

# Supplementary Materials

## Uncovering the anti-lung cancer mechanisms of the herbal drug FDY2004 by network pharmacology

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## Supplementary Figures

	Category	Term name	Count	Percent [%]	p-value
Gene ontology	Biological process	Cellular response to chemical stimulus	101	2.95	1.93E-39
		Cellular response to chemical stress	27	7.34	1.25E-15
		Cellular response to cytokine stimulus	43	3.76	1.74E-15
		Cellular response to growth factor stimulus	21	2.87	4.45E-04
		Cellular response to radiation	14	7.25	6.53E-07
		Cellular response to stimulus	117	1.50	9.93E-20
		Cytokine-mediated signaling pathway	37	4.57	1.54E-15
		Integrated stress response signaling	4	18.18	4.58E-02
		Lymphocyte activation	19	2.45	1.82E-02
		Lymphocyte differentiation	13	3.46	1.52E-02
		Regulation of angiogenesis	16	3.88	2.69E-04
		Regulation of apoptotic process	63	3.92	2.56E-26
		Regulation of apoptotic signaling pathway	25	6.01	3.09E-12
		Regulation of catabolic process	24	2.31	3.01E-03
		Regulation of catalytic activity	59	2.46	6.18E-14
		Regulation of cell death	67	3.80	1.04E-27
		Regulation of cell growth	15	3.55	2.07E-03
		Regulation of cell migration	37	3.73	1.09E-12
		Regulation of cell motility	38	3.61	1.17E-12
		Regulation of cell population proliferation	55	3.09	3.85E-17
		Regulation of cellular localization	24	2.39	1.62E-03
		Regulation of cellular response to oxidative stress	7	7.37	1.84E-02
		Regulation of cellular response to stress	25	3.19	3.17E-06
		Regulation of cytokine production	23	2.76	2.19E-04
		Regulation of immune response	23	2.26	7.20E-03
		Regulation of immune system process	44	2.67	1.86E-10
		Regulation of inflammatory response	23	5.30	6.66E-10
		Regulation of kinase activity	28	3.04	8.36E-07
		Regulation of leukocyte adhesion to vascular endothelial cell	7	18.42	3.04E-05
		Regulation of leukocyte cell-cell adhesion	19	5.65	2.96E-08
		Regulation of leukocyte differentiation	14	4.76	1.44E-04
		Regulation of metabolic process	95	1.31	6.28E-08
		Regulation of programmed cell death	65	3.98	8.24E-28
		Regulation of response to oxidative stress	7	6.73	3.34E-02
		Regulation of response to stimulus	84	1.91	5.69E-16
		Regulation of response to stress	46	2.98	7.02E-13
		Regulation of signal transduction	71	2.19	2.10E-15
		Regulation of signaling	76	2.05	2.22E-15
		Reponse to chemical	113	2.35	1.82E-37
		Reponse to cytokine	46	3.72	1.18E-16
Reponse to drug	27	6.44	3.42E-14		
Reponse to growth factor	21	2.77	8.26E-04		
Reponse to radiation	28	6.03	4.45E-14		
Reponse to stimulus	124	1.31	7.20E-17		
Reponse to toxic substance	13	5.20	1.56E-04		

	Category	Term name	Count	Percent [%]	p-value
Gene ontology	Cellular components	Cell surface	24	2.64	1.83E-05
		Chromatin	22	1.75	4.57E-02
		Cytoplasm	113	0.96	1.12E-03
		Cytosol	61	1.17	1.28E-02
		Death-inducing signaling complex	3	33.33	9.92E-03
		Endoplasmic reticulum	37	2.01	3.84E-06
		Extracellular matrix	14	2.53	2.01E-02
		Extracellular region	56	1.22	9.27E-03
		Membrane region	12	3.51	2.95E-03
		Nucleoplasm	49	1.22	4.29E-02
		Organelle	127	0.91	2.44E-04
		Plasma membrane	65	1.15	9.60E-03
		Protein-containing complex	63	1.14	1.77E-02
		Transcription regulator complex	13	2.91	9.09E-03
	Vesicle	54	1.34	8.84E-04	
	Molecular function	Catalytic activity	96	1.63	3.39E-16
		Drug binding	7	6.86	8.59E-03
		Enzyme binding	55	2.41	3.71E-13
		Hormone binding	6	6.98	3.34E-02
		Kinase activity	23	2.85	2.86E-05
		Kinase binding	22	2.91	3.88E-05
		Ligand-activated transcription factor activity	9	20.45	2.47E-08
		Molecular transducer activity	26	1.76	2.88E-02
		Nuclear receptor activity	9	20.45	2.47E-08
		Phosphatase binding	13	6.63	2.20E-06
		Signaling receptor activity	26	1.76	2.88E-02
		Signaling receptor binding	35	2.09	1.49E-05
		Small molecule binding	49	1.90	1.98E-07
Steroid hormone receptor activity		9	16.36	2.07E-07	
Transcription factor binding	28	3.97	3.14E-10		
Pathway	KEGG	Apoptosis	13	9.56	2.00E-05
		Cellular senescence	11	7.05	3.31E-03
		EGFR tyrosine kinase inhibitor resistance	11	13.92	3.67E-06
		ErbB signaling pathway	8	9.52	4.78E-03
		Estrogen signaling pathway	11	8.03	9.77E-04
		Focal adhesion	13	6.50	1.53E-03
		HIF-1 signaling pathway	12	11.01	1.26E-05
		MAPK signaling pathway	17	5.78	3.57E-04
		Non-small cell lung cancer	9	13.24	1.02E-04
		p53 signaling pathway	8	10.96	1.71E-03
		Pathways in cancer	39	7.37	1.17E-14
		PD-L1 expression and PD-1 checkpoint pathway in cancer	11	12.36	1.29E-05
		PI3K-Akt signaling pathway	22	6.23	3.03E-06
		Platinum drug resistance	9	12.50	1.67E-04
		Ras signaling pathway	14	6.06	1.59E-03
		Small cell lung cancer	10	10.87	1.63E-04
		TNF signaling pathway	17	15.18	1.38E-10
VEGF signaling pathway	8	13.56	3.40E-04		

