Original Article

Analyzing the multi-target pharmacological mechanism of folium *Artemisia argyi* acting on breast cancer: a network pharmacology approach

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Background: Folium *Artemisia argyi* (FAA) is a traditional Chinese herbal medicine that is widely used in the clinic. However, the underlying mechanisms of its anticancer effects have not been fully elucidated.

Methods: In this study, we applied a network pharmacology approach to identify the potential mechanisms of FAA against breast cancer. To be specific, we screened the active ingredients and potential targets of the FAA through the Traditional Chinese Medicine Systems Pharmacology (TCMSP) database. Meanwhile, we employed the oral bioavailability (OB) and drug-likeness (DL) to search for potential bioactive compounds of FAA. Breast cancer-related target genes data were gathered from the GeneCards and Online Mendelian Inheritance in Man (OMIM) databases, and the protein-protein interaction (PPI) data were acquired from the Search Tool for the Retrieval of Interacting Genes (STRING) database. In addition, we constructed the network and performed Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) Pathway Enrichment Analysis.

Results: We obtained a total of nine active ingredients and 236 potential targets from FAA to construct a network, which showed that quercetin served as the major ingredient in FAA. *AKT1* (RAC-alpha serine/threonine-protein kinase), *MYC* (Myc proto-oncogene protein), *CASP3* (Caspase-3), *EGFR* (Epidermal growth factor receptor), *JUN* (Transcription factor AP-1), *CCND1* (G1/S-specific cyclin-D1), *VEGFA* (Vascular endothelial growth factor A), *ESR1* (Estrogen receptor), *MAPK1* (Mitogen-activated protein kinase 1), and *EGF* (pro-epidermal growth factor) were identified as key targets of FAA in the treatment of breast cancer. The PPI cluster demonstrated that *AKT1* was the seed in this cluster, indicating that *AKT1* played a crucial role in connecting other nodes in the PPI network. This enrichment demonstrated that FAA was highly related to signal transduction, endocrine system, replication and repair, as well as cell growth and death. The enrichment results also verified that the underlying mechanisms of FAA against breast cancer might be attributed to the coordinated regulation of several cancer-related pathways, such as the MAPK and mammalian target of rapamycin (mTOR) signaling pathways, among others.

Conclusions: This study identified the potential targets and pathways of FAA in the treatment of breast cancer using a network pharmacology approach, and systematically elucidated the mechanisms of FAA in the treatment of breast cancer.

Keywords: Folium *Artemisia argyi* (FAA); breast cancer; network pharmacology; herb

Submitted Nov 03, 2022. Accepted for publication Dec 15, 2022.
doi: 10.21037/atm-22-5769
View this article at: https://dx.doi.org/10.21037/atm-22-5769

Introduction

Breast cancer is the most frequent malignancy occurring in women with 1.38 million new cases each year and nearly 0.46 million related deaths globally (1,2). According to current projections, there will be approximately 3.2 million new cases per year by 2050 (3). Meanwhile, breast cancer is a kind of heterogeneous disease, with differences in occurrence, development, treatment, and prognosis (4). At present, comprehensive adjuvant treatments containing chemotherapy, radiotherapy, endocrine, and HER2-targeted therapies are widely used according to the five major molecular subtypes of breast cancer (5). However, these treatments are costly and usually result in a series of short- and long-term side effects, such as febrile neutropenia (6), alopecia (7), peripheral neuropathy (8) and cardiotoxicity (9), all of which significantly decrease the patient's quality of life. Furthermore, older patients in the terminal stages may also be more intolerant to these adverse reactions.

Folium *Artemisia argyi* (FAA), commonly called wormwood, is a perennial herb belonging to Artemisia in the Asteraceae family and rich in volatile oils, polysaccharides, flavonoids and other trace elements. FAA has strong adaptability and distributes in most parts of China. It is also cultivated in Mongolia, Korea, Russia's Far East and Japan. As a traditional Chinese herbal medicine, FAA has antipyretic, analgesic, and hemostatic effects (10). For thousands of years, it has been used internally to warm channels, arrest bleeding, dispel cold, and relieve pain, and is applied externally to eliminate dampness and relieve itching (11). Recently, owing to the various limitations of Western medicine, such as the toxicity and adverse side effects, increasing attention has been paid to the role of traditional Chinese medicine in the prevention and treatment of cancer (12). At the same time, Chinese herbs can target multiple points to achieve synergistic actions (13,14). According to pharmacology research, FAA contains multiple active chemical constituents, such as flavonoids, terpenoids, phenolic acids, and volatile oils (15,16), and exhibits a variety of effects, including anticancer, anti-inflammation, and anti-oxidation (17,18). For example, Shafi *et al.* suggested that FAA inhibited the proliferation and promoted apoptosis in breast cancer cells through Bcl-2 family proteins and the MEK/ERK pathway (10). It was also reported that FAA exhibited a dose-dependent inhibitory effect on hepatoma cells (11). However, although many studies have verified that FAA exerts remarkable antitumor functions, the underlying mechanisms have not yet been comprehensively understood (10,11,17,18).

