

### Electronic Supplementary Information

Network Pharmacology Study on Mechanism of Traditional Chinese Medicine for  
Upper Respiratory Tract Infection

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The supplementary information has five tables: Table S1 and Table S2 list the information of both 46 molecules in RDN and 45 target proteins related to URTIs for molecular docking. Table S3 and Table S4 list the two topological parameters (degree and betweenness) of the nodes (molecules or target proteins) in DTN, DDN and TTN. The relationship between target protein and diseases in TTD, as well as the classification of the diseases are listed in Table S5.

**Table S1 46 molecules contained in RDN**

<b>index</b>	<b>CAS_NO.</b>	<b>UNPD ID <sup>a</sup></b>	<b>Chemical_Name</b>
1	14965-20-9	UNPD186030	Chrysosplenol-D
2	537-98-4	UNPD12047	(E)-ferulic acid
3	1014-83-1	UNPD142498	(Z)-ferulic acid
4	114653-46-2	UNPD125055	6"-p-coumaroyl genipin gentiobioside
5	63968-64-9	UNPD189689	Artemisinin
6	546-49-6	UNPD102035	Artemisia ketone
7	331-39-5	UNPD133665	Caffeic acid
8	76-22-2	UNPD59933	Camphor
9	479-91-4	UNPD186353	Casticine
10	327-97-9	UNPD106185	chlorogenic acid
11	470-82-6	UNPD63596	Cineole
12	91-64-5	UNPD21132	Coumarin
13	82638-22-0	UNPD164733	3alpha,5alpha-dihydroxy-4alpha-O-caffeoylq Uinic acid
14	5373-11-5	UNPD51223	Luteoloside
15	19587-65-6	UNPD135322	Eupatin
16	470-08-6	UNPD22238	(+)-beta-fenchol
17	1632-73-1	UNPD26605	(-)-beta-fenchol
18	4695-62-9	UNPD30210	(-)-alpha-fenchol
19	2217-2-9	UNPD7069	(+)-alpha-fenchol
20	1135-24-6	UNPD168255	3-O-methyl caffeic acid
21	6902-77-8	UNPD70448	Genipin
22	29307-60-6	UNPD158162	Genipin-1-beta-gentiobioside
23	27741-01-1	UNPD106583	Geniposidinsaeure
24	106-24-1	UNPD171634	Geraniol
25	482-36-0	UNPD127168	Hyperoside
26	89919-61-9	UNPD101522	Isochlorogenic acid A
27	17912-89-9	UNPD13564	4,5-di-O-caffeoylquinic acid
28	480-19-3	UNPD60650	Isorhamnetin
29	78-70-6	UNPD106513	(3R)-()-Linalool
30	126-90-9	UNPD139439	(3S)-()-Linalool
31	491-70-3	UNPD149880	Luteolin
32	906-33-2	UNPD129293	neochlorogenic acid

33	99-50-3	UNPD60430	Protocatechuic acid
34	117-39-5	UNPD49205	Quercetin
35	153-18-4	UNPD150726	Rutin
36	69-72-7	UNPD59192	salicylic acid
37	21149-19-9	UNPD49553	Santolina alcohol
38	301-16-6	UNPD130563	Scoparin
39	92-61-5	UNPD123796	Scopoetine
40	22864-93-3	UNPD138269	Secologansaeure
41	58822-47-2	UNPD26834	Secoxyloganin
42	60077-47-6	UNPD86130	7-epi-vogeloside
43	57378-72-0	UNPD124411	Isochlorogenic acid C
44	123372-74-7	UNPD48475	Methyl 4-O-caffeoylquinat
45	114637-83-1	UNPD189327	4,5- <i>di-O</i> -caffeoylquinat
46	29708-87-0	UNPD148585	Methyl 5- <i>O</i> -caffeoylquinat

<sup>a</sup> UNPD: universal natural product database, which was constructed by Xiao-Jie Xu professor et al ( <http://pkuxxj.pku.edu.cn/UNPD/> ).