**Supplementary Figure S1. Functional enrichment analysis for the lung cancer-related targets of FDY2004.**

## Supplementary Tables

**Supplementary Table S1. General information and reports on evidence of biological activities of FDY2004 and its herbal constituents**

	Herbal medicines			
	Moutan Radicis Cortex	Persicae Semen	Rhei Radix et Rhizoma	FDY2004
Scientific name	<i>Paeonia suffruticosa</i> Andrews	<i>Prunus persica</i> Batsch	<i>Rheum palmatum</i> Linné	-
Vernacular name	<i>Mudanpi</i>	<i>Taoren</i>	<i>Dahuang</i>	-
Species	Paeoniaceae	Rosaceae	Rheum	-
Traditional uses	Treatment for allergic diseases, atherosclerosis, cutaneous diseases, diabetes, infection, and inflammation [1-4]	Treatment for dysmenorrhea, endometriosis, hypermenorrhea, and infertility [5-8]	Treatment for abdominal pain, constipation, fever, and intense and profuse sweating [9, 10]	-
Parts used	Root barks	Dried ripe seed	Dried root and rhizome	-
Collection site	China	Republic of South Africa	China	-
Yield	-	-	-	19.07 ± 2.14 % (w/w) [11]

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Biological activities	Analgesic, anti-allergic, anticancer, antidiabetic, anti-inflammatory, anti-oxidative, antipyretic, hepatoprotective, immunomodulatory, and neuroprotective activities [4, 12-14]	Anti-allergic, anticancer, antidiabetic, anti-inflammatory, and anti-oxidative activities [15-20]	Anticancer, anti-fibrotic, anti-inflammatory, anti-oxidative, and gastrointestinal function regulatory activities [21-23]	Anticancer and antioxidant activities [11]
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**Supplementary Table S2. Chemical components of FDY2004.**

Herbal medicines	Chemical compounds	OB	Caco-2	DL
MRC	(+)-Catechin	54.83	-0.03	0.24
MRC	5-[[5-(4-methoxyphenyl)-2-furyl]methylene]barbituric acid {ZINC9320615}	43.44	0.09	0.3
MRC	Caffeic acid	25.76	0.21	0.05
MRC	Kaempferol	41.88	0.26	0.24
MRC	Mairin	55.38	0.73	0.78
MRC	Paeoniflorin	10.22	-1.69	0.79
MRC	Paeoniflorin_qt	68.18	-0.34	0.4
MRC	Paeonol	28.79	0.93	0.04
MRC	Pentagalloylglucose	3.01	-3.08	0.21
MRC	Quercetin	46.43	0.05	0.28
MRC	(1R)-()-Nopinone	57.86	1.23	0.05
MRC	1-(2,3-dihydroxy-4-methoxyphenyl)ethanone	32.96	0.81	0.05

MRC	3-[(2S,3R,4S,5S,6R)-6-[[[(2R,3R,4R)-3,4-dihydroxy-4-(hydroxymethyl)oxolan-2-yl]oxymethyl]-3,4,5-trihydroxyoxan-2-yl]oxy-4,5-dihydroxybenzoic acid	5.6	-2.54	0.63
MRC	3-acetyl-4-hydroxybenzoic acid	37.58	-0.04	0.05
MRC	3-Hydroxy-4-methoxyacetophenone	22.32	0.85	0.04
MRC	4-O-Methylpaeoniflorin	25.71	-1.27	0.78
MRC	4-O-Methylpaeoniflorin_qt	67.24	0.15	0.43
MRC	6-Hydroxycoumarin	15.8	0.73	0.05
MRC	6-o-vanillyoxypaeoniflorin	10.91	-1.58	0.54
MRC	6-o-vanillyoxypaeoniflorin_qt 2	17.71	-0.61	0.37
MRC	apiopaeonoside	16.73	-1.79	0.64
MRC	Apocynin	31.71	0.74	0.04
MRC	Benzoyl paeoniflorin	31.14	-1.35	0.54
MRC	Beta-D-Apiose	118.53	-1.46	0.03
MRC	Beta-sitosterol-beta-d-glucoside	19.58	-0.17	0.62
MRC	Beta-sitosterol-beta-d-glucoside_qt	25.32	1.28	0.75