It is widely known that herbal medicines include multi-component, multi-target, and multi-pathway features (19,20). Traditional Chinese medicine network pharmacology is a systematic research method based on the interaction network of herbs, compounds, targets, diseases, and genes (21). This approach emphasizes the integration of bioinformatics, systems biology, and pharmacology, which not only explains the complex interactions between herbs and diseases at a systematic level but also conforms to the systematic and holistic perspective of the traditional Chinese medicine theory (22,23). Thus, we utilized a network pharmacology approach in this study to explore the pharmacological mechanisms of FAA as a treatment for breast cancer. Firstly, we screened for active ingredients of FAA by estimating their oral bioavailability (OB) and drug-likeness (DL) (24). Next, we selected the common targets shared by the FAA compound targets and the breast

Highlight box

Key findings

- We explore the pharmacological mechanisms of FAA for breast cancer by a network pharmacology approach.

What is known and what is new?

- Many studies have verified that FAA exerts remarkable antitumor functions.
- The quercetin served as the major ingredient of FAA and might exert its anti-tumor effect mainly by acting on AKT pathway in breast cancer. The anti-tumor mechanism of FAA might be attributed to the coordinated regulation of several cancer-related pathways.

What is the implication, and what should change now?

- It provides a new theoretical basis and some new ideas for the studies of the treatment of breast cancer. It provides the feasibility of experimental research to study the mechanism of FAA in breast cancer, and then provides the possibility to find a new treatment strategy of breast cancer.

cancer-related targets using two databases [GeneCards and Online Mendelian Inheritance in Man (OMIM)] and then constructed the network by investigating the potential interactions between the various target nodes. In addition, the protein-protein interaction (PPI) data were obtained from the Search Tool for the Retrieval of Interacting Genes (STRING) database, and enrichment analyses [Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG)] were performed to explore the potential mechanisms of FAA against breast cancer. In summary, this study aimed to identify the potential targets and pathways of FAA as a treatment for breast cancer using the network pharmacology approach, and systematically elucidate the mechanisms of FAA in the treatment of breast cancer. We present the following article in accordance with the STREGA reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5769/rc).

Methods

Data preparation

Active ingredients and targets against breast cancer in FAA

FAA ingredients were acquired from the Traditional Chinese Medicine Systems Pharmacology (TCMSP) database, which serves as a systematic platform to study herbs, including the identification of compounds and the screening of compound targets (25). In addition, to identify the corresponding targets of FAA compounds against breast cancer, the TCMSP database was utilized to identify potential targets. Finally, nine active herbal ingredients of FAA were selected (*Table 1*) by linking the active ingredients of FAA to the breast cancer targets. A total of 236 targets of FAA compounds were obtained in total (the specific targets are not shown).

Table 1 Active ingredients of FAA

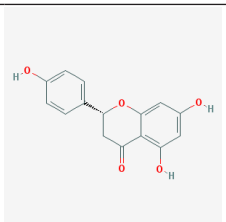
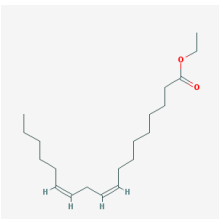
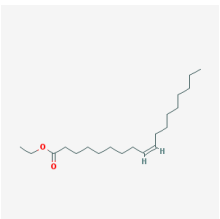
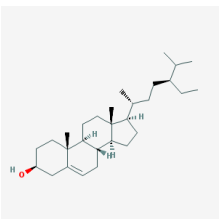
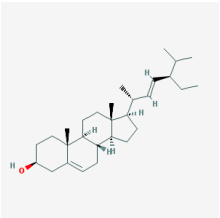
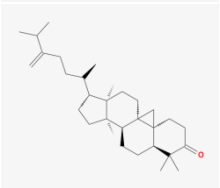
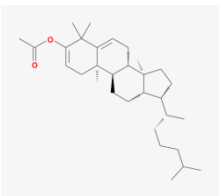
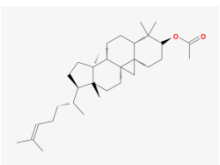
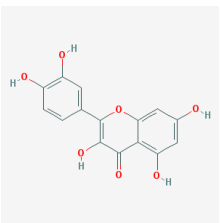
Mol ID	Mol name	2D structure	OB (%)	DL
MOL001040	(2R)-5,7-dihydroxy-2-(4-hydroxyphenyl) chroman-4-one		42.36	0.21
MOL001494	Mandenol		42	0.19
MOL002883	Ethyl oleate (NF)		32.4	0.19
MOL000358	beta-sitosterol		36.91	0.75

Table 1 (*continued*)

Table 1 (*continued*)

Mol ID	Mol name	2D structure	OB (%)	DL
MOL000449	Stigmasterol		43.83	0.76
MOL005720	24-methylenecyloartanone		41.11	0.79
MOL005735	dammaradienyl acetate		44.83	0.83
MOL005741	cycloartenol acetate		41.11	0.8
MOL000098	quercetin		46.43	0.28

FAA, folium *Artemisia argyi*; Mol, molecular; OB, oral bioavailability; DL, drug-likeness.

Pharmacokinetic predictions

In a pharmaceutical study, ADME (absorption, distribution, metabolism, and excretion) is a critical pattern to identify (24). Therefore, we employed two major ADME-related properties, namely, OB and DL to search for potential bioactive compounds of FAA. Ingredients with OB ≥30% and DL ≥0.18 were considered to be suggested drug screening criteria. The screening criteria of OB ≥30% and DL ≥0.18 to select ingredients was set based on previous studies (26,27). This criterion allows for more accurate screening of active ingredients. Detailed information on all of the ingredients before screening is listed in Table S1.

