A1	GC02M189560	2.3
CAT	GC11P034460	6.43	LCK	GC01P032251	2.29
HMOX1	GC22P035380	6.28	EIF2AK3	GC02M088637	2.27
SOD1	GC21P031659	6.25	POU5F1	GC06M031177	2.25
G6PD	GC0XM154531	6.06	VAPA	GC18P009904	2.15
CD4	GC12P006786	6.01	CARD9	GC09M136361	2.15
TF	GC03P133666	5.96	TRIM25	GC17M056836	2.13
CTRL	GC16M067927	5.95	HNRNPA1	GC12P054280	2.05
IL1A	GC02M112773	5.93	CCND3	GC06M041934	1.99
PIK3C2A	GC11M017165	5.92	MYOM2	GC08P002045	1.97
PARP1	GC01M226360	5.91	PRKRA	GC02M178431	1.96
RFLA	GC11M065653	5.89	SOCS3	GC17M078356	1.95
NOS2	GC17M027756	5.85	LCN1	GC09P135521	1.90
EIE2AK2	CC02M037099	5.83	EIEAE	CC04M098871	1.01
	GC0210037099	5.05	LITAL ICAM2	GC04W090071	1.91
GAPDII	GC12F000050	5.61	ICANIZ DCT2	GC17M004002	1.09
NU55	GC0/P150990	5.77	D512	GC19M017405	1.00
CISB	GC08M011842	5.72	IFTI MZ	GCTIP000300	1.87
CCL4	GC17P036103	5.69	KPNA4	GC03M160494	1.83
CASP8	GC02P201233	5.65	DROSHA	GC05M031401	1.78
ANXA5	GC04M121667	5.59	USP7	GC16M008892	1.78
F8	GC0XM154835	5.58	CD46	GC01P207752	1.74
CREB1	GC02P207529	5.55	AHSG	GC03P186612	1.73
SH2D3A	GC19M006752	5.54	BAG3	GC10P119651	1.72
HLA-DRB1	GC06M032578	5.48	TMPRSS11A	GC04M067909	1.69
TMPRSS11D	GC04M067820	5.38	APOD	GC03M195568	1.66
BMP6	GC06P007726	5.32	PRKCB	GC16P023872	1.64
SMAD3	GC15P067063	5.2	RHOB	GC02P020447	1.64
MASP2	GC01M011026	5.13	ITGA6	GC02P172427	1.63
IFITM3	GC11M000319	5.11	STAT2	GC12M056341	1.62
HLA-C	GC06M031272	5.11	CALM1	GC14P090396	1.61
BAD	GC11M064273	5.04	OAS1	GC12P112906	1.6
CANX	GC05P179678	4 97	BCL2L2	GC14P025033	16
MCI 1	GC01M150673	4 77	IFI27	GC14P094104	1.6
CCL7	GC17P034270	4 71	PSMC6	GC14P052707	1.55
CASP6	CC04M100688	47	TEP2	CC07M100620	1.55
ECP1	GC04W1109000	4.7	SDI1	CC11M059694	1.5
EGKI ITCP1	GC001 100400	4.00		GC11W1059094	1.45
IIGDI	GC10M052900	4.64	IGAC	GC02IN089081	1.44
KNASE3	GC14P020891	4.63	PHB2	GC12M006965	1.44
STINGI	GC05M139476	4.5	CD151	GC11P000883	1.42
CD34	GC01M207880	4.48	IIGA1	GC05P052788	1.42
DUSP1	GC05M172768	4.42	FAH	GC15P080152	1.4
RB1	GC13P048303	4.41	NUDT2	GC09P034329	1.36
ADAM17	GC02M009488	4.4	AQP1	GC07P030911	1.35
HSPB1	GC07P076302	4.33	TMPRSS13	GC11M117900	1.32
EEF1A1	GC06M073515	4.33	CD3G	GC11P118344	1.28
TOLLIP	GC11M001274	4.31	PCSK5	GC09P075890	1.23
CCR1	GC03M046218	4.3	CBLB	GC03M105655	1.21
EZR	GC06M158765	4.27	TMEM233	GC12P119594	1.18
LCN2	GC09P128149	4.26	ANXA11	GC10M080150	1.13
TRAF3	GC14P104312	4.23	CLEC4D	GC12P008509	1.1
SMAD7	GC18M048919	4.18	NMRAL1	GC16M004461	1.07
TXN	GC09M110243	4.17	HPGDS	GC04M094298	0.84
ICAM3	GC19M010335	4.15	SLC39A14	GC08P022367	0.83
VCP	GC09M035056	4 15	OR8U9	GC11Pi00193	0.35
NI RP12	GC19M053792	4 1 4	C8G	GC09P136944	0.31
ANXA?	GC15M060347	4 1 2	200	50001 100000	0.01
	CT0111000011	1.14			



Figure 3. Ingredient-target network of SFJDC. The blue ovals represent target genes; the green, light blue, yellow, pink, purple and light yellow rectangulars represent the ingredients from PR, IR, HP, RB, PCRR, FF; the red rectangulars represent the ingredients from mlti-herb. PR: Phragmitis Rhizoma; IR: Isatidis Radix; HP: Herba Patriniae; RB:Radix Bupleuri; PCRR: Polygoni Cuspidati Rhizoma Et Radix; FF: Forsythiae Fructus.



Figure 4. PPI network of SFJDC against NCP. (A) The whole network of SFJDC against NCP contained 2,407 nodes and 53,639 edges. (B) A subnetwork of significant genes from A consisted of 766 nodes and 28872 edges. (C) PPI network of more significant genes from B with 169 nodes and 4238 edges. BC: Betweenness Centrality; DC: Degree Centrality.