MRC	BOX	31.55	0.54	0.02
MRC	Sitosterol	36.91	1.32	0.75
MRC	Delta 7-stigmastenol	25.32	1.31	0.75
MRC	DEP	52.19	0.72	0.07
MRC	Eugenol	56.24	1.35	0.04
MRC	Galloyl-oxypaeoniflorin	3.2	-2.18	0.39
MRC	Galloyl-oxypaeoniflorin Qt 2	26.21	-0.54	0.44
MRC	Hexanoic acid	73.08	0.8	0.01
MRC	Methyl salicylate	42.55	1.05	0.03
MRC	Mudanoside A	13.39	-1.42	0.29
MRC	Mudanpinoic,acid,a	13.86	0.6	0.65
MRC	Mudanpioside H	6.77	-1.63	0.61
MRC	Mudanpioside H Qt 2	42.36	-0.39	0.37
MRC	octadecyl (E)-3-(3,4-dihydroxyphenyl)prop-2-enoate	3.18	0.98	0.55
MRC	Oleanic acid	8.41	1.14	0.77



MRC	Oleanolic acid	29.02	0.59	0.76
MRC	Oleic acid	33.13	1.17	0.14
MRC	Oxypaeoniflorin	12.98	-1.91	0.78
MRC	Oxypaeoniflorin_qt	19.4	-0.77	0.44
MRC	Paeonidanin	24.64	-1.28	0.78
MRC	Paeonidanin_qt	65.31	-0.09	0.35
MRC	Paeonolide	6.3	-1.42	0.64
MRC	Paeonoside	18.52	-0.86	0.24
MRC	PHB	30.15	0.39	0.03
MRC	Trochol	15.48	0.84	0.78
MRC	Vanillic acid	35.47	0.43	0.04
MRC	WLN: QR CQ DV1	36.49	0.67	0.03
PS	(+)-Epicatechin	48.96	0.02	0.24
PS	Amygdalin	4.42	-1.91	0.61
PS	Campesterol	37.58	1.31	0.71

PS	GA120	84.85	0.38	0.45
PS	GA121-Isolactone	72.7	-0.26	0.54
PS	GA122	64.79	-0.17	0.5
PS	GA122-Isolactone	88.11	-0.18	0.54
PS	Gibberellin A119	76.36	-0.12	0.49
PS	Gibberellin A44	101.61	-0.13	0.54
PS	Gibberellin A7	73.8	-0.18	0.5
PS	Hederagenin	36.91	1.32	0.75
PS	$\alpha$ 1-Sitosterol	43.28	1.41	0.78
PS	(2S)-2-phenyl-2-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyacetic acid	8.27	-1.22	0.2
PS	(2S,3R,4S,5S,6R)-2-(benzyloxy)-6-methylol-tetrahydropyran-3,4,5-triol	17.14	-0.71	0.14
PS	[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl] (E)-3-(4-hydroxyphenyl)prop-2-enoate	9.8	-1.09	0.26
PS	[2-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyphenyl]methyl (E)-3-(3,4-dihydroxyphenyl)prop-2-enoate	8.22	-1.05	0.69

PS	2,3-didehydro GA69	14.28	-0.17	0.5
PS	2,3-didehydro GA77	88.08	-0.67	0.53
PS	2,3-didehydro GA9	17.03	0.37	0.45
PS	24-Methylenecycloartanol	10.4	1.42	0.79
PS	3-feruloylquinic acid	19.31	-1.01	0.36
PS	3-O-p-coumaroylquinic acid	37.63	-1.2	0.29
PS	4a-formyl-7alpha-hydroxy-1-methyl-8-methylidene-4aalpha,4bbeta-gibbane-1alpha,10beta-dicarboxylic acid	88.6	-0.75	0.46
PS	7-dehydroavenasterol	10.03	1.36	0.76
PS	alexandrin	20.63	-0.2	0.63
PS	Amygdalinic acid	4.15	-2.32	0.63
PS	Benzyl Beta -gentiobioside	3.46	-2.07	0.56
PS	Benzyl glucopyranoside	12.39	-0.7	0.14
PS	Beta-D-Glucopyranoside, 2-((benzoyloxy)methyl)-4-hydroxyphenyl	13.51	-1.03	0.53
PS	Campesterol-3-O-β-D-(6-O-oleyl)glucopyranoside	27.03	0.04	0.17