Potential target genes of breast cancer

Breast cancer-related target genes data were gathered from the GeneCards and OMIM databases. The species was set to Homo sapiens. GeneCards is an extensive platform that provides insight into predicted and annotated human genes. All of the gene-centric data were collected from 150 web resources, including genetic, genomic, proteomic, transcriptomic, and functional information (28). *Search strategy*: we set the keyword as "breast cancer" and the score30 after logging in to Genecards. The detailed information is listed in Table S2.

The OMIM is a comprehensive, authoritative, and

timely knowledgebase that links and catalogues all known diseases with a genetic component and provides further references to the genomic analyses of catalogued genes (29). Search strategy: we chose "gene map" on the website and then set the keyword as "breast cancer". The detailed information is listed in Table S3.

PPI data

We acquired the PPI data from the STRING database, which defines PPI with confidence ranges for data scores (high >0.7; medium >0.4; low >0.15) (30). In this study, we selected a confidence score of >0.4 to construct our PPI network.

Network construction

The PPI network has been widely applied to display many different interactions between proteins in the context of complex diseases (23,31), including breast cancer, prostate cancer, lung cancer, gastric cancer, etc. In this study, we constructed the network as follows: (I) we acquired the targets shared by the FAA compound targets and the breast cancer-related targets; (II) we entered these targets into the STRING database and obtained the FAA against breast cancer targets PPI network; and (III) we exported the PPI results as a simple tabular text output (.tsv) and then imported the .tsv file into Cytoscape (version 3.6.1, National Resource for Network Biology (NRNB), USA) to reconstruct the network to achieve better visualization and understanding for further analysis (32).

GO and KEGG pathway enrichment analysis

In this study, we used the Cluster Profiler package of R3.5.2 (Bioconductor, China) to perform GO enrichment analysis of the targets; the higher the score, the greater the importance of the genes represented in the list (33). The Cluster Profiler package of R3.5.2 was also used to analyze the KEGG pathway enrichment of overlapping target genes. KEGG analysis was used to explore the biological pathways and potential biological functions based on the enrichment analysis of functional items (34). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Results

Active ingredients

In this study, we acquired a total of nine active ingredients in FAA after ADME identification. Detailed information is shown in *Table 1* (all Mol IDs (Bioconductor, China) could be tracked in the TCMSP database). All of the FAA compounds before screening are presented in Table S1.

FAA compound-target network

To further uncover the potential pharmacological mechanisms of FAA against breast cancer, target genes common to both the active ingredients of FAA and breast cancer were selected in different databases. A total of 75 genes (Figure S1) belonging to both the FAA target gene and breast cancer target gene networks were screened via Venn analysis (*Figure 1A*). The compound-target network is presented in *Figure 1B* and includes 82 nodes and 171 edges, with a network density of 0.051 and a network diameter of 3. Detailed information on this network is depicted in *Table 2*.

PPI network

To explore the underlying mechanisms of FAA as a therapy against breast cancer, a PPI network of the FAA compound targets against breast cancer was constructed by connecting the targets of the FAA compounds and breast cancer. First, we obtained a total of 75 target genes belonging to both the FAA target gene and breast cancer target gene and obtained target symbol names using UniProt. Next, all of these 75 target genes were imported into the STRING database to generate the PPI results (settings: Homo sapiens and confidence>0.4). The original STRING PPI network is presented in Figure S2. Next, we imported the PPI data generated in the STRING database into Cytoscape (version 3.6.1).

As shown in *Figure 2A*, this PPI network included 75 nodes and 1,247 edges, with a network diameter of 3, a clustering coefficient of 0.733, and an average number of 33.253 neighbors. The average node degree was 33.3 (the degree was indicated both by the different colors and the size of the circles). Detailed information on this network is displayed in *Table 3*. All target degrees were calculated using this network. In *Figure 2B*, the 10 targets with the greatest degrees were *AKT1* (degree =67), *MYC* (degree =65), *CASP3* (degree =63), *EGFR* (degree =62), *JUN* (degree =61), *CCND1* (degree =60), *VEGFA* (degree =60), *ESR1* (degree =59), *MAPK1* (degree =57), and *EGF* (degree =55). As shown in *Figure 2C*, the cluster consisted of 68 nodes and 1,155 edges. The average node degree was 34 and the