Table 5. The data of top twenty GO terms including BP, CC, MF

IPF COM0246 response to hypophysic-thride 1.27F-17 2.31F-14 1.3 IPF COM0222 cellular response to molecule of bucchel of argin 2.10F-17 2.31F-14 1.3 IPF COM071219 cellular response to biolicit of thread is gaining pathway 1.39F-12 1.04F-09 9 IPF COM071216 cellular response to biolicit signiling pathway 1.39F-12 2.18F-09 9 IPF COM01216 response to incide of bucchel signiling pathway 1.39F-13 1.07F-07 9 IPF COM01458 response to incide thread is more and incide is gaining pathway 1.07F-07 9 IPF COM0458 response to incide thread is more and incide is gaining pathway 1.07F-07 9 IPF COM04548 response to incide is gaining pathway 1.07F-07 9 1.07F-07 9 IPF COM04548 response to incide incide is gaining pathway 1.07F-07 9 1.07F-07 9 IPF COM04549 gial cell apoptoic irgonome 1.07F-07 3.05F-07 9 IPF <td< th=""><th>GO category</th><th>ID</th><th>Description</th><th>P-value</th><th>P.adiust</th><th>Count</th></td<>	GO category	ID	Description	P-value	P.adiust	Count
mmCOUNT227response to impolynomic or bacterial origin2.186-172.156-141.3IPCOUNT216cellular response to molecule of bacterial origin1.987-121.046-099IPCOUNT216cellular response to molecule of bacterial origin1.987-121.046-099IPCOUNT216cellular response to molecule of bacterial origin2.987-107.245-088IPCOUNT216response to molecul of bacterial origin2.987-107.245-089IPCOUNT216response to molecul of bacterial origin bacterial origin2.987-107.245-089IPCOUNT216response to molecul origin bacterial origin bacterial origin2.987-107.245-089IPCOUNT216response to molecul origin bacterial or	BP	CO:0032496	response to linopolysaccharide	1 27E-17	2 31F-14	13
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mm colcollidar response to indecide of laceital origin pathows198–12191.600191BPCO071216cultur response to indecide of laceital origin pathows196-10218-1049BPCO2010728response to media ion aportoric signaling pathows1361-10218-1079BPCO2010128response to media ion aportoric signaling pathows1361-10218-1079BPCO2010128response to steroid hormone3381-10117-1079BPCO2010128response to valcative system development117-107238-1079BPCO20010391response to valcative system development117-1073.162-078BPCO20010391response to valcative system development217-1073.162-078BPCO2001297megnotic protein217-1073.162-078BPCO2001297megnotic protein217-1073.162-078BPCO2001297megnotic protein3.178-1073.162-078BPCO2001297megnotic protein3.178-1073.162-078CCCO2001997neuron conh3.178-1073.162-078CCCO2001971membrane region1.201-1673.162-078CCCO2001977membrane region1.201-1673.162-071.201-167CCCO2001977membrane region1.201-1673.178-1073.178-107CCCO20019707membrane region1.201-1673.178-107 <td>BD BD</td> <td>CO:0071222</td> <td>callular response to linenelyzascharide</td> <td>1 20E 12</td> <td>1.02E.00</td> <td>0</td>	BD BD	CO:0071222	callular response to linenelyzascharide	1 20E 12	1.02E.00	0
nnC. Controlcalling heapboxe instruction (https://control1.961-121.910-191.910-19PPC. COUD1244calgebra instruction (https://spinling pathway)1.961-191.910-1971.910-197PPC. COUD1245responses to struction forme3.997-107.917-4079PPC. COUD1247responses to struction forme3.997-101.912-1979PPC. COUD1247responses to struction forme3.997-101.912-1979PPC. COUD1248responses to calculation1.812-192.561-079PPC. COUD1249responses to calculation1.912-192.561-079PPC. COUD1249responses to calculation3.912-193.161-079PPC. COUD1249responses to calculation3.912-193.161-079PPC. COUD1249glad-off-appoints process2.175-193.251-074PPC. COUD1249glad-off-appoints process2.175-193.251-074PPC. COUD1249glad-off-appoints process2.175-193.251-074PPC. COUD1249grad-profess3.176-0777PPC. COUD1249grad-off-appoints process2.175-193.251-074PPC. COUD1249grad-off-appoints process2.175-193.251-074PPC. COUD1249grad-off-appoints process2.175-193.251-074PPC. COUD1249grad-off-appoints process2.175-193.251-07 <t< td=""><td>DF PD</td><td>GO.0071222</td><td>cellular response to inpopolysaccharide</td><td>1.39E-12</td><td>1.02E-09</td><td>9</td></t<>	DF PD	GO.0071222	cellular response to inpopolysaccharide	1.39E-12	1.02E-09	9
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BP GO003845 response to steam latername 3.898-10 1.425-67 9 BP GO002407 reproductive structure development 1.126-69 2.234-67 9 BP GO0006079 response to radiation 1.126-69 2.234-67 9 BP GO0006079 response to radiation 1.126-69 2.656-67 9 BP GO0006079 response to radiation 2.116-69 3.256-67 8 BP GO0006079 response to radiation 3.256-94 3.256-67 8 BP GO0002575 method langerptic groeces 3.256-94 3.256-67 7 BP GO000257 methodana 3.156-94 4.566-67 7 BP GO000257 methodana 1.356-69 4.356-67 6 CCC GO0005121 methodana 1.356-60 6.176-45 6 CCC GO000521 methodana 1.356-60 1.366-60 6 CCC GO000521 methodana 1.356-60 1.366-60 6 CCC GO000521 methodana 1.356-60 1.366-60 1.366-60 1.366-60 CCC GO000571 methodana 1.366-60 1.366-60 1.366-60	BP	GO:0010038	response to metal ion	2.37E-10	7.45E-08	9
BP COUNDEX247 regulation of celluedi adhesion 5.821-10 1.216-07 9 BP COUNDEX16 reproductive system development 1.126-09 2.236-07 9 BP COUNDEX14 response to radiation 1.481-09 2.661-07 9 BP COUNDEX14 response to radiation stress 2.191-09 3.228-07 8 BP COUNDEX147 response to function 3.181-09 4.991-07 8 BP COUNDEX17 response to function 3.581-09 4.991-07 8 BP COUNDEX77 neuron death 3.181-07 6.3112-07 8 CC COUNDEX71 neuron death 1.172-08 6.3112-07 8 CC COUNDEX71 neuron death 1.272-08 6.172-05 8 CC COUNDEX71 neuron more conspan few 4.574-05 6.172-05 8 CC COUNDEX71 neuron more conspan few 4.574-05 0.00134544 4 CC COUNDEX71 neuron more conspan few 4.574-05 0.00134544 4 CC COUNDEX71 neuron more conspan few 4.574-05 0.00134544 4 CC COUNDEX71 neuron more conspan few 4.574-05	BP	GO:0048545	response to steroid hormone	3.89E-10	1.07E-07	9
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and COUNDERSE Field of the set of a	BP	CO:0070997	neuron death	5.00E 09	6 31E 07	8
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nr C.0.004952 response to oxygen leves 1.38-18 1.301-b0 6 CC CO.0049512 membrane microdomain 1.301-66 6.172-65 6 CC CO.0098857 membrane region 1.611-66 6.172-65 6 CC CO.0005741 mitochondrial outer membrane 571-65 0.001243834 4 CC CO.0005741 mitochondrial outer membrane 5.971-65 0.001361141 4 CC CO.0005847 ergenselie outer membrane 2.976-05 0.001361141 4 CC CO.0005819 optical enter membrane 2.976-05 0.001361141 4 CC CO.0005819 spindle 0.00054171 0.00501704 3 CC CO.0000573 RNA polymerase II transcription factor complex 0.001489462 0.001493458 2 CC CO.0000574 epindle protein transcription factor complex 0.001499568 2 CC CO.0000577 RNA polymerase II transcription factor complex 0.001499568 2 CC	DP	GO.007/191	extrinsic apoptotic signaling pathway	0.76E-09	1 505 00	/