**Table S2 45 proteins related to URTIs and their PDB entry**

<b>Protein</b>	<b>Protein_name</b>	<b>PDB code</b>	<b>Uniprot code</b>
3C proteases (CVA16)	3C proteases (Polyprotein)	3SJI	C8CIL7
3C protease (EV71)	3C proteases (Polyprotein)	3SJO	E0WWC7
RdRp (3D(pol)) (EV71)	RNA-dependent RNA polymerase(Polyprotein)	3N6M	D3K0N8
HA (infl A)	Hemagglutinin	3EYM	P03437
PB2 (infl A)	Polymerase basic protein 2	2VQZ	P31345
M2 (infl A)	Matrix protein 2	2RLF	P63231
NP (infl A)	Nucleocapsid protein	3RO5	Q1K9H2
PA (infl A)	Polymerase acidic protein	3HW4	Q9Q0U9
NA (infl A)	Neuraminidase	1XOE	P03472
NA (infl B)	Neuraminidase	1NSD	P27907
HN (PIV 3)	Haemagglutinin-neuraminidase Glycoprotein	1V3E	Q6WJ03
3C protease (HRV A2)	Type 2 rhinovirus 3C protease	1CQQ	P04936
VP1 (HRV 1A)	Rhinovirus coat protein (Subunit VP1)	2HWD	P23008
VP1 (HRV B14)	Coat protein VP1	1NCQ	P03303

F protein (RSV)	Fusion glycoprotein F0	3KPE	P03420
PDE 4A	cAMP-specific 3',5'-cyclic Phosphodiesterase 4A	2QYK	P27815
H1R	Histamine H1 receptor	3RZE	P35367
PDE 4B	cAMP-specific 3',5'-cyclic Phosphodiesterase 4B	1XLX	Q07343
PDE 4D	cAMP-specific 3',5'-cyclic Phosphodiesterase 4D	3G4K	Q08499
COX-2	Prostaglandin G/H synthase 2	3LN1	P35354
COX-1	Prostaglandin G/H synthase 1	3N8X	P23219
sPLA2	Phospholipase A2,membrane associated	1J1A	P14555
Na, K-ATPase $\alpha$	Sodium/potassium-transporting ATPase subunit alpha-1	3N23	P05024
LSD1	Lysine-specific histone demethylase 1	2Z3Y	O60341
TNF- $\alpha$	Tumor necrosis factor	2AZ5	P01375
eNOS	Endothelial Nitric-oxide synthase	1M9M	P29474
iNOS	Inducible Nitric oxide synthase	4NOS	P35228
CXCR4	C-X-C chemokine receptor type 4	3ODU	P61073
p38 MAPK	Mitogen-activated protein kinase 12	1KV1	Q16539
JNK2	Mitogen-activated protein kinase 9	3NPC	P45984
JNK1	Mitogen-activated protein kinase 8	3ELJ	P45983
JNK3	Mitogen-activated protein kinase 10	3TTI	P53779
ERK1	Mitogen-activated protein kinase 3	2ZOQ	P27361
ERK2	Mitogen-activated protein kinase 1	1PME	P28482
PIK3C3	Phosphatidylinositol 3-kinase catalytic subunit type 3	3LS8	Q8NEB9
PKC- $\beta$	Protein kinase C beta type	2I0E	P05771
PKC- $\alpha$	Protein kinase C alpha type	3IW4	P17252
Caspase-3	Caspase-3	1GFW	P42574
IRAK4	Interleukin-1 receptor-associated kinase-4	2NRU	Q9NWZ3
SAH	Human S-adenosylhomocysteine hydrolase	1LI4	P23526
MEK1	Dual specificity mitogen-activated protein kinase kinase 1	1S9J	Q02750
mPGES-1	Prostaglandin E synthase	3DWW	O14684
OMP decarboxylase	Orotidine 5'-monophosphate decarboxylase	1EIX	P08244