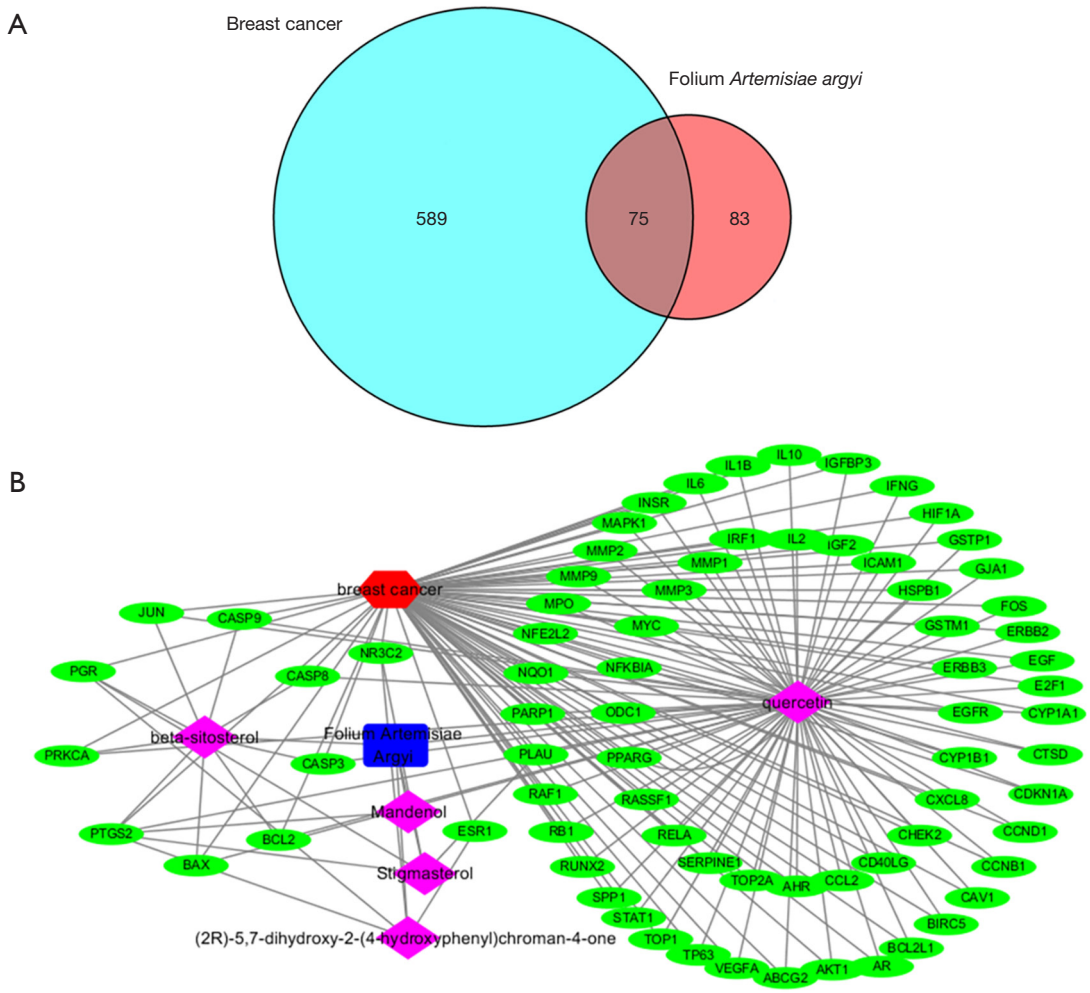


Figure 1 Seventy-five target genes for FAA against breast cancer. (A) Venn diagram showing the overlapping target genes for FAA against breast cancer. (B) Network of target genes for FAA against breast cancer. Pink diamond represents the active ingredients of FAA compounds; green ellipse represents the target genes of both FAA and breast cancer. FAA, folium *Artemisia argyi*.

Table 2 The FAA compound-candidate target network parameters

Network parameters	Values
Number of nodes	82
Network density	0.051
Network diameter	3
Network heterogeneity	2.678
Average number of neighbors	4.146
Characteristic path length	2.035
Shortest paths	6,642 (100%)
Network centralization	0.897

FAA, folium *Artemisia argyi*.

clustering coefficient was 0.77. *AKT1* (The red diamond in *Figure 2C*) was the seed in this cluster and interacted with the other FAA targets.

GO enrichment

To further discuss the multiple mechanisms of FAA as a treatment against breast cancer, we conducted GO enrichment analysis on the 75 common targets shared by the FAA compound targets and the breast cancer-related targets (35). Specifically, the top 30 targets are as follows (*Figure 2B*): *AKT1*, *MYC*, *CASP3*, *EGFR*, *JUN*, *CCND1*, *VEGFA*, *ESR1*, *MAPK1*, *EGF*, *IL6*, *PTGS2*, *ERBB2*, *FOS*, *MMP9*, *CXCL8*,