CC COUMP3121 membrane rank 1.21-bb 6.171-05 6 CC CO0098589 membrane region 1.61-b6 6.172-05 6 CC CO0005667 transcription factor complex 5.41-b5 0.001243834 4 CC CO0005667 transcription factor complex 5.41-b5 0.001361141 4 CC CO0019967 outer membrane 2.97E-b5 0.001361141 4 CC CO0199687 outer membrane 0.00032171 0.005011074 3 CC CO01904813 foolin-1-rch granule lumen 0.00039217 0.00501074 3 CC CO0009077 cyclin-dependent protein kinase holeexyme complex 0.00089346 0.01035148 3 CC CO0000037 cyclin-dependent protein kinase holeexyme complex 0.01089450 0.01086456 3 CC CO0000377 cyclin-dependent protein kinase complex 0.01089409 0.02985711 2 CC CO0000377 cyclin-dependent protein kinase complex 0.01089409 0.000894091 3	BP	GO:0070482	response to oxygen levels	1.36E-08	1.50E-06	8
CC CG009887 membrane engin 1.31-06 6.17E-05 6 CC CG00005741 mitochondrial outer membrane 4.97L-05 0.001243834 4 CC GC00005767 transcription factor complex 5.41E-05 0.001243834 4 CC GC00019667 outer membrane 2.97E-05 0.001361141 4 CC GC0019667 outer membrane 0.00032441 0.000664842 2 CC GC00196690 pore complex 0.00032411 0.000664842 2 CC GC00009075 RNA polymerase II transcription factor complex 0.001089812 0.00093090 3 CC GC00000975 RNA polymerase II transcription factor complex 0.001089812 0.01089816 2 CC GC000001002 ficolin-1-rich granule 0.00135428 0.01089016 2 CC GC000010102 ficolin-1-rich granule 0.0013640840 0.003564081 2 CC GC0000102 ficolin-1-rich granule 0.0013640840 0.003510445 3	CC	GO:0045121	membrane raft	1.27E-06	6.17E-05	6
CC COM08889 membrane region 1.61-06 5.776-05 6 CC COM003567 transcription factor complex 5.417-05 0.001243844 5 CC GOM003567 transcription factor complex 7.976-05 0.001361141 4 CC GOM019867 outer membrane 9.976-05 0.001361141 4 CC GOM019867 outer membrane 0.000392171 0.005011074 3 CC GOM003957 RNA polymerase II transcription factor complex 0.000640704 0.007566992 4 CC GOM00307 cyclin-dependent protein kinase holecaryme complex 0.00189466 0.010199568 2 CC GOM00307 cyclin-dependent protein kinase complex 0.00189478 0.0113962616 3 CC GOM013974 secretory granule lumen 0.00389711 2 2 CC GOM03578 secretory granule lumen 0.00850473 0.00389511 2 CC GOM03574 secretory granule lumen 0.00850476 0.00389511 2 <tr< td=""><td>CC</td><td>GO:0098857</td><td>membrane microdomain</td><td>1.30E-06</td><td>6.17E-05</td><td>6</td></tr<>	CC	GO:0098857	membrane microdomain	1.30E-06	6.17E-05	6
CCCOM005741mitochondrial outer membrane97F-050.001243844CCGOM005767transcription factor complex5.41E-050.0013611414CCGOM01968organelle outer membrane8.29E-050.0013611414CCGOM01967pore complex0.0003214410.0046638422CCGOM09575RNA polymerase II transcription factor complex0.0006902710.0005690924CCGOM090575RNA polymerase II transcription factor complex0.0008698260.0009399093CCGOM01002ficalin-trich granule lumen0.0012534680.0110395682CCGOM01002ficalin-trich granule sclopenzyme complex0.00129847840.010395682CCGOM01002ficalin-trich granule sclopenzyme complex0.00129847840.010395613CCGOM04794azarophil granule lumen0.0059468040.003369112CCGOM04774secretory granule lumen0.0065946950.035108453CCGOM04774secretory granule lumen0.0065946800.000170884MFGOM01902philosphatase binding2.9E-071.91E-053MFGOM02020probasis binding2.9E-071.91E-053MFGOM02020probase binding0.000176864MFGOM02020probase binding0.00017550.000242525MFGOM02020probase binding0.00017550.000242525MF	CC	GO:0098589	membrane region	1.61E-06	6.17E-05	6
CC COM056/7 transcription factor complex 5411-65 0.00124854 5 CC GOM01969 organelle outer membrane 7971-65 0.001361141 4 CC GOM01967 outer membrane 8297-65 0.000361141 0.0006311074 3 CC GOM04930 pore complex 0.000392171 0.000511074 3 CC GOM00375 RNA polymerase II transcription factor complex 0.0006955 0.00099909 3 CC GOM00037 cyclin-dependent protein kinase holeenzyme complex 0.00189346 0.011369518 3 CC GOM00479 nuclear transcription factor complex 0.00189340 0.01363511 2 CC GOM0591 caveola nuclear transcription factor complex 0.00189401 0.01363511 2 CC GOM0597 serine/ threonine protein kinase complex 0.00159021 0.0136311 2 CC GOM0597 aztrophil granule lumen 0.00504375 0.03551045 3 CC GOM06025 cytoplasmic vesice lumen	CC	GO:0005741	mitochondrial outer membrane	4.97E-05	0.001243834	4
CCGO001968organelle outer membrane7.97E-050.0013611414CCGO0019697outer membrane7.97E-050.003611414CCGO10046930pore complex0.0003241410.00063912710.00050110743CCGO1009575RNA polymerase II transcription factor complex0.000698520.000999903CCGO000077eyclin-dependent protein kinase holeenzyme complex0.000898520.0019895682CCGO101002ficolin-1-rich granule0.001590310.011080153CCGO0044798nuclear transcription factor complex0.0016903730.013080512CCGO1002554serine/thronine protein kinase complex0.0069043730.033695112CCGO1003774secretory granule lumen0.0061904370.033695112CCGO1004774secretory granule lumen0.006194730.0355108453CCGO1005140H1 domain binding2.98E-071.91E-053MFGO005140H1 domain binding2.98E-071.91E-053MFGO005126eytoplastic vesicle lumen0.006127950.000549254MFGO0005126probabates binding2.48E-050.000708984MFGO0005126probabates binding2.48E-050.0006294255MFGO0005126eytokine receptor binding2.82E-050.0006294252MFGO0005126ubiquitin protein ligase binding0.001278970.0	CC	GO:0005667	transcription factor complex	5.41E-05	0.001243834	5
CCGO0019867outer membrane8.29E-050.0013611414CCGO0004693pore complex0.000532110.0006439422CCGO1004813ficolin-1-ich granule lumen0.000640740.0073680924CCGO000575RNA polymerase II transcription factor complex0.000893400.000939903CCGO0000575eyclin-dependent protein kinase holeenzyme complex0.001893460.0104395682CCGO000070cyclin-dependent protein kinase holeenzyme complex0.001893460.010893163CCGO000501eaveola0.00059010.023857112CCGO000575azveola0.000849100.023857112CCGO000577azveola0.000849730.033851142CCGO000577azveola0.000649150.035508453CCGO000577azveola0.000649150.035508453CCGO000577azveola0.000649150.0035108453CCGO000573azveola0.000649150.000570843CCGO000574ATPae complex0.000617750.0355108453CCGO000713detth domain binding229E-071.91E-053MFGO0007163ethidomain binding229E-071.91E-053MFGO0007163ethidomain binding229E-071.91E-053MFGO0007165ethidomain binding229E-071.91E-053MFGO	CC	GO:0031968	organelle outer membrane	7.97E-05	0.001361141	4