IMPDH2	Inosine-5'-monophosphate dehydrogenase 2	1NF7	P12268
IMPDH1	Inosine-5'-monophosphate dehydrogenase 1	1JCN	P20839

**Table S3 the degree and betweenness of the molecules in the DDN and DTN**

Molecules	DTN		Molecules	DDN	
	Betweenness	Degree		Betweenness	Degree
UNPD189689	0.428	24	UNPD70448	0.308	16
UNPD149880	0.165	14	UNPD189689	0.158	21
UNPD49205	0.055	8	UNPD51223	0.132	18
UNPD51223	0.133	8	UNPD133665	0.065	10
UNPD130563	0.054	7	UNPD149880	0.045	16
UNPD124411	0.044	6	UNPD130563	0.031	14
UNPD127168	0.024	5	UNPD127168	0.029	14
UNPD60650	0.017	5	UNPD106583	0.026	14
UNPD106583	0.014	4	UNPD135322	0.025	12
UNPD135322	0.021	4	UNPD60650	0.022	9
UNPD164733	0.012	4	UNPD124411	0.021	16
UNPD70448	0.197	4	UNPD49205	0.017	14
UNPD13564	0.009	3	UNPD164733	0.015	10
UNPD186353	0.007	3	UNPD101522	0.006	12
UNPD101522	0.002	2	UNPD13564	0.004	9
UNPD133665	0.029	2	UNPD186353	0.003	8
UNPD148585	0.001	2	UNPD148585	0.003	9
UNPD186030	0.001	2	UNPD186030	0.001	10
UNPD48475	0.001	2	UNPD48475	0.000	6
UNPD102035	0	1	UNPD189327	0	1
UNPD106185	0	1	UNPD125055	0	7
UNPD125055	0	1	UNPD158162	0	5
UNPD129293	0	1	UNPD22238	0	8
UNPD158162	0	1	UNPD26605	0	8
UNPD189327	0	1	UNPD30210	0	8
UNPD21132	0	1	UNPD59933	0	8
UNPD22238	0	1	UNPD102035	0	8
UNPD26605	0	1	UNPD63596	0	8

UNPD30210	0	1	UNPD7069	0	8
UNPD59933	0	1	UNPD21132	0	2
UNPD63596	0	1	UNPD129293	0	7
UNPD7069	0	1			

**Table S4 the degree and betweenness of the target proteins in the TTN and DTN**

Protein	DTN		Protein	TTN	
	Betweenness	Degree		Betweenness	Degree
O14684	0.212	9	P29474	0.039	30
O60341	0.074	8	P05771	0.038	31
P14555	0.110	8	P14555	0.038	29
P29474	0.096	8	O60341	0.036	31
P17252	0.047	6	P23219	0.028	27
P23008	0.061	6	P17252	0.026	30
P23219	0.115	5	P23008	0.021	30
P35228	0.027	5	Q02750	0.020	20
P53779	0.027	5	P35228	0.019	28
Q16539	0.029	5	P03437	0.016	29
P03437	0.018	4	P20839	0.016	29
P05771	0.040	4	P63231	0.015	26
P35354	0.051	4	Q9Q0U9	0.015	26
Q02750	0.067	4	Q16539	0.014	26
P08244	0.069	3	P35354	0.013	18
P20839	0.009	3	P05024	0.010	28
P27815	0.008	3	P28482	0.010	28
P28482	0.008	3	P45984	0.010	28
Q9Q0U9	0.013	3	P53779	0.008	25
D3K0N8	0.002	2	P08244	0.006	8
P05024	0.004	2	Q8NEB9	0.006	25
P12268	0.002	2	P12268	0.003	16
P45984	0.004	2	P27815	0.002	11
P61073	0.030	2	Q08499	0.001	24
P63231	0.009	2	O14684	0.001	4
Q08499	0.004	2	D3K0N8	0.000	7
Q8NEB9	0.003	2	P03472	0	13