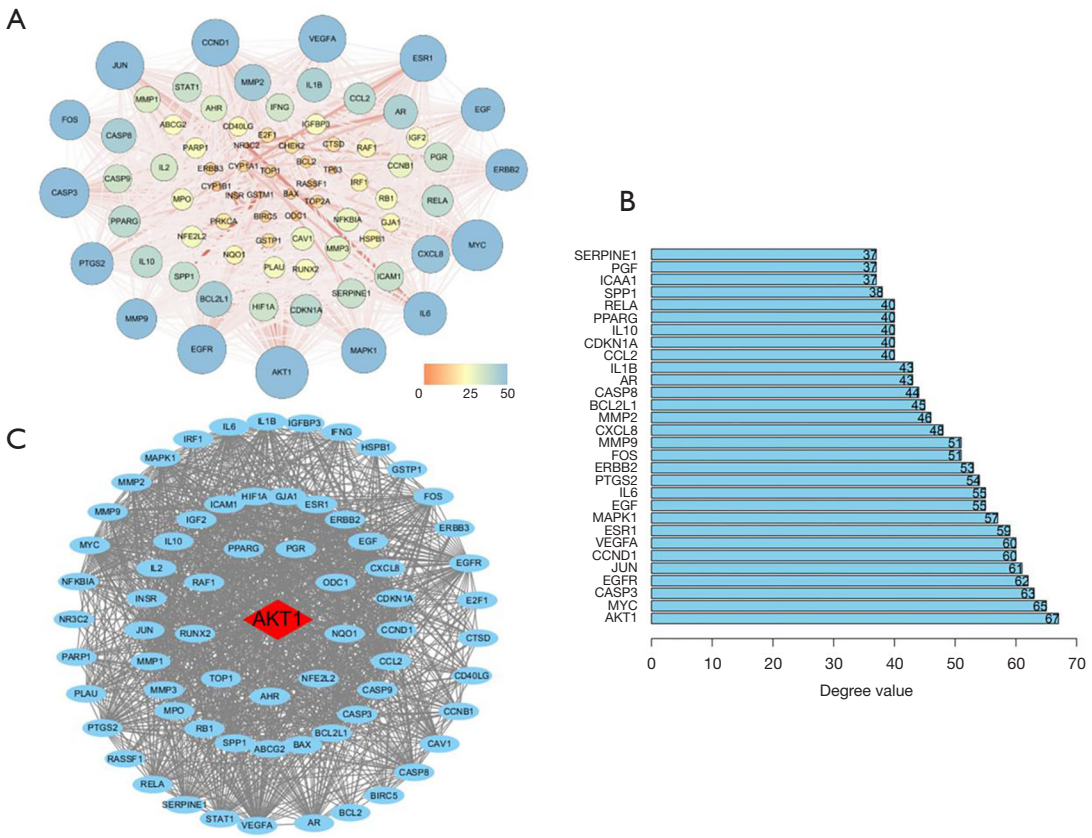


Figure 2 PPI network of FAA compound targets against breast cancer. (A) The PPI network was constructed using Cytoscape. Different colors represent the degree, as indicated by the scale. The size of the circle also indicates the degree. (B) The top 30 target genes of FAA against breast cancer screened by the PPI network. The X-axis represents degree values. (C) The cluster generated from (A). The red diamond in (C), AKT1, was the seed in this cluster and interacted with other FAA targets. PPI, protein-protein interaction; FAA, folium *Artemisia argyi*.

Table 3 The network parameters of FAA compound targets against breast cancer

Network parameters	Values
Number of nodes	75
Number of edges	1,247
Network diameter	3
Clustering coefficient	0.733
Average number of neighbors	33.253
Average node degree	33.3

FAA, folium *Artemisia argyi*.

MMP2, *BCL2L1*, *CASP8*, *AR*, *IL1B*, *CCL2*, *CDKN1A*, *IL10*, *PPARG*, *RELA*, *SPP1*, *ICAM1*, *PGR*, and *SERPINE1*. The significantly enriched GO targets are presented (adjusted P value <0.001) in *Figure 3*. The top five GO enrichment targets included (I) transcription factor activity, RNA polymerase II proximal promoter sequence-specific DNA binding (GO:0000982); (II) transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific DNA binding (GO:0001228); (III) ubiquitin-like protein ligase binding (GO:0044389); (IV) cytokine receptor binding (GO:0005126); and (V) transcriptional activator activity, RNA polymerase II proximal promoter sequence-specific DNA binding (GO:0001077). Detailed

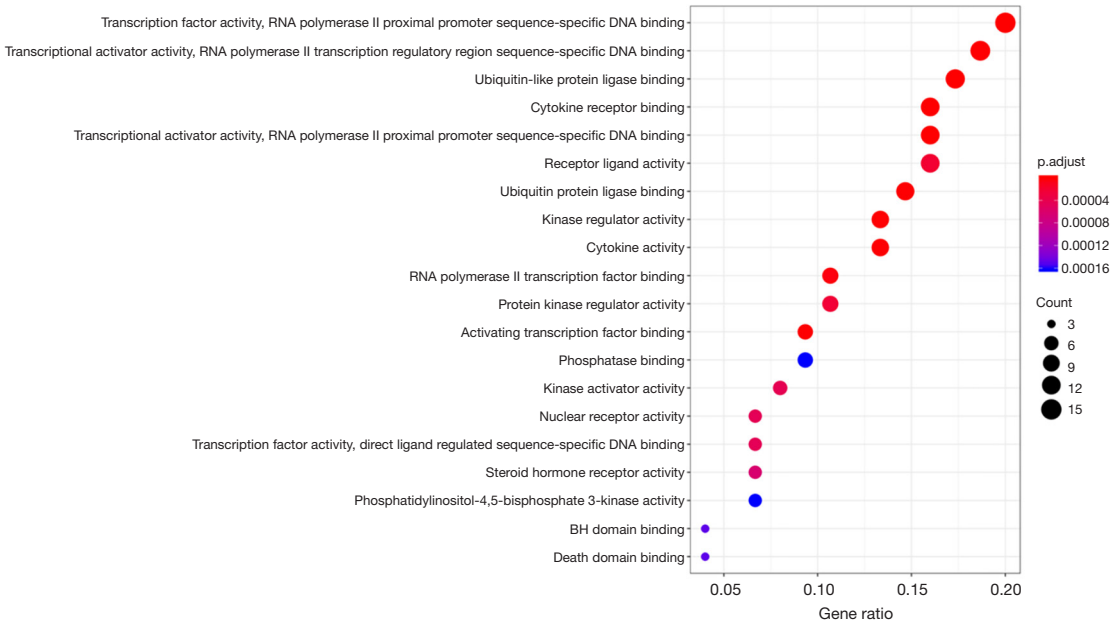


Figure 3 GO enrichment analysis of the 75 common targets shared by the FAA compound targets and breast cancer-related targets. The color represents the different adjusted P values, while the size of the circle represents the count. GO, Gene Ontology; FAA, folium *Artemisia argyi*.

GO enrichment information was shown in *Table 4*. Thus, we speculated that FAA probably executed its pharmacological effects on breast cancer by simultaneously involving these molecular functions.