CCGO0046930pore complex0.00324110.00463422CCGO0190813ficulin-1-rich granule lumen0.003921710.0073680924CCGO009057RNA polymerase II transcription factor complex0.008940740.0073680923CCGO0000307cyclin-dependent protein kinase holeenzyme complex0.001893460.010439563CCGO0001002ficolin-1-rich granule0.0015902310.0103056163CCGO0044798naclear transcription factor complex0.0018991010.0298379112CCGO0005911caveola0.0005910330.0339551142CCGO003578azurophi granule lumen0.0059103730.0339551142CCGO003774secretory granule lumen0.006568950.03355108453CCGO0005103death domain binding2.92F-071.91E-053MFGO001902phosphatase binding3.42E-640.000719884MFGO0005120protess binding2.82E-050.000624254MFGO0005120protess binding3.02E-050.000624255MFGO0005120protess binding3.02E-050.000624254MFGO0005120protess binding3.02E-050.000624255MFGO0005120protess binding3.02E-050.000624255MFGO0005120protess binding0.00154540.000740642MFGO0005120protesi binding <t< td=""><td>CC</td><td>GO:0019867</td><td>outer membrane</td><td>8.29E-05</td><td>0.001361141</td><td>4</td></t<>	CC	GO:0019867	outer membrane	8.29E-05	0.001361141	4
CCGO 3904813Ítcolin-1-rick granule lumen0.000392710.000510749CCGO 0003975RNA polymerase II transcription factor complex0.0006898520.009099903CCGO 0000307cyclin-dependent protein kinase holoenzyme complex0.001893460.010495682CCGO 0001002ficolin-1-rick granule0.0015902310.0110880153CCGO 0001002ficolin-1-rick granule0.0015902310.0130626163CCGO 00044798nuclear transcription factor complex0.0018991010.0298379112CCGO 0003578serine/ threonine protein kinase complex0.005043730.033695112CCGO 00034774serine/ threonine protein kinase complex0.0050468010.03355108453CCGO 00034774serine/ threonine protein kinase complex0.0059468040.03355108453CCGO 0004275exteriory granule lumen0.006568950.0355108453CCGO 0004025cytoplasmic vesicle lumen0.006568950.000519863MFGO 0007513death domain binding2.98F-071.91F-053MFGO 0001992protein plase binding3.42F-060.0000294254MFGO 0005126eytokine receptor binding2.98F-050.0000294255MFGO 0005126eytokine receptor binding2.98F-050.0000294255MFGO 0001528protein phosphatase binding0.001769822MF </td <td>CC</td> <td>GO:0046930</td> <td>pore complex</td> <td>0.000324441</td> <td>0.004663842</td> <td>2</td>	CC	GO:0046930	pore complex	0.000324441	0.004663842	2
CC GO:0005819 spindle 0.000640704 0.007368092 4 CC GO:0000575 KNA polymerase II transcription factor complex 0.00089852 0.009093909 3 CC GO:001002 ficolin-1-rich granule 0.001253428 0.011089316 3 CC GO:004778 nuclear transcription factor complex 0.001250312 0.03369511 2 CC GO:0035578 azurophil granule lumen 0.0005004373 0.033895311 2 CC GO:003578 azurophil granule lumen 0.0065004373 0.035510845 3 CC GO:003578 azurophil granule lumen 0.006856899 0.00510845 3 CC GO:0040751 death domain binding 2.29E-07 1.91E-05 3 MF GO:00070513 death domain binding 2.32E-06 0.00070898 5 MF GO:0001200 protease binding 3.42E-06 0.00070898 5 MF GO:0001202 protein phosphatase binding 3.2E-05 0.000629425 5	CC	GO:1904813	ficolin-1-rich granule lumen	0.000392171	0.005011074	3
CC GO.0090575 RNA polymerase II transcription factor complex 0.000869852 0.009093909 3 CC GO.0000307 cyclin-dependent protein kinase holenzyme complex 0.00125342 0.011053956 3 CC GO.0004798 nuclear transcription factor complex 0.00125342 0.013062616 3 CC GO.0005901 caveola 0.003891901 0.029837911 2 CC GO.0035578 azurophil granule lumen 0.005946804 0.0035916845 3 CC GO.0004774 secretory granule lumen 0.006946804 0.003510845 3 CC GO.0006025 cytoplasmic vesicle lumen 0.00686985 0.035510845 3 CC GO.00070513 death domain binding 2.29E-07 1.91E-05 3 MF GO.001902 phosphatse binding 3.42E-06 0.000170898 4 MF GO.0002020 protease binding 3.02E-05 0.000629425 5 MF GO.0003516 cytokine receptor binding 3.02E-05 0.000629425 5	CC	GO:0005819	spindle	0.000640704	0.007368092	4
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CC GOUNDAGE Form approximate protein make nonceasing to compare to constraine to overlations of a constraine of the protein sector of the pro	CC C	GQ:0000307	cyclin-dependent protein kinase holoenzyme complex	0.001089346	0.010439568	2
CC COMPLATE COMPLATE <thcomplate< th=""> COMPLATE CO</thcomplate<>	CC	CO:0101002	ficelin 1 rich granulo	0.001053428	0.011088015	3
CC CO0049795 Inductar transcription nactor Controlet 000159/231 000159/231 2 CC GO0005501 caveola 000389010 0.029837911 2 CC GO003578 azurophil granule lumen 0.00504373 0.03380511 2 CC GO0034774 secretory granule lumen 0.0054804 0.035510845 3 CC GO000505 cytoplasmic vesicle lumen 0.006856895 0.035510845 3 CC GO00051400 BH domain binding 2.29E-07 1.91E-05 3 MF GO0005126 cytoplasmic vesicle lumen 0.006856895 0.00070898 5 MF GO0007513 death domain binding 2.29E-07 1.91E-05 3 MF GO0003513 activating transcription factor binding 4.09E-06 0.000170898 4 MF GO0005126 cytokine receptor binding 2.96E-05 0.000629425 5 MF GO0005123 ubiquitin rotein ligase binding 3.02E-05 0.000629425 5 MF	CC	CO:0044708	nuclear transcription factor complex	0.001200420	0.012062616	3
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CC GC1942954 serme/Introduce protein kinase complex 0.004088015 0.0339911 2 CC GC0035778 azurophil granule lumen 0.00504473 0.0338511 2 CC GC01904949 ATPase complex 0.006129775 0.035510845 3 CC GC0000505 cytoplasmic vesicle lumen 0.006856895 0.035510845 3 MF GC00070513 death domain binding 2.29E-07 1.91E-05 3 MF GC00070513 death domain binding 2.29E-07 1.91E-05 3 MF GC00070513 death domain binding 2.42E-06 0.000170898 5 MF GC0002020 protease binding 4.09E-06 0.000170898 4 MF GC0002126 cytokine receptor binding 2.96E-05 0.000629425 4 MF GC0001902 protease binding 3.02E-05 0.000740542 2 MF GC0001903 ubiquitin protein ligase binding 3.02E-05 0.00074052 2 MF GC0.0004707<		GO:0003901	caveola	0.003891901	0.029837911	2
CC GC000557/s aztropin granule iumen 0.00004373 0.0338511 2 CC GC0190474 scretory granule iumen 0.006544684 0.035510845 3 CC GC00060205 cytoplasmic vesicle lumen 0.006546804 0.035510845 3 MF GC00070513 death domain binding 2.29E-07 1.91E-05 3 MF GC00070513 death domain binding 2.29E-07 1.91E-05 3 MF GC00070513 death domain binding 2.29E-07 1.91E-05 3 MF GC00070513 activating transcription factor binding 4.09E-06 0.000170898 5 MF GC0002020 protease binding 2.82E-05 0.000629425 4 MF GC00019903 protein bigase binding 3.02E-05 0.000629425 4 MF GC0004707 MAP kinase activity 0.000145644 0.0024925 5 MF GC00097153 cysteine-type endopeptidase activity involved in 0.00017918 0.002549304 2 MF </td <td></td> <td>GO:1902554</td> <td>serine/threonine protein kinase complex</td> <td>0.004688015</td> <td>0.03369511</td> <td>2</td>		GO:1902554	serine/threonine protein kinase complex	0.004688015	0.03369511	2