P01375	0	1	P04936	0	5
P03303	0	1	P01375	0	23
P03472	0	1	P03303	0	23
P04936	0	1	P35367	0	7
P23526	0	1	P23526	0	13
P31345	0	1	Q07343	0	23
P35367	0	1	P61073	0	23
Q07343	0	1	Q9NWZ3	0	7
Q1K9H2	0	1	Q1K9H2	0	23
Q9NWZ3	0	1			

**Table S5 the relationship between potential targets and diseases from Therapeutic Target database, and the classification of diseases**

Protein	Disease	Classification	Protein	Disease	Classification
P29474	Sepsis	Bacterial Infections and Mycoses	P35354	Cancer	Neoplasms
Q16539	Endotoxemia	Bacterial Infections and Mycoses	P35354	Carcinoma in situ	Neoplasms
Q9NWZ3	Sepsis	Bacterial Infections and Mycoses	P35354	Colorectal cancer	Neoplasms
P01375	Behcet's disease	Cardiovascular Diseases	P35354	Lung cancer	Neoplasms
P01375	Congestive heart failure	Cardiovascular Diseases	P35354	Meningioma	Neoplasms
P01375	Heart failure	Cardiovascular Diseases	P35354	Peutz-Jeghers syndrome	Neoplasms
P05771	Diabetic retinopathy	Cardiovascular Diseases	P35354	Prostate cancer	Neoplasms
P14555	Atherosclerosis	Cardiovascular Diseases	P35354	Renal cell carcinoma	Neoplasms
P14555	Coronary Artery Disease	Cardiovascular Diseases	P45984	Cancer	Neoplasms
P23219	Cardiovascular disease	Cardiovascular Diseases	P61073	Breast cancer	Neoplasms
P29474	Cardiovascular disease	Cardiovascular Diseases	P61073	Multiple Myeloma	Neoplasms
P29474	Coronary	Cardiovascular	P61073	Non-Hod	Neoplasms

	Artery Disease	Diseases		gkin's Lymphom a	
P29474	Hypertension	Cardiovascular Diseases	P61073	Ovarian cancer	Neoplasms
P35228	Ischemia reperfusion injuries	Cardiovascular Diseases	Q02750	Breast cancer	Neoplasms
P35354	Abdominal aortic aneurysm	Cardiovascular Diseases	Q02750	Prostate cancer	Neoplasms
P35354	Gestational hypertension	Cardiovascular Diseases	Q07343	Chronic lymphocy tic leukemia	Neoplasms
P35354	Myocardial infarction	Cardiovascular Diseases	Q16539	Multiple myeloma	Neoplasms
P35354	Stroke	Cardiovascular Diseases	P35354	Malignant mesotheli oma	Neoplasms
P35367	Hypotension	Cardiovascular Diseases	P35367	Acute lymphobl astic leukaemia	Neoplasms
P61073	Multiple Myeloma	Cardiovascular Diseases	P35354	Genitouri nary tumors	Neoplasms
Q16539	Multiple myeloma	Cardiovascular Diseases	P35354	Orophary ngeal squamous cell carcinoma	Neoplasms
Q16539	Thrombosis	Cardiovascular Diseases	P61073	Prostate cancer (metastati c)	Neoplasms
P53779	Ischemic stroke	Cardiovascular Diseases	P01375	Solid tumor	Neoplasms
P01375	Hyperimmuno globulinemia D	Congenital, Hereditary, and Neonatal Diseases and Abnormalities	P05771	B-lineage malignanc ies	Neoplasms
P35354	Adenomatous	Congenital,	P61073	Late-stage	Neoplasms