KEGG enrichment

We obtained a total of 74 pathways belonging to several categories, including human diseases, cellular processes, and drug resistance, among others. Among these, the top 30 significantly enriched KEGG targets are presented (adjusted P value <0.001) in *Figure 4*. In the cancer-related disease, prostate cancer (hsa05215), bladder cancer (hsa05219), pancreatic cancer (hsa05212), breast cancer (hsa05224), colorectal cancer (hsa05210), non-small cell lung cancer (hsa05223), small cell lung cancer (hsa05222), gastric cancer (hsa05226), endometrial cancer (hsa05226), renal cell carcinoma (hsa05211), thyroid cancer (hsa05216), and small cell lung cancer (hsa05222) data were processed using KEGG enrichment analysis. Detailed KEGG information is shown in *Table 5*.

Discussion

As demonstrated in *Figure 1B*, quercetin was the most critical component of FAA, which was connected to the most targets. It is a flavonoid found in natural plants and exhibits a variety of activities such as antioxidant, anti-inflammatory, antiviral, and antimicrobial effects through multiple signal transduction pathways (35,36). Several studies have validated that quercetin can inhibit the progression of various tumors, including breast cancer (37), prostate cancer (38), gastric cancer (39), ovarian cancer (40), and colorectal cancer (41). Moreover, some studies have also reported that it not only has a synergistic effect when combined with chemotherapeutic or radiotherapy agents but can also mitigate the expected adverse side effects and toxic reactions (42,43).

In addition, our results showed that numerous targets were affected by two or more compounds. For instance, Prostaglandin G/H synthase 1 (*PTGS1*) and Prostaglandin G/H synthase 2 (*PTGS2*) were both modulated by quercetin, stigmasterol, mandenol, etc. Constitutive *PTGS1* and inducible *PTGS2* belong to two isozymes of *PTGS*, which have pivotal effects both as a peroxidase and a dioxygenase (44). Other studies have suggested that *PTGS2* might inversely control the metastasis and chemoresistance of breast cancer via the regulation of *EMT* (Epithelial-mesenchymal transition), apoptosis, and senescence (45-47). Also, nuclear receptor coactivator 2 (*NCOA2*), a member

Table 4 GO enrichment results

ID	Description	Count	Adjust P value
GO:0000982	Transcription factor activity, RNA polymerase II proximal promoter sequence-specific DNA binding	15	<0.0001
GO:0001228	Transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific DNA binding	14	<0.0001
GO:0044389	Ubiquitin-like protein ligase binding	13	<0.0001
GO:0005126	Cytokine receptor binding	12	<0.0001
GO:0001077	Transcriptional activator activity, RNA polymerase II proximal promoter sequence-specific DNA binding	12	<0.0001
GO:0048018	Receptor ligand activity	12	<0.0001
GO:0031625	Ubiquitin protein ligase binding	11	<0.0001
GO:0019207	Kinase regulator activity	10	<0.0001
GO:0005125	Cytokine activity	10	<0.0001
GO:0001085	RNA polymerase II transcription factor binding	8	<0.0001
GO:0019887	Protein kinase regulator activity	8	<0.0001
GO:0033613	Activating transcription factor binding	7	<0.0001
GO:0019902	Phosphatase binding	7	0.0002
GO:0019209	Kinase activator activity	6	<0.0001
GO:0004879	Nuclear receptor activity	5	<0.0001
GO:0098531	Transcription factor activity, direct ligand regulated sequence-specific DNA binding	5	<0.0001
GO:0003707	Steroid hormone receptor activity	5	<0.0001
GO:0046934	Phosphatidylinositol-4,5-bisphosphate 3-kinase activity	5	0.0002
GO:0051400	BH domain binding	3	0.0001
GO:0070513	Death domain binding	3	0.0001

GO, Gene Ontology.

of the p160 family, performs key roles in many different physiological and pathological processes, including cell growth, energy metabolism, endocrine regulation, and circadian rhythms (48). More importantly, *NCOA2* gene expression plays crucial roles in the development, progression, and metastasis of malignant tumors, including breast cancer (49). In prostate cancer patients, the high expression of *NCOA2* is more likely to relapse after androgen deprivation therapy (50).

Similarly, Beta-2 adrenergic receptor (*ADRB2*), Gamma-aminobutyric acid receptor subunit alpha-1 (*GABRA1*), Heat shock protein HSP 90, Progesterone receptor (*PGR*), and Sodium channel protein type 5 subunit alpha (*SCN5A*) could also be regulated by more than two active ingredients. In this study, we obtained an approximate observation of the relationship between these active ingredients and targets and also discovered the potential pharmacological effects of FAA from this network (*Figure 1B*).

Figure 2C intuitively indicated that *AKT1* played an important role in connecting other nodes in this PPI network. It is well-known that the serine/threonine kinase, *AKT1*, one of the three isoforms of the Akt family, emerged as a downstream effector of *PI3K* (51). *AKT* inhibits apoptosis by suppressing the actions of BAD (BCL2 Associated Agonist of Cell Death) and caspase-9 (52). In breast cancer, *AKT1* activation accelerates cell proliferation, while Akt1 inhibition promotes epithelial-to-mesenchymal transition (53).