PS	Campesterol-3-O- $\beta$ -D-(6-O-palmityl)glucopyranoside	25.65	0.02	0.19
PS	Campesterol-3-O- $\beta$ -D-glucopyranoside	20.49	-0.22	0.67
PS	Campesterol-3-O- $\beta$ -D-glucopyranoside_qt	7.86	1.29	0.72
PS	cis-p-Coumarate	45.98	0.46	0.04
PS	D-mandelonitrile	48.26	0.67	0.02
PS	EIC	41.9	1.16	0.14
PS	GA118	10.41	-0.6	0.53
PS	GA121	14.13	-0.26	0.5
PS	GA126	11.8	-0.64	0.53
PS	GA16	14.26	-0.63	0.53
PS	GA30	61.72	-0.83	0.54
PS	GA54	64.21	-0.5	0.53
PS	GA60	93.17	-0.79	0.53
PS	GA61	14.82	-0.22	0.49
PS	GA63	65.54	-0.57	0.54

PS	GA69	17.67	-0.21	0.49
PS	GA70	14.04	-0.23	0.49
PS	GA77	87.89	-0.64	0.53
PS	GA87	68.85	-1.14	0.57
PS	GA95	20.01	-0.24	0.49
PS	GA97	10.12	-0.89	0.47
PS	Gibberellin 17	94.64	-0.87	0.49
PS	Grandidentatin	10.56	-0.9	0.54
PS	Heriguard	11.93	-1.03	0.33
PS	Methyl-alpha-D-fructofuranoside	65.63	-1.09	0.05
PS	MGL	24.46	-1.13	0.05
PS	MNN	48.36	0.68	0.02
PS	Triolein	27.27	0.97	0.13
PS	Prunasin	12.61	-0.79	0.18
PS	RMN	43.67	0.11	0.03

PS	Salireposide_qt	24.3	0.63	0.12
PS	WLN: Q1R	58.68	1.08	0.01
PS	$\beta$ -sitosterol 3-O- $\beta$ -D-(6-O-oleyl)glucopyranoside	26.94	-0.02	0.16
PS	$\beta$ -sitosterol-3-(6-palmitoyl)glucopyranoside	26.07	0.1	0.18
RRR	(-)-Catechin	49.68	-0.03	0.24
RRR	Aloe-emodin	83.38	-0.12	0.24
RRR	Chrysophanol	18.64	0.62	0.21
RRR	Daucosterol {Sitogluside}	20.18	0.09	0.69
RRR	Daucosterol_qt	35.89	1.35	0.7
RRR	Emodin	24.4	0.22	0.24
RRR	Eupatin	50.8	0.53	0.41
RRR	Mutatochrome {Citroxanthin}	48.64	1.97	0.61
RRR	Palmidin A	32.45	-0.36	0.65
RRR	Physcion	22.29	0.52	0.27
RRR	Rhein	47.07	-0.2	0.28

RRR	Toralactone	46.46	0.86	0.24
RRR	Hispidulin	29.95	0.47	0.27
RRR	Procyanidin B2 3,3'-di-O-gallate	42.63	-1.86	
RRR	Palmidin B	1.21	-0.11	0.69
RRR	(-)-Epicatechin-pentaacetate	8	-0.59	0.77
RRR	(+)-Catechin-pentaacetate	27.58	-0.65	0.77
RRR	(9S)-9-[(9R)-2-carboxy-4,5-dihydroxy-10-oxo-9H-anthracen-9-yl]-4,5-dihydroxy-10-oxo-9H-anthracene-2-carboxylic acid	27.75	-0.91	0.57
RRR	[(2R,3R,4S,5R,6R)-3,5-dihydroxy-2-(3,4,5-trihydroxybenzoyl)oxy-6-[(3,4,5-trihydroxybenzoyl)oxymethyl]oxan-4-yl] 3,4,5-trihydroxybenzoate	3.01	-2.22	0.54
RRR	[(2R,3S,4S,5R,6S)-6-[4-[(Z)-2-(3,5-dihydroxyphenyl)ethenyl]phenoxy]-3,4,5-trihydroxyoxan-2-yl]methyl 3,4,5-trihydroxybenzoate	2.69	-1.17	0.73
RRR	[Epicatechin-(48)]5-epicatechin	4.02	-4.48	0
RRR	1,8-dihydroxy-3-methoxy-2,6-dimethyl-9,10-anthraquinone	5.53	0.63	0.29
RRR	10beta-Hydroxy-6beta-isobutyryl furanoeremophilane	16.94	0.88	0.29
RRR	1-Cinnamoyl-3-hydroxy-11-methoxymeliacarpinin	35.72	-0.58	0.07