	polyposis	Hereditary, and Neonatal Diseases and Abnormalities		Solid tumors	
P35354	Peutz-Jeghers syndrome	Hereditary, and Neonatal Diseases and Abnormalities	P01375	Hyperimmunoglobulinemia D	Nervous System Diseases
P01375	Crohn's disease	Digestive System Diseases	P28482	Neurodegenerative diseases	Nervous System Diseases
P20839	Inflammatory bowel disease	Digestive System Diseases	P35354	Alzheimer's disease	Nervous System Diseases
P29474	Colon cancer	Digestive System Diseases	P35354	Carpal tunnel syndrome	Nervous System Diseases
P35354	Adenomatous polyposis	Digestive System Diseases	P35354	Meningioma	Nervous System Diseases
P35354	Colorectal cancer	Digestive System Diseases	P35354	Stroke	Nervous System Diseases
P35354	Peutz-Jeghers syndrome	Digestive System Diseases	P35367	Epilepsy	Nervous System Diseases
P45984	Crohn's disease	Digestive System Diseases	Q16539	Alzheimer's disease	Nervous System Diseases
Q16539	Crohn's disease	Digestive System Diseases	P53779	Ischemic stroke	Nervous System Diseases
P01375	Diabetes Mellitus Type 2	Endocrine System Diseases	P53779	Neurological diseases	Nervous System Diseases
P05771	Diabetes mellitus	Endocrine System Diseases	P01375	Diabetes Mellitus Type 2	Nutritional and Metabolic Diseases
P05771	Diabetic retinopathy	Endocrine System Diseases	P01375	Hyperimmunoglobulinemia D	Nutritional and Metabolic Diseases

P61073	Ovarian cancer	Endocrine System Diseases	P05771	Diabetes mellitus	Nutritional and Metabolic Diseases
P01375	Behcet's disease	Eye Diseases	P45984	Obesity	Nutritional and Metabolic Diseases
P05771	Diabetic retinopathy	Eye Diseases	Q16539	Insulin resistance	Nutritional and Metabolic Diseases
P05771	Macular edema	Eye Diseases	P01375	Periodic fever syndrome	Pathological Conditions, Signs and Symptoms
P35354	Bladder cancer	Female Urogenital Diseases and Pregnancy Complications	P35354	Pyresis	Pathological Conditions, Signs and Symptoms
P35354	Endometriosis	Female Urogenital Diseases and Pregnancy Complications	P35354	Vascular lesion regression	Pathological Conditions, Signs and Symptoms
P35354	Gestational hypertension	Female Urogenital Diseases and Pregnancy Complications	P35367	Systemic arterial vasodilation	Pathological Conditions, Signs and Symptoms
P35354	Renal cell carcinoma	Female Urogenital Diseases and Pregnancy Complications	Q16539	Cytokine-mediated diseases	Pathological Conditions, Signs and Symptoms
P61073	Ovarian cancer	Female Urogenital Diseases and Pregnancy Complications	P01375	Chronic inflammatory diseases	Pathological Conditions, Signs and Symptoms
Q16539	Crescentic glomerulonephritis	Female Urogenital Diseases and	P23219	Chronic inflammatory	Pathological Conditions, Signs and