Detailed GO enrichment information is shown in *Table 4*. We speculated that FAA probably executed its

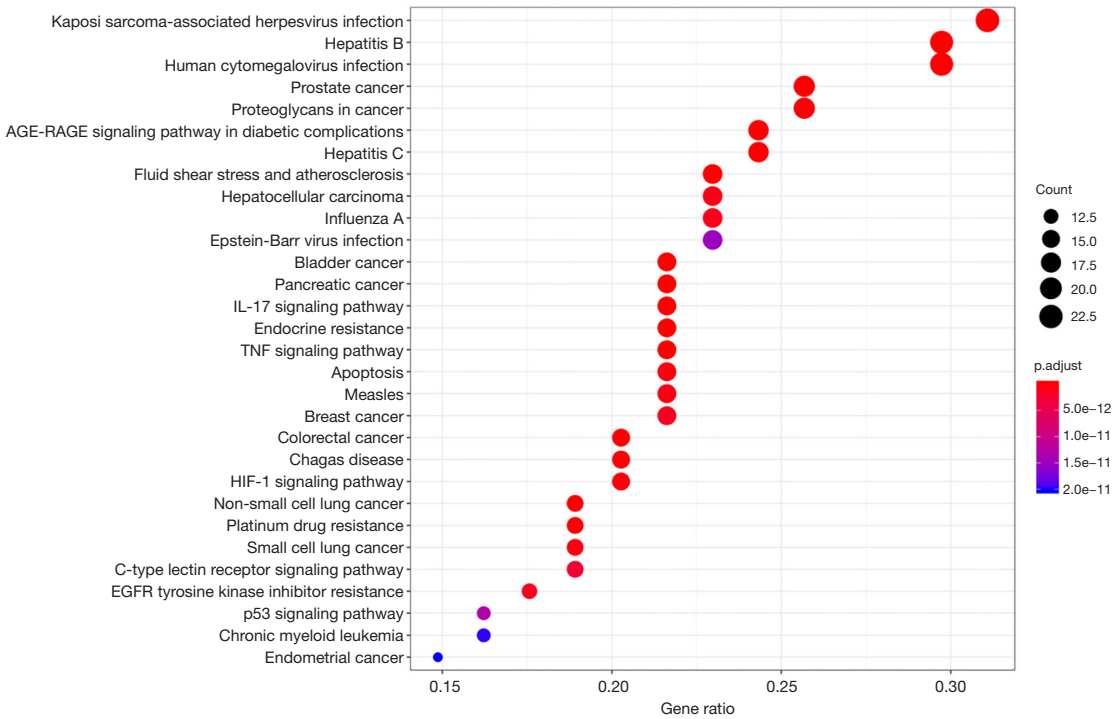


Figure 4 KEGG enrichment analysis of the 75 common targets shared by the FAA compound targets and breast cancer-related targets. The color represents the different adjusted P value, while the size of circle represents the count. KEGG, Kyoto Encyclopedia of Genes and Genomes; FAA, folium *Artemisia argyi*.

pharmacological effects on breast cancer by simultaneously involving these molecular functions. We further carried out KEGG (34) enrichment analysis on 75 common targets to clarify the integral regulation of FAA in the treatment of breast cancer. The results (shown in *Table 5*) indicated that FAA has a significant potential to treat a wide range of cancers, such as breast cancer (10), prostate cancer (54), bladder cancer (55), colorectal cancer (56), and gastric cancer (57), which is consistent with previous research. Furthermore, the results also verified that these signaling pathways remarkably enriched by potential targets of FAA in breast cancer were strongly associated with signal transduction, endocrine system, replication, repair, as well as cell growth and death, most of which played an essential role in the development and progression of cancers, such as the PI3K/AKT signaling pathway (hsa04151) (58), the MAPK signaling pathway (hsa04010) (59), the mammalian target of rapamycin (mTOR) signaling pathway (hsa04150) (60), apoptosis (hsa04210), and the cell cycle signaling pathway (hsa04110) (61). Therefore, we speculated that the underlying mechanism of FAA against breast cancer might be attributed to the coordinated regulation of several cancer-related pathways. About 30% of breast cancer patients who have poor prognosis show overexpression and amplification of *HER2* gene. The high receptor concentration on the membranes of HER2 overexpressing cells can activate the PI3K/AKT and the RAS/RAF/MAPK pathways, which initiates cell proliferation, growth, survival, invasion and angiogenesis. It is considered that FAA is related to the above signaling pathways in breast cancer. FAA may inhibit the recurrence and metastasis of HER2-positive breast cancer patients, which needs further verification (62,63).

Although breast cancer patients get better after various treatments, most patients still have drug resistance and show disease progression. This process involves multiple signaling pathways. According to our results, FAA may be related to multiple signaling pathways in breast cancer. Quercetin was the most critical component of FAA, several studies have validated that quercetin can inhibit the progression of various tumors (38,41,42). Therefore, FAA may be considered as a therapeutic agent against various cancers including breast cancer in the future. The absence of experimental data is indeed the weakness of this