RRR	1-O-Galloyl-glycerol	63.21	-0.81	0.1
RRR	1-O-Galloylpedunculagin	38.09	-2.9	0.04
RRR	2,3-Digalloylglucose	2.99	-2.25	0.66
RRR	2-Cinnamoyl-glucose	17.02	-0.73	0.22
RRR	2-Methyl cardol	3.56	1.46	0.28
RRR	2-Methyl-5-carboxymethyl-7-hydroxychromanone	14.8	0.06	0.12
RRR	3,5-Di-O-galloyl-4-O-digalloylquinic acid	3.01	-2.61	0.31
RRR	3-Carboxy-4-hydroxy-phenoxy glucoside	13.85	-1.44	0.22
RRR	3-Hydroxy-25-norfriedel-3,1(10)-dien-2-one-30-oic acid	18.4	0.41	0.78
RRR	5-[(Z)-2-(3-hydroxy-4-methoxy-phenyl)vinyl]resorcinol	76.25	0.66	0.15
RRR	5-acetyl-7-hydroxy-2-methyl-chromone	30.25	0.37	0.1
RRR	5-Carboxy-7-hydroxy-2-methyl-benzopyran-gamma-one	34.4	0.14	0.11
RRR	Aloeemodin-omega-O-beta-D-glucopyranoside	9.04	-1.34	0.81
RRR	Anthraglycoside B	27.06	-1.29	0.8
RRR	Barolub	16.29	0.88	0.22



RRR	Beta-Glucogallin	17.89	-1.58	0.25
RRR	Chrysophanol glucoside	20.06	-1.17	0.76
RRR	Chrysophanol-8-O-beta-D-(6'-O-galloyl)-glucopyranoside	1.92	-1.48	0.69
RRR	Cinnamic acid	19.68	0.91	0.03
RRR	cis-Zimtsaeure	38.19	0.91	0.03
RRR	Citric acid	56.22	-1.11	0.05
RRR	DLA	44.51	-0.21	0.01
RRR	DMR	68.62	-1.09	0.02
RRR	Docosanoate	15.69	1.21	0.26
RRR	Emodin-1-O-beta-D-glucopyranoside	44.81	-1.12	0.8
RRR	Emodin-6-glucoside	16.09	-1.28	0.8
RRR	Emodinanthrone	24.72	0.8	0.21
RRR	Gallic acid-3-O-(6'-O-galloyl)-glucoside	30.25	-1.96	0.67
RRR	Gallic acid-4-O-(6'-O-galloyl)-glucoside	27.06	-1.82	0.67
RRR	Gallocatechin	2.26	-0.27	0.27

RRR	Glycerite	7.28	-4.71	0.03
RRR	Laccaic acid D	2.06	-0.56	0.31
RRR	MAE	65.06	-0.46	0.01
RRR	o-Acetyltoluene	38.96	1.47	0.02
RRR	OXL	29.68	-0.64	0.01
RRR	Palmidin C	2.35	0.18	0.69
RRR	Physcion-8-O-beta-D-glucopyranoside	8.2	-1.19	0.85
RRR	Physcion-9-O-beta-D-glucopyranoside_qt	20.3	0.56	0.3
RRR	Physciendiglucoside	41.65	-2.64	0.63
RRR	Physcione	19.38	0.02	0.27
RRR	PIT	72.29	0.64	0.13
RRR	Procyanidin B-5,3'-O-gallate {Procyanidin}	31.99	-1.61	0.32
RRR	RHAPONTIN	9	-0.86	0.55
RRR	Rhapontisterone	4.39	-1.84	0.82
RRR	Rheidin B	1.21	-0.19	0.65

RRR	Rheidin C	1.24	-0.18	0.58
RRR	Rhein diglucoside	2.93	-2.79	0.63
RRR	Rheinoside A	0.82	-3.17	0.68
RRR	Rheinoside A_qt	26.28	-1.87	0.75
RRR	Rheochrysin	18.31	-1.14	0.82
RRR	Rheosmin	26.79	0.97	0.04
RRR	Rheumin	9.16	-0.23	0.17
RRR	Sennidin C	1.28	-0.62	0.61
RRR	Sennoside A	3.34	-3.7	0.08
RRR	Sennoside B	3.34	-3.85	0.08
RRR	Sennoside C	3.99	-3.54	0.09
RRR	Sennoside D	3.99	-3.48	0.09
RRR	Sennoside D_qt	61.06	-0.7	0.61
RRR	Sennoside E	3.02	-3.67	0.06
RRR	Sennoside E_qt	50.69	-0.74	0.61

RRR	Serotonin	42.99	0.59	0.06
RRR	Strumaroside	20.78	-0.23	0.67
RRR	Succinic acid	29.62	-0.44	0.01
RRR	Torachryson-8-O-beta-D-(6'-oxayl)-glucoside	43.02	-1.23	0.74
RRR	TPBO	24.23	1.42	0.03
RRR	ZINC04081604	15.23	0.88	0.44
MRC/RRR	3,4,5-trihydroxybenzoic acid {Gallic acid}	31.69	-0.09	0.04
PS/RRR	$\beta$ -Sitosterol	36.91	1.32	0.75

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MRC, Moutan Radicis Cortex; PS, Persicae Semen; RRR, Rhei Radix et Rhizoma; OB, oral bioavailability; Caco-2, Caco-2 cell permeability; DL, drug-likeness score. Synonyms of certain chemical compounds are given in braces { }.