		Pregnancy Complications			diseases	Symptoms
P01375	Hyperimmunoglobulinemia D	Hemic Lymphatic Diseases	and	P35354	Inflammatory diseases	Pathological Conditions, Signs and Symptoms
P27815	Chronic lymphocytic leukemia	Hemic Lymphatic Diseases	and	P35367	Intimal hyperplasia	Pathological Conditions, Signs and Symptoms
P61073	Non-Hodgkin's Lymphoma	Hemic Lymphatic Diseases	and	P35367	Nausea and vomiting	Pathological Conditions, Signs and Symptoms
Q07343	Chronic lymphocytic leukemia	Hemic Lymphatic Diseases	and	P29474	Inflammation	Pathological Conditions, Signs and Symptoms
P28482	Proliferative diseases	Hemic Lymphatic Diseases	and	P29474	Sepsis	Pathological Conditions, Signs and Symptoms
P35367	Acute lymphoblastic leukaemia	Hemic Lymphatic Diseases	and	P35228	Ischemia reperfusion injuries	Pathological Conditions, Signs and Symptoms
P01375	Hyperimmunoglobulinemia D	Immune System Diseases		P35354	Dysmenorrhea	Pathological Conditions, Signs and Symptoms
P27815	Chronic lymphocytic leukemia	Immune System Diseases		P35354	Inflammation	Pathological Conditions, Signs and Symptoms
P35367	Seasonal allergic rhinitis	Immune System Diseases		P35354	Pain	Pathological Conditions, Signs and Symptoms
P61073	Acquired Immune Deficiency Syndrome	Immune System Diseases		P35354	Pathological angiogenesis	Pathological Conditions, Signs and Symptoms
P61073	HIV Infection	Immune System Diseases		P35367	Ischemia	Pathological Conditions,



						Diseases
P35354	Renal carcinoma	cell	Male Urogenital Diseases	P23008	Acute nasopharyngitis	Respiratory Tract Diseases
Q02750	Prostate cancer		Male Urogenital Diseases	P35354	Lung cancer	Respiratory Tract Diseases
P61073	Prostate cancer (metastatic)		Male Urogenital Diseases	P35367	Seasonal allergic rhinitis	Respiratory Tract Diseases
Q16539	Crescentic glomerulonephritis		Male Urogenital Diseases	Q07343	Asthma	Respiratory Tract Diseases
P29474	Schizophrenia		Mental Disorders	Q08499	Asthma	Respiratory Tract Diseases
P35354	Alzheimer's disease		Mental Disorders	Q16539	Adult respiratory distress syndrome	Respiratory Tract Diseases
P35367	Anxiety disorder		Mental Disorders	P35367	Chronic urticaria	Skin and Connective Tissue Diseases
Q16539	Alzheimer's disease		Mental Disorders	P01375	Behcet's disease	Skin and Connective Tissue Diseases
O14684	Rheumatoid arthritis		Musculoskeletal Diseases	P35354	Breast cancer	Skin and Connective Tissue Diseases
P01375	Rheumatic diseases		Musculoskeletal Diseases	P35354	Peutz-Jeghers syndrome	Skin and Connective Tissue Diseases
P01375	Rheumatoid arthritis		Musculoskeletal Diseases	P61073	Breast cancer	Skin and Connective Tissue Diseases
P35354	Arthritis		Musculoskeletal Diseases	Q02750	Breast cancer	Skin and Connective Tissue Diseases

P35354	Osteoarthritis	Musculoskeletal Diseases	Q16539	Psoriasis	Skin and Connective Tissue Diseases
P35354	Rheumatoid arthritis	Musculoskeletal Diseases	Q16539	Skin diseases	Skin and Connective Tissue Diseases
Q16539	Rheumatoid arthritis	Musculoskeletal Diseases	P01375	Behcet's disease	Stomatognathic Diseases
P12268	Leukemia	Neoplasms	P35367	Epidermal hyperplasia	Virus Diseases
P17252	Leukemia	Neoplasms	P63231	Influenza	Virus Diseases
P17252	Prostate cancer	Neoplasms	P03437	Influenza A virus infection	Virus Diseases
P27815	Chronic lymphocytic leukemia	Neoplasms	P23008	Acute nasopharyngitis	Virus Diseases
P29474	Colon cancer	Neoplasms	P23526	Viral infection	Virus Diseases
P35354	Adenomatous polyposis	Neoplasms	P61073	Acquired Immune Deficiency Syndrome	Virus Diseases
P35354	Bladder cancer	Neoplasms	P61073	HIV Infection	Virus Diseases
P35354	Breast cancer	Neoplasms	P35354	Carpal tunnel syndrome	Wounds and Injuries

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