CC GO:00347/4 secretory granule lumen 0.00594804 0.035510845 3 CC GO:1904949 ATPase complex 0.006129753 0.035510845 3 CC GO:0060205 cytoplasmic vesicle lumen 0.006856895 0.035510845 3 MF GO:0070513 death domain binding 2.29E-07 1.91E-05 3 MF GO:003613 activating transcription factor binding 4.09E-06 0.000170898 4 MF GO:0002020 protease binding 2.08E-05 0.000629425 5 MF GO:0005126 cytokine receptor binding 2.96E-05 0.000629425 5 MF GO:0001625 ubiquitin protein ligase binding 3.02E-05 0.000629425 5 MF GO:0004707 MAP kinase activity 0.0014564 0.0023226 2 MF GO:0004707 MAP kinase activity involved in apoptotic process 0.002649325 2 MF GO:0004708 MAP Kinase kinase activity involved in apoptotic process 0.00268588 2 MF <td></td> <td>GO:0035578</td> <td>azurophil granule lumen</td> <td>0.005004373</td> <td>0.03385311</td> <td>2</td>		GO:0035578	azurophil granule lumen	0.005004373	0.03385311	2
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CCGC:0060205cytoplasmic vesicle lumen0.0068568950.0355108453MFGC:0070513deth domain binding2.29E-071.91E-053MFGC:0019902phosphatase binding3.42E-060.0001708985MFGC:00031613activating transcription factor binding4.09E-060.0001708984MFGC:0005126protease binding2.82E-050.0006294255MFGC:0005126cytokine receptor binding2.82E-050.0006294255MFGC:0005126ubiquitin protein ligase binding3.02E-050.0006294255MFGC:0004702ubiquitin protein ligase binding3.02E-050.0006294255MFGC:0004702MAP kinase activity0.001456440.00243262MFGC:0004707MAP kinase activity involved in apoptotic process0.000179180.0025493042MFGO:0004708MAP kinase kinase activity involved in apoptotic process0.00017150.002685882MFGO:0004708MAP kinase kinase activity0.001917550.002685882MFGO:0009718disordered domain specific binding0.008324590.00830783MFGO:0007718disordered domain specific binding0.001261330.00830783MFGO:0001085RNA polymerase II transcription factor binding0.001261330.0097074693MFGO:0001075RNA polymerase II transcription factor binding0.001261330.009707469	CC	GO:1904949	ATPase complex	0.006127975	0.035510845	2
MFGC:0051400BH domain binding229E-071.91E-053MFGC:0070513death domain binding2.29E-071.91E-053MFGC:0019902phosphatse binding3.42E-060.0001708985MFGC:00033613activating transcription factor binding4.09E-060.0001708984MFGC:0005126cytokine receptor binding2.08E-050.0006294255MFGC:0031625ubiquitin protein ligase binding2.96E-050.0006294255MFGC:0031625ubiquitin protein ligase binding3.02E-050.0006294255MFGC:0044389ubiquitin-like protein ligase binding4.02E-050.0007460425MFGC:00097153cysteine-type endopeptidase activity involved in apoptotic process0.0001757180.0025493042MFGC:00097153cysteine-type endopeptidase activity involved in apoptotic process0.000271550.0006294572MFGC:0009718death receptor binding0.0001757180.002685882MFGC:00097718death receptor binding0.0008324590.00830783MFGC:00097718disordered domain specific binding0.0008324590.008830783MFGC:0001085RNA polymerase II transcription factor binding0.00110261330.0097074693MFGC:00101085RNA polymerase II transcription factor binding0.001104330.0097074693MFGC:00101085RNA polymerase II transcripti	CC	GO:0060205	cytoplasmic vesicle lumen	0.006856895	0.035510845	3
MFGO:0070513death domain binding2.29E-071.91E-053MFGO:001902phosphatase binding3.42E-060.0001708985MFGO:0033613activating transcription factor binding4.09E-060.0001708984MFGO:0002020protease binding2.08E-050.0006294254MFGO:001903protein phosphatase binding2.82E-050.0006294254MFGO:0031625ubiquitin protein ligase binding3.02E-050.0006294255MFGO:0044389ubiquitin-like protein ligase binding3.02E-050.0007460425MFGO:004707MAP kinase activity0.0001456440.002432262MFGO:0097153cysteine-type endopeptidase activity involved in apoptotic process0.0001679180.0026893042MFGO:000778MAP kinase kinase activity involved in apoptotic process0.00026942542MFGO:000778MAP kinase kinase activity involved in apoptotic process0.000117570.002685882MFGO:000778MAP kinase kinase activity0.0001917550.0026805883MFGO:000778heme binding0.000860630.00880783MFGO:000778heme binding0.0011026130.0097074693MFGO:000785RNA polymerase II transcription factor binding0.001261330.0097074693MFGO:0016248channel inhibitor activity0.0011039990.0097074693 <td>MF</td> <td>GO:0051400</td> <td>BH domain binding</td> <td>2.29E-07</td> <td>1.91E-05</td> <td>3</td>	MF	GO:0051400	BH domain binding	2.29E-07	1.91E-05	3
MFGC0:0019902phosphatase binding3.42E-060.0001708985MFGC0:0033613activating transcription factor binding4.09E-060.0001708984MFGC0:0002020protease binding2.08E-050.0006294254MFGC0:0019903protein phosphatase binding2.96E-050.0006294254MFGC0:0016264ubiquitin protein ligase binding3.02E-050.0006294254MFGC0:001625ubiquitin protein ligase binding3.02E-050.0007460425MFGC0:0004707MAP kinase activity0.001145640.00243262MFGC0:0097153crysteine-type endopeptidase activity involved in apoptotic process0.0006875480.002689582MFGC0:0004708MAP kinase kinase activity0.000871540.00281693MFGC0:0007718death receptor binding0.000875480.008830782MFGC0:0007718disordered domain specific binding0.000874590.008830783MFGC0:0007718disordered domain specific binding0.00088307833MFGC0:0016248channel inhibitor activity0.0011039990.009774693MFGC0:0016248channel inhibitor activity0.0011044340.009774692MFGC0:0016248channel inhibitor activity0.0011044390.009774693MFGC0:0016248channel inhibitor activity0.0011044390.009774693MFGC0:0016	MF	GO:0070513	death domain binding	2.29E-07	1.91E-05	3
MFGC:0033613activating transcription factor binding4.09E-060.0001708984MFGC:0002020protease binding2.08E-050.0006294255MFGC:0019903protein phosphatase binding2.96E-050.0006294255MFGC:0031625ubiquitin protein ligase binding3.02E-050.0006294255MFGC:0044389ubiquitin-like protein ligase binding4.02E-050.0007406425MFGC:0004707MAP kinase activity0.0001456440.00232262MFGC:00097153cysteine-type endopeptidase activity involved in apoptotic process0.000217150.002687882MFGC:0005123death receptor binding0.000217150.002895472MFGC:00097718disordered domain specific binding0.0008874880.00830783MFGC:0016285kerpayrole binding0.0008875480.00830783MFGC:0016286RNA polymerase II transcription factor binding0.001123090.009774693MFGC:0016248channel inhibitor activity0.0011030990.0097074693MFGC:0016248channel inhibitor activity0.0011030990.0097074692MFGC:0016248channel inhibitor activity0.0011044330.0097074692MFGC:0016248channel inhibitor activity0.0011024920.0117273162	MF	GO:0019902	phosphatase binding	3.42E-06	0.000170898	5