**Supplementary Table S3. Active chemical components of FDY2004.**

Herbal medicines	Chemical compounds	OB	Caco-2	DL
MRC	(+)-Catechin	54.83	-0.03	0.24
MRC	5-[[5-(4-methoxyphenyl)-2-furyl]methylene]barbituric acid {ZINC9320615}	43.44	0.09	0.3
MRC	Caffeic acid	25.76	0.21	0.05
MRC	Kaempferol	41.88	0.26	0.24
MRC	Mairin	55.38	0.73	0.78
MRC	Paeoniflorin	10.22	-1.69	0.79
MRC	Paeonol	28.79	0.93	0.04
MRC	Pentagalloylglucose	3.01	-3.08	0.21
MRC	Quercetin	46.43	0.05	0.28
MRC	Sitosterol	36.91	1.32	0.75
PS	(+)-Epicatechin	48.96	0.02	0.24
PS	Amygdalin	4.42	-1.91	0.61

PS	Campesterol	37.58	1.31	0.71
PS	GA120	84.85	0.38	0.45
PS	GA121-Isolactone	72.7	-0.26	0.54
PS	GA122	64.79	-0.17	0.5
PS	GA122-Isolactone	88.11	-0.18	0.54
PS	Gibberellin A119	76.36	-0.12	0.49
PS	Gibberellin A44	101.61	-0.13	0.54
PS	Gibberellin A7	73.8	-0.18	0.5
PS	Hederagenin	36.91	1.32	0.75
PS	$\alpha$ 1-Sitosterol	43.28	1.41	0.78
RRR	(-)-Catechin	49.68	-0.03	0.24
RRR	Aloe-emodin	83.38	-0.12	0.24
RRR	Chrysophanol	18.64	0.62	0.21
RRR	Daucosterol {Sitogluside}	20.18	0.09	0.69
RRR	Emodin	24.4	0.22	0.24

RRR	Eupatin	50.8	0.53	0.41
RRR	Mutatochrome {Citroxanthin}	48.64	1.97	0.61
RRR	Palmidin A	32.45	-0.36	0.65
RRR	Phycion	22.29	0.52	0.27
RRR	Rhein	47.07	-0.2	0.28
RRR	Toralactone	46.46	0.86	0.24
MRC/RRR	3,4,5-trihydroxybenzoic acid {Gallic acid}	31.69	-0.09	0.04
PS/RRR	$\beta$ -Sitosterol	36.91	1.32	0.75

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MRC, Moutan Radicis Cortex; PS, Persicae Semen; RRR, Rhei Radix et Rhizoma; OB, oral bioavailability; Caco-2, Caco-2 cell permeability; DL, drug-likeness score. Synonyms of certain chemical compounds are given in braces { }.

**Supplementary Table S4. Targets of active chemical components of FDY2004.**

Herbal medicines	Chemical compounds	Targets
MRC	(+)-Catechin	ALPL*, APOB*, BACE1*, CA1, CA2, CA3, CA4*, CA5A, CA5B, CA6, CA7, CA9*, CA12*, CSF2*, DNMT1*, FUT4*, HMOX1*, KIAA1149, PGD*, PGF*, PON1*, PTGS2*, SLC22A11, SLC47A1
MRC	Caffeic acid	ALOX5*, CA1, CA2, CA3, CA5A, CA5B, CA6, CA7, CA9*, CA12*, CA14, MMP1*, MMP2*, MMP9*, NR0B2*, PTPN1*, SLC22A6
MRC	Kaempferol	ABCB1*, ABCC1*, ABCG2*, AHR*, AKR1B1*, ALOX5*, AR*, CA2, CA7, CA12*, CDK1*, CISD1, CTDSP1, CYP1A2*, CYP1B1*, CYP2D6*, DAPK1, ESRRA*, FLT3*, HSD17B1*, HSD17B2*, MPO*, NOX4*, NR1I2*, P4HB, PTPRS, RPS6KA3*, SLC2A1*, TYR*, UGT1A3, UGT1A7*, UGT1A8, UGT1A9*, UGT3A1, XDH*
MRC	Mairin	A1CF, AKR1B10*, AMD1, ARHGEF7*, CDCA8*, CPSF4*, CYP2R1, DHPS, EIF2AK2*, EME1, FOLH1*, GPBAR1, HIGD1B, MDM2*, MEX3D, MMAB, MTOR*, POLB*, PTPRN, RAC1*, RNF31, RPS3, S100A8*, SAE1, UBA2*, USF1
MRC	Mutatochrome {Citroxanthin}	DRAP1, NR1D2*, RANBP2, RUVBL1*, TJP1*, TPK1, YAP1*
MRC	Paeoniflorin	BLVRA, F13A1*, FRS3, HNRNPR, NUCB1, STRBP*
MRC	Paeonol	CASP8*, CASP10*, ICAM1*, MTNR1A*, MTNR1B, PTGS2*, TYR*, VCAM1*



MRC	Pentagalloylglucose	ABCC11*, AMY1A, AMY1B, AMY1C, BACE1*, EGFR*, ESR1*, F10*, HMOX1*, MCL1, NFE2L2*, PTPN1*, PTPN2*, SERPINE1*, SQLE*, TMPRSS11D
MRC	Quercetin	ABCB1*, ABCC1*, ABCG2*, AKR1B1*, AKT1*, ALK*, ALOX12*, ALOX15*, ALOX5*, ATP5B, AURKB*, AVPR2*, AXL*, BACE1*, CA1, CA2, CA3, CA4*, CA5A, CA6, CA7, CA9*, CA12*, CA14, CAMK2B, CCR4*, CDK1*, CSNK2A1*, CXCR1*, CYP1A1*, CYP1A2*, CYP1B1*, CYP2C8*, CYP2C9*, DAPK1, DRD4*, EGFR*, ELAVL1*, F2*, FLT3*, GLO1, GPR35, GSK3B*, HCK, HIBCH, HSD17B2*, IGF1R*, KDR*, MAOA*, MCL1, MET*, MMP2*, MMP3*, MMP9*, MMP13*, MPO*, NEK2*, NEK6, NOX4*, NUAK1, P4HB*, PIK3R1, PIM1*, PKN1, PLA2G1B*, PTK2*, PTPRS, PYGL, SLC2A2, STK17B, XDH*
MRC	Sitosterol	CALML3, CYP17A1, DHPS, DRAP1, GPBAR1, HDLBP, LTF*, NPC1L1, NR1D2*, RAC1*, RUVBL1*, USF1
PS	(+)-Epicatechin	ALPL, APOB, BACE1, CA1, CA2, CA3, CA4, CA5A, CA5B, CA6, CA7, CA9, CA12, CSF2, DNMT1, FUT4, HMOX1, KIAA1149, PGD*, PGF*, PON1*, PTGS2*, SLC22A11, SLC47A1
PS	Campesterol	AMD1, ARHGEF7, CALML3, CDCA8, CYP17A1, DHPS, DRAP1, EIF2AK2, GPBAR1, LTF*, MDM2*, MEX3D, MTOR*, NPC1L1, NR1D2*, PTPRN, RAC1*, RPS3, S100A8*, SHBG*, SLC10A1, SRD5A2*, TNNC1, USF1, USP8*
PS	GA120	ACBD7, AMD1, CALML3, EIF2AK2, MDM2*, MEX3D, MTOR*, RAC1*, RPS3, S100A8*

PS	GA121-Isolactone	ARHGEF7, CPSF4, CYP2R1, DHRS1, EIF2AK2, FOLH1, MDM2*, MEX3D, MMAB, MTOR*, MTRR*, PHO85, PTPRN, RAC1*, RGS18, RPS3
PS	GA122-Isolactone	DHRS1, MTRR*, RGS18
PS	Gibberellin A44	BRD7, DHRS1
PS	Gibberellin A7	ACBD7, EIF2AK2*, MDM2*, MEX3D, MTOR*, RAC1*
PS	Hederagenin	F3*, PNP1, PTPN2*
PS	$\alpha$ 1-Sitosterol	ACBD7, AMD1, CALML3*, CDCA8*, DHPS, DRAP1, EIF2AK2*, HDLBP, LTF*, MDM2*, MEX3D, MTOR*, NR1D2*, RAC1*, RANBP2, RNF31, RUVBL1*, TNNC1, USF1, USP8*
RRR	(-)-Catechin	ALPL*, APOB*, BACE1*, CA1, CA2, CA3, CA4*, CA5A, CA5B, CA6, CA7, CA9*, CA12*, CSF2*, DNMT1*, FUT4*, HMOX1*, KIAA1149, PGD*, PGF*, PON1*, PTGS2*, SLC22A11, SLC47A1
RRR	Aloe-emodin	CASP3*, CASP8*, CASP9*, EIF2S1, HSP90AA1*, TP53*, UGT1A9*, XBP1*
RRR	Chrysophanol	NLRP3*, UGT1A9*
RRR	Daucosterol {Sitogluside}	CYP17A1*, NPC1L1, NR1D2*, RUVBL1*
RRR	Emodin	AKR1B1*, CASP3*, CSNK2A1*, CSNK2B, CXCR4*, CYP1B1*, ERBB2*, ESR1*, ESR2*, LCK*, MCL1, PIM1*, PTP4A3*, TNF*, TP53*, VEGFA*

RRR	Eupatin	CREB1*, CYP1B1*
RRR	Phycion	ELANE*, UGT1A9*
RRR	Rhein	DNM1L*, FTO*, NFKB1*, PPARA*, PPARG*, RELA*, RXRA*, SLC37A4, TPMT*, UCP1, VEGFA*
MRC/RRR	3,4,5-trihydroxybenzoic acid { Gallic acid }	ABCB1*, ATM*, CA1, CA2, CA3, CA4*, CA5A, CA5B, CA6, CA7, CA9*, CA12*, CA14, CASP3*, EIF2AK3*, FUT7*, GATA3*, JUN*, MMP2*, SERPINE1*, TPMT*, TYR*, UGT2B17*
PS/RRR	$\beta$ -Sitosterol	ACBD7, CYP17A1*, DHPS, DRAP1, GPBAR1, LTF*, MDM2*, MEX3D, MTOR*, NPC1L1, NR1D2, RAC1*, RANBP2, RUVBL1*, TNNC1, USF1

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MRC, Moutan Radicis Cortex; PS, Persicae Semen; RRR, Rhei Radix et Rhizoma; \*, lung cancer-associated targets. Synonyms of certain chemical compounds are given in braces {}.