MFGO:002020protease binding2.08E-050.0006294254MFGO:001526cytokine receptor binding2.82E-050.0006294255MFGO:001903protein phosphatase binding2.96E-050.0006294254MFGO:004389ubiquitin protein ligase binding3.02E-050.0007460425MFGO:004707MAP kinase activity0.0001456440.00243262MFGO:0097153cysteine-type endopeptidase activity involved in apoptotic process0.000197550.002685882MFGO:00020037death receptor binding0.0001917550.002685882MFGO:0009718disordered domain specific binding0.0008324590.008830782MFGO:00097718disordered domain specific binding0.0008824590.008830782MFGO:0016248tetrapyrole binding0.001103990.0097074693MFGO:0016248channel inhibitor activity, acting on paired donors, with nor or eduction of molecular oxygen0.00111424920.0117273162	MF	GO:0033613	activating transcription factor binding	4.09E-06	0.000170898	4
MFGO:0005126cytokine receptor binding2.82E-050.0006294255MFGO:0019903protein phosphatase binding2.96E-050.0006294254MFGO:0031625ubiquitin protein ligase binding3.02E-050.0006294255MFGO:0044389ubiquitin-like protein ligase binding4.02E-050.0007460425MFGO:0004707MAP kinase activity0.001456440.002432262MFGO:0004707MAP kinase activity involved in apoptotic process0.00197550.002685882MFGO:0004708MAP kinase kinase activity0.000197550.002685882MFGO:0005123death receptor binding0.0001917550.002685882MFGO:00097718disordered domain specific binding0.0008324590.008830783MFGO:001085RNA polymerase II transcription factor binding0.001261330.0097074693MFGO:016248channel inhibitor activity, acting on paired donos, with incorporation or molecular oxygen0.0011424320.0017273162	MF	GO:0002020	protease binding	2.08E-05	0.000629425	4
MFGO:0019903protein phosphatase binding2.96E-050.0006294254MFGO:0031625ubiquitin protein ligase binding3.02E-050.0006294255MFGO:0044389ubiquitin-like protein ligase binding4.02E-050.0007460425MFGO:004707MAP kinase activity0.0001456440.002432262MFGO:0097153cysteine-type endopeptidase activity involved in apoptotic process0.000147070.0026685882MFGO:0004708MAP kinase kinase activity0.000117550.0026685882MFGO:0005123death receptor binding0.000217150.0027895472MFGO:00097718disordered domain specific binding0.0008875480.008830783MFGO:001085RNA polymerase II transcription factor binding0.0010261330.0097074693MFGO:0016248channel inhibitor activity, acting on paired donors, with incorporation or reduction of molecular oxygen0.0011044330.0097074692MFGO:0007712protein serine/threonine/tyrosine kinase activity0.001104124920.0117273162	MF	GO:0005126	cytokine receptor binding	2.82E-05	0.000629425	5
MFGO:0031625ubiquitin protein ligase binding3.02E-050.0006294255MFGO:0044389ubiquitin-like protein ligase binding4.02E-050.0007460425MFGO:0004707MAP kinase activity0.0001456440.002432262MFGO:0097153cysteine-type endopeptidase activity involved in apoptotic process0.000197550.0026685882MFGO:0004708MAP kinase kinase activity0.0001917550.0026685882MFGO:0005123death receptor binding0.000217150.0027895472MFGO:0020037heme binding0.0008824590.008830783MFGO:0046906tetrapyrrole binding0.0008460630.008830783MFGO:001085RNA polymerase II transcription factor binding0.0011039990.0097074693MFGO:0016248channel inhibitor activity, acting on paired donors, with incorporation or reduction of molecular oxygen0.0011424920.0117273162	MF	GO:0019903	protein phosphatase binding	2.96E-05	0.000629425	4
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MFGO:0007125GO:002795042MFGO:0002037MAP kinase kinase activity0.0001917550.0026685882MFGO:0020037heme binding0.000875480.0082014683MFGO:0020037heme binding0.0008875480.008830782MFGO:0046906tetrapyrole binding0.0008460630.008830783MFGO:001085RNA polymerase II transcription factor binding0.0010261330.0097074693MFGO:0016248channel inhibitor activity, acting on paired donors, with incorporation or reduction of molecular oxygen0.0011044430.0097074693MFGO:0016705protein serine/threonine/tyrosine kinase activity0.0011424920.0117273162	ME	CO:0097153	cysteine-type endopentidase activity involved in	0.000167918	0.002549304	2
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MF GO:0020037 heme binding 0.000687548 0.008201468 3 MF GO:0097718 disordered domain specific binding 0.000832459 0.00883078 2 MF GO:0010850 tetrapyrrole binding 0.000846063 0.00883078 3 MF GO:001085 RNA polymerase II transcription factor binding 0.00126133 0.009707469 3 MF GO:0016248 channel inhibitor activity, acting on paired donors, with normal construction or reduction or molecular oxygen 0.00110443 0.009707469 3 MF GO:0016705 oxidoreductase activity, acting on paired donors, with normal construction or reduction or molecular oxygen 0.001142492 0.011727316 2	MF	GO:0005123	death receptor binding	0.00021715	0.002789547	2
MFGO:0097718disordered domain specific binding0.0008324590.008830782MFGO:0046906tetrapyrole binding0.0008460630.008830783MFGO:001085RNA polymerase II transcription factor binding0.0010261330.0097074693MFGO:0016248channel inhibitor activity0.0011039990.0097074692MFGO:0016705oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen0.0011242920.0117273162	MF	GO:0020037	heme binding	0.000687548	0.008201468	3
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MF GO:0001085 RNA polymerase II transcription factor binding 0.001026133 0.009707469 3 MF GO:0016248 channel inhibitor activity 0.001103999 0.009707469 2 MF GO:0016705 oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen 0.001104443 0.009707469 3 MF GO:0004712 protein serine/threonine/tyrosine kinase activity 0.001412492 0.011727316 2	MF	GO:0046906	tetrapyrrole binding	0.000846063	0.00883078	3
MF GO:0016248 channel inhibitor activity 0.001103999 0.009707469 2 MF GO:0016705 oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen 0.001104443 0.009707469 3 MF GO:0004712 protein serine/threonine/tyrosine kinase activity 0.001412492 0.011727316 2	MF	GO:0001085	RNA polymerase II transcription factor binding	0.001026133	0.009707469	3
MF GO:0016705 oxidoreductase activity, acting on paired donors, with 0.001104443 0.009707469 3 incorporation or reduction of molecular oxygen MF GO:0004712 protein serine/threonine/tyrosine kinase activity 0.00142492 0.011727316 2	MF	GO:0016248	channel inhibitor activity	0.001103999	0.009707469	2
MF GO:0004712 protein serine/threonine/tyrosine kinase activity 0.001412492 0.011727316 2	MF	GO:0016705	oxidoreductase activity, acting on paired donors, with	0.001104443	0.009707469	3
MF GO:0004712 protein serine/threonine/tyrosine kinase activity 0.001412492 0.011727316 2			incorporation or reduction of molecular oxygen			-
	MF	GO:0004712	protein serine/threonine/tyrosine kinase activity	0.001412492	0.011727316	2