**Supplementary Table S5. Docking scores between active chemical components of FDY2004 and the lung cancer-associated targets.**

Chemical compounds	Targets											
	AKT1	EGFR	ESR1	HSP90AA1	JUN	NFKB1	PIK3R1	PTK2	RAC1	TNF	TP53	VEGFA
(-)-Catechin	-5.7	-7.7	-7.0	-6.7	-5.3	-6.3	-6.1	-6.0	-8.5	-6.2	-7.3	-6.9
(+)-Catechin	-6.0	-7.7	-7.0	-6.7	-5.3	-6.3	-6.1	-6.0	-9.0	-6.2	-7.3	-6.9
(+)-Epicatechin	-5.6	-7.7	-7.0	-6.7	-5.3	-6.4	-6.1	-6.0	-9.0	-6.3	-7.3	-6.9
Aloe-emodin	-6.1	-8.3	-7.4	-7.2	-5.4	-6.4	-6.0	-6.1	-9.6	-6.4	-7.1	-6.8
Caffeic acid	-5.2	-6.5	-5.1	-5.8	-4.6	-5.3	-5.0	-4.8	-6.8	-4.9	-5.8	-5.5
Campesterol	-6.0	-9.4	-6.4	-5.7	-5.8	-5.8	-6.0	-5.9	-8.3	-5.6	-6.2	-7.9
Chrysophanol	-5.7	-8.5	-7.6	-7.3	-5.4	-6.5	-5.8	-6.0	-9.8	-6.7	-7.3	-7.0
Daucosterol	-5.3	-7.2	-8.1	-5.1	-5.8	-6.9	-6.0	-6.7	-8.8	-5.9	-6.6	-7.9
Emodin	-6.0	-8.3	-7.8	-7.2	-5.6	-6.5	-5.8	-6.2	-10.1	-6.8	-7.3	-7.0
Eupatin	-5.5	-8.7	-6.8	-6.0	-5.4	-6.8	-5.7	-6.0	-9.3	-6.7	-6.6	-7.1
GA120	-6.9	-8.2	-7.3	-7.4	-6.7	-6.5	-6.7	-6.2	-8.4	-6.1	-7.1	-7.5
Gallic acid	-5.4	-6.4	-5.4	-5.2	-5.1	-5.2	-4.9	-4.6	-6.3	-4.8	-5.4	-5.6

Gibberellin A7	-6.0	-7.9	-7.0	-7.2	-6.5	-6.4	-6.5	-6.2	-8.1	-6.4	-6.9	-7.4
Hederagenin	-6.5	-10.0	-7.9	-5.0	-6.6	-6.5	-7.5	-6.9	-7.7	-6.5	-7.4	-7.8
Kaempferol	-6.3	-7.9	-6.6	-6.3	-5.4	-6.4	-6.1	-5.7	-8.8	-6.3	-6.7	-6.9
Mairin	-5.0	-9.8	-7.9	-6.5	-6.8	-6.5	-6.8	-6.7	-6.8	-6.6	-7.8	-8.3
Mutatochrome	-6.9	-5.4	-7.3	-6.5	-7.3	-7.7	-7.8	-7.2	-10.3	-6.2	-7.6	-9.6
Paeoniflorin	-6.0	-8.6	-7.0	-6.1	-6.1	-6.8	-6.7	-7.2	-8.4	-5.7	-6.6	-7.6
Paeonol	-5.3	-5.7	-5.0	-5.4	-3.9	-4.9	-4.5	-4.1	-6.3	-4.9	-5.2	-5.1
Pentagalloylglucose	-6.0	-8.9	-7.0	-3.0	-6.0	-8.7	-6.3	-7.0	-8.9	-7.0	-8.3	-8.4
Physcion	-8.1	-11.2	-9.9	-6.3	-7.8	-8.8	-8.0	-9.1	-12.7	-8.3	-8.8	-10.4
Quercetin	-6.4	-7.9	-6.5	-6.1	-5.4	-6.6	-6.3	-6.1	-9.3	-6.5	-7.0	-7.2
Rhein	-5.4	-8.7	-7.6	-6.7	-5.6	-6.8	-6.1	-6.2	-10.2	-6.4	-7.3	-7.1
Sitosterol	-4.5	-8.8	-6.2	-5.5	-5.8	-5.3	-5.9	-5.9	-8.1	-5.6	-6.4	-7.8
$\alpha$ 1-Sitosterol	-4.8	-9.7	-6.3	-6.8	-6.3	-5.5	-5.9	-5.9	-7.8	-5.5	-7.0	-8.5
-Sitosterol	-4.5	-8.8	-6.2	-5.2	-5.9	-5.3	-5.8	-5.8	-7.0	-5.6	-6.8	-7.9

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