In addition, they have high OB and acacetin from 2 herbs (PR, IR) of SFJDC. The three main ingredients were anti-inflammatory and COVID-19 caused by a series of inflammatory storms. Hence, they might be the crucial effective compounds of SFJDC according the network.

PPI network of SFJDC against NCP were visualized using Cytoscape software to obtain the candidate target genes. In order to obtain the more accurate genes, two parameters including DC and BC were used to screen nodes and structure a new network. 169 genes were eventually identified for SFJDC against NCP including 156 other human genes and 13 target genes.

Twenty-three candidate genes (CGs) were identified by using the VennDiagram package. CGs were enriched in BP, CC, MF by GO enrichment analysis. Based on GO terms data, we found that some terms were response to lipopolysaccharide or raft, bacterial origin, membrane membrane microdomain, BH domain binding and cytokine receptor binding. COVID-19 infections leaded to a strong immune response and inflammatory storm in which a large number of cytokines were activated, so SFJDC might regulate COVID-19 through the above biological processes.

SFJDC, as a TCM formula, has multi-component, multi-target-gene, multi-pathway. In the present study, 110 KEGG pathways were significantly enriched. Seven of the top 20 pathways were associated with viral infection including Kaposi sarcoma-associated herpesvirus infection, Human cytomegalovirus infection, Hepatitis B, Influenza A, Epstein-Barr virus infection, Human immunodeficiency virus 1 infection and Measles, and three were associated with lung disease contained tuberculosis, pertussis and small cell lung cancer. Multiple targets of SFJDC may also inhibit the activation of cytokines and reduce inflammation by regulating cytokine pathways, such as IL-17 signaling pathway and TNF signaling pathway. In this study, we obtained 20 functional annotation clusters through DAVID. Annotation Cluster1 including Asthma, Bronchiolitis Viral, Respiratory Syncytial Virus Infections, respiratory syncytial virus bronchiolitis were lung related diseases and Virus infection disease.

Gene-pathway network was constructed to the core and key target genes. The network showed that RELA had largest degree, was the core target gene. Other top five genes such as MAPK1, MAPK14, CASP3, CASP8 and IL6 might be the key target genes. The pathophysiological process of Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-COV-2) infection is similar to that of SARS-CoV infection, with a strong inflammatory response. The SARS-COV-2 virus mainly targets respiratory epithelial cells, alveolar epithelial cells, vascular endothelial cells and pulmonary macrophages, all of which express Angiotensin converting enzyme 2 (ACE2) of proreceptor, triggering the generation inflammatory cytokines and chemokines (including IL-6, TNF, IL-10 and MCP1) [41]. The NF-kB family member RELA is a widely expressed and effective transcriptional activator that activates the expression of many inflammatory through exposure to pathogens and inflammatory cytokines [42]. RELA may play an important role in the infection of COVID-19. MAPK1 and MAPK14 are members of the MAPK family, which can regulate multiple cellular processes, such as response to oxidative stress, antiinflammatory, immune response, apoptosis and cell proliferation [43]. Joseph et al showed SASR-CoV-2 could induce severe inflammation by directly activating p38 MAPK pathway and many p38 MAPK inhibitors are in the clinical stage and should be considered for clinical trial for severe COVID-19 infection [44]. CASP3 and CASP8, a family of cysteine-dependent proteases, play an important role in these events through activation of other apoptotic proteins mediated by proteolysis and cleavage of nuclear proteins [45]. In Krahling's study, infection of 293/ACE2 cells with SARS-CoV activated apoptosisassociated events, such as caspase3, caspase 8[46]. Therefore, we conclude that CASP3 and CASP8 may be activated and play an important role in the pathophysiological process of COVID-19. Higher plasma level of IL-6 was found in ICU patients with COVID-19[47]. Tocilizumab, recombinant а humanized anti-human IL-6 receptor monoclonal antibody, improved the clinical outcome in 20 severe and critical COVID-19 patients and is an effective treatment to reduce mortality [48].



Figure 6. Gene ontology terms of CGs. The top 20 GO functional terms were selected (P<0.05). BP: biological processes; CC: cellular components; MF: molecular functions.

protein serine/threonine/tyrosine kinase activity

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Figure 7. KEGG pathway enrichment of CGs. The top 20 pathways were identified. Color represented P value and size of the spot represented count of genes.

Table 6. The data of top twenty KEGG pathway

ID	Description	P-value	P.adjust	Count
hsa05167	Kaposi sarcoma-associated herpesvirus infection	5.39E-16	8.46E-14	13
hsa04933	AGE-RAGE signaling pathway in diabetic complications	1.13E-15	8.85E-14	11
hsa05163	Human cytomegalovirus infection	6.58E-15	3.45E-13	13
hsa04657	IL-17 signaling pathway	4.27E-14	1.68E-12	10
hsa05161	Hepatitis B	2.60E-13	6.81E-12	11
hsa04668	TNF signaling pathway	2.60E-13	6.81E-12	10
hsa05164	Influenza A	1.78E-11	4.00E-10	10
hsa05133	Pertussis	2.57E-11	5.04E-10	8
hsa05152	Tuberculosis	3.16E-11	5.50E-10	10
hsa05169	Epstein-Barr virus infection	9.46E-11	1.48E-09	10
hsa05170	Human immunodeficiency virus 1 infection	1.60E-10	2.29E-09	10
hsa05142	Chagas disease (American trypanosomiasis)	2.86E-10	3.74E-09	8
hsa05140	Leishmaniasis	1.57E-09	1.90E-08	7
hsa04210	Apoptosis	2.89E-09	3.24E-08	8
hsa05162	Measles	3.24E-09	3.40E-08	8
hsa05132	Salmonella infection	4.64E-09	4.55E-08	9
hsa01522	Endocrine resistance	8.69E-09	8.03E-08	7
hsa04625	C-type lectin receptor signaling pathway	1.32E-08	1.15E-07	7
hsa05145	Toxoplasmosis	2.22E-08	1.83E-07	7
hsa05130	Pathogenic Escherichia coli infection	6.53E-08	5.13E-07	8

It has been clinically confirmed that SFJDC is effective in the treatment of COVID-19. Wang et al shown that conventional treatment combined with SFJDC treatment for 4 cases of COVID-19 patients could significantly improve symptoms and promote viral negative conversion [49]. Another study including 70 COVID-19 patients found that SFJDC combined with Arbidol for COVID-19 compared with single using Arbidol could significantly shorten the time of clinical symptoms improvement and COVID-19 negative conversion [50].

To summarise, the compound and targets of SFJDC were systematically studied by applying

network pharmacology. Wogonin, licochalcone a and acacetin regulated the most targets associated with NCP. RELA, MAPK1, MAPK14, CASP3, CASP8 and IL6 were the core and key genes in the gene-network of SFJDC for the treatment of NCP. SFJDC regulated novel coronavirus pneumonia by multi-compound and multi-target, which provided theoretical support for SFJDC against COVID-19. More mechanism and roles require further clinical validation.

Abbreviations

ACE2: Angiotensin converting enzyme 2; ARDS: acute respiratory distress syndrome; BBB: bloodbrain barrier; BC: Betweenness Centrality; BP: biological processes; Caco-2: Caco-2 permeability; CC: cellular components; CC: Colseness Centrality; CG: candidate genes; DC: Degree Centrality; DL: drug-likeness (DL); EC: Eigenvector Centrality; FF: Forsythiae Fructus; GO: Gene Ontology; HP: Herba Patriniae; I: licorice; IR: Isatidis Radix; KEGG: Kyoto Encyclopedia of Genes and Genomes; LAC: Local average connectivity-based method; LHQWG: granules; LianHua QingWen MF: molecular functions; NC: Network Centrality; NCP: Novel Coronavirus Pneumonia; **OB**: oral bioavailability; PCRR: Polygoni Cuspidati Rhizoma Et Radix; PPI: protein-protein interaction; PR: Phragmitis Rhizoma; **RB:** Radix Bupleuri; **SFJDC:** ShuFeng JieDu capsule; SARS-COV-2: Severe Acute Respiratory Syndrome-Coronavirus-2; TCM: Traditional Chinese Medicine; TCMSP: Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform; VH: Verbenae Herb.

Annotation Cluster	Term	Count	<i>P</i> -value
Annotation Cluster 1	Asthma Bronchiolitis, Viral Respiratory Syncytial Virus Infections	7	8.50E-07
(Score:6.04)	respiratory syncytial virus bronchiolitis	7	8.50E-07
	Bronchiolitis, Viral Respiratory Syncytial Virus Infections	7	1.04E-06
Annotation Cluster 2	Coronary Artery Disease Inflammation	5	5.45E-07
(Score:4.91)	non-Hodgkin lymphoma	4	1.90E-06
	Recurrence Venous Thromboembolism	5	2.48E-06
	Arthritis	5	2.66E-06
	Brain Ischemia Hypertension Osteoporosis Stroke	5	3.69E-06
	diabetes, type 1	5	1.38E-05 2.10E.05
	Inflammation Venous Thromboembolism	4	2.10E-05
	Chlamydia Infections Inflammation Trachoma	4	2.24E-05
	Brain Ischemia Inflammation Stroke	4	2.24E-05
	Pre-Eclampsia	4	3.32E-04
	Migraine Disorders	4	4.52E-04
Annotation Cluster 3	Chorioamnionitis Fetal Membranes, Premature Rupture Infection of amniotic sac and membranes	7	4.94E-07
(Score:4.89)	Chorioamnionitis Fetal Membranes, Premature Rupture Infection of amniotic sac and membranes Obstetric Labor, Premature Pre-Eclampsia Premature Birth	7	5.10E-07
	Coronary Artery Disease	7	1.56E-04
	Alzheimer's disease	8	7.10E-04
Annotation Cluster 4	Hodgkin Disease Inflammation	4	3.40E-06
(Score:4.44)	Sarcoidosis	5	4.99E-06
	Adenocarcinoma Stomach Neoplasms	4	5.74E-05
	kidney failure, chronic	5	2.02E-04
Apportation Cluster 5	umphama Nan Hadakin II umphama Nan Hadakin's	5	3.20E-04 3.30E-05
(Score:4.26)	Leukemia Myelogenous Chronic BCR-ABI Positive Neovascularization Pathologic	4	4.02E-05
()	Leukemia, Myelogenous, Chronic, BCR-ABL Positive	4	1.02E 00
Annotation Cluster 6	Tuberculosis, Pulmonary	5	2.31E-06
(Score:4.09)	systemic lupus erythematosus	5	8.88E-05
	hepatitis C, chronic	4	3.56E-04
	Tuberculosis	4	6.16E-04
Annotation Cluster 7	Helicobacter Infections Inflammation Precancerous Conditions Stomach Neoplasms	4	9.23E-07
(Score:4.04)	Stomach Neoplasms	5	3.54E-05
	patent ductus arteriosus	5	6.13E-05
	Cystic Fibrosis	4	1.29E-04
	stomach cancer	4	5.46E-04
	rheumatoid arthritis	4	0.003880586
Annotation Cluster 8	Infection Inflammation Premature Birth	5	5.26E-05
(50010.5.94)	Inflammation Premature Birth	5	5.77E-05
	Hematologic Premature Birth Skin Diseases	5	9.96E 04
Apportation Cluster 9	Atherosclerosis	4 7	2.07E-05
(Score:3.84)	Myocardial Infarction	7	2.07E-03
	Alzheimer's disease	8	7.10E-04
Annotation Cluster 10	Brain Ischemia Stroke	5	1.86E-05
(Score:3.78)	Peripheral Vascular Diseases	4	4.02E-05
	Cardiovascular Diseases	5	2.60E-04
	Hypercholesterolemia LDLC levels	4	0.004054968
Annotation Cluster 11	Restenosis	4	1.81E-04
(Score:3.55)	Arthritis, Rheumatoid Rheumatoid Arthritis	5	1.98E-04
A	Endometriosis	4	6.16E-04
Annotation Cluster 12 (Score:3.28)	Alcoholism Liver Cirrhosis, Alcoholic	3	2.12E-04
(50010.5.20)	Esophageai Neoplasms Hypergiycemia Oesophageai neoplasm	3	2.12E-04
	Arthritic Description Description arthropathy	3	5.00E-04
	cardiovascular	3	0.002488197
Annotation Cluster 13	Otitis Media Recurrence	3	2 47E-04
(Score:3.18)	Brucellosis	3	5.12E-04
	Graft vs Host Disease Hematologic Neoplasms Neoplasm Recurrence, Local	3	5.12E-04
	Kawasaki disease	3	6.21E-04
	Atopy	3	0.003077333
Annotation Cluster 14	Atherosclerosis Inflammation Retinal Vein Occlusion	3	1.23E-04
(Score:2.82)	Dermatitis, Atopic Eczema allergic	3	7.41E-04
	juvenile arthritis	3	0.001084437
	graft-versus-host disease	3	0.002834545
	Graft vs Host Disease	3	0.005354403
A	hepatitis C	3	0.008600238
Annotation Cluster 15 (Score: 2 80)	Uveilis, Anterior	3	1.23E-04
(00010.2.00)	rancieauus, Chronic	3	0.03E-04

	stroke, ischemic	3	0.004142278
	Glomerulonephritis, IGA	3	0.016033469
Annotation Cluster 16	giant cell arteritis	3	5.12E-04
(Score:2.76)	Malaria, Falciparum	3	0.002163435
	Malaria	3	0.004882851
Annotation Cluster 17 (Score:2.72)	Cardiovascular Diseases Inflammation	3	1.50E-04
	skin cancer, non-melanoma	3	0.001084437
	Adenoma Colorectal Neoplasms	3	0.002954755
	Depression	3	0.028362664
Annotation Cluster 18 (Score:2.68)	Endometriosis Uterine Diseases	3	1.50E-04
	Hepatitis B, Chronic	3	0.006357795
	Pulmonary Disease, Chronic Obstructive	3	0.009415863
Annotation Cluster 19 (Score:2.63)	respiratory syncytial virus	3	3.68E-04
	Q fever	3	4.61E-04
	Graves' disease Graves' disease	3	0.001490775
	Graves' disease	3	0.001579503
	Diabetes Mellitus, Insulin-Dependent Diabetes Mellitus, Type 1	3	0.006532757
	Premature Birth	3	0.01182929
	Kidney Diseases	3	0.012294446
Annotation Cluster 20	Carcinoma, Squamous Cell Mouth Neoplasms	3	0.001084437
(Score:2.47)	Helicobacter Infections Stomach Neoplasms	3	0.002377534
	Precursor Cell Lymphoblastic Leukemia-Lymphoma	3	0.015509841



Figure 8. Gene-pathway network of SFJDC against NCP. The V shapes represented pathway and the squares represent target genes in the network.

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Author contributions

YQQ, XC designed the study; YHY and MYZ performed the data collection; JYL and RL analyzed the data; XC drafted the manuscript; YQQ revised the manuscript. All authors read and approved the final manuscript.

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Data Accessibility

Publicly available databases were analyzed in our study. The active ingredients and putative target genes of SFJDC from TCMSP can be found in http://tcmspw.com/tcmsp.php. NCP-related target genes were from GeneCards (https://www. genecards.org/).

Competing Interests

The authors have declared that no competing interest exists.

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