Table 5 KEGG enrichment results

ID	Description	Count	Adjust P value
hsa05167	Kaposi sarcoma-associated herpes virus infection	23	<0.0001
hsa05161	Hepatitis B	22	<0.0001
hsa05163	Human cytomegalovirus infection	22	<0.0001
hsa04151	PI3K-Akt signaling pathway	21	<0.0001
hsa05215	Prostate cancer	19	<0.0001
hsa05205	Proteoglycans in cancer	19	<0.0001
hsa05206	MicroRNAs in cancer	19	<0.0001
hsa04933	AGE-RAGE signaling pathway in diabetic complications	18	<0.0001
hsa05160	Hepatitis C	18	<0.0001
hsa04010	MAPK signaling pathway	18	<0.0001
hsa05165	Human papillomavirus infection	18	<0.0001
hsa05418	Fluid shear stress and atherosclerosis	17	<0.0001
hsa05225	Hepatocellular carcinoma	17	<0.0001
hsa05164	Influenza A	17	<0.0001
hsa05169	Epstein-Barr virus infection	17	<0.0001
hsa05166	Human T-cell leukemia virus 1 infection	17	<0.0001
hsa05219	Bladder cancer	16	<0.0001
hsa05212	Pancreatic cancer	16	<0.0001
hsa04657	IL-17 signaling pathway	16	<0.0001
hsa01522	Endocrine resistance	16	<0.0001
hsa04668	TNF signaling pathway	16	<0.0001
hsa04210	Apoptosis	16	<0.0001
hsa05162	Measles	16	<0.0001
hsa05224	Breast cancer	16	<0.0001
hsa05210	Colorectal cancer	15	<0.0001
hsa05142	Chagas disease	15	<0.0001
hsa04066	HIF-1 signaling pathway	15	<0.0001
hsa04218	Cellular senescence	15	<0.0001
hsa05152	Tuberculosis	15	<0.0001
hsa05170	Human immunodeficiency virus 1 infection	15	<0.0001

KEGG, Kyoto Encyclopedia of Genes and Genomes.

study. In fact, the relevant experiments are carrying out to validate the representative active ingredients of FAA, but have not been completed. We are very pleased to report the experimental results in the subsequent studies.

Conclusions

At present, although many studies have verified that FAA exhibits arresting antitumor activities, the underlying mechanisms of its antitumor activities have not yet been

fully elucidated. Network pharmacology emphasizes the integration of bioinformatics, systems biology, and pharmacology, which not only explain the complex interactions between diseases and Chinese herbs at a systematic level but also conform to the systematic and holistic perspective of traditional Chinese medicine theory (12). To better explore the pharmacological mechanisms of FAA as a treatment for breast cancer, we applied the network pharmacology approach to identify the potential mechanisms of FAA as a breast cancer treatment by compound-target network construction, PPI network, and GO and KEGG enrichment analyses. We took advantage of OB and DL to explore the potential active ingredients of FAA. At present, there are few studies on the pharmacokinetics of FAA. Choi *et al*. found that FAA exerted anticancer activities through the inhibition of cell growth and the induction of apoptosis in breast cancer cells (17).

In this study, we acquired nine active ingredients and 236 potential targets from FAA and validated a synergistic herb strategy featuring multi-component, multi-target, and multi-pathway characteristics. The compound-target network confirmed that quercetin served as the major ingredient in FAA. Moreover, the PPI network provided information concerning the source of the interactions. PPI analysis indicated that FAA had a significant effect on breast cancer by influencing the whole biological network, including targets such as *AKT1*, *MYC*, *CASP3*, *EGFR*, *JUN*, *CCND1*, *VEGFA*, *ESR1*, *MAPK1*, and *EGF*. The PPI cluster demonstrated that *AKT1* was the seed, suggesting that *AKT1* played a crucial role in connecting other nodes in the PPI network. Next, enrichment analysis indicated that FAA was strongly related to signal transduction, the endocrine system, replication and repair, and cell growth and death. The enrichment results also showed that the underlying mechanism of FAA against breast cancer might be attributed to the coordinated regulation of several cancer-related pathways, such as the MAPK and mTOR signaling pathways, among others.

In conclusion, this study applied a network approach demonstrating how FAA compounds alter different pathways against breast cancer, which was supplementary to other studies on drugs against breast cancer. Furthermore, we confirmed that FAA substantially influenced numerous breast cancer-related targets, a finding that was consistent with present cancer study trends showing that the occurrence and development of breast cancer is a result of the gradual accumulation of distinct genome modifications in cancer cells (64,65). We fully expect that our research can help to promote the employment of network pharmacology in uncovering the potential mechanisms of anticancer Chinese herbs and provide clues to assess the synergy of herbs in the treatment of other complex diseases, especially cancer.

Acknowledgments

Funding: This study was supported by Heilongjiang Science Foundation (Grant No. H2018046).

Footnote

Reporting Checklist: The authors have completed the STREGA reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-5769/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5769/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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(English Language Editor: A. Kassem)

Cite this article as: Song Y, Wang J, Wang X, Zhang H, Niu X, Yang Y, Yang X, Yin L, Wang Y, Zhang C, Shui R, Zhang Q, Ji H. Analyzing the multi-target pharmacological mechanism of folium *Artemisia argyi* acting on breast cancer: a network pharmacology approach. Ann Transl Med 2022;10(24):1368. doi: 10.21037/atm-22-5769

AKT1, MYC, CASP3, EGFR, JUN, CCND1, VEGFA, ESR1, MAPK1, EGF, IL6, PTGS2, ERBB2, FOS, MMP9, CXCL8, MMP2, BCL2L1, CASP8, AR, IL1B, CCL2, CDKN1A, IL10, PPARG, RELA, SPP1, ICAM1, PGR, SERPINE1, STAT1, HIF1A, CASP9, IFNG, IL2, AHR, MMP1, MMP3, CCNB1, NFKBIA, CAV1, RB1, PLAU, IGF2, NFE2L2, MPO, IGFBP3, PARP1, RUNX2, ABCG2, CD40LG, RAF1, HSPB1, NQO1, GJA1, IRF1, PRKCA, E2F1, CTSD, CHEK2, GSTP1, TOP2A, TOP1, BCL2, ERBB3, CYP1A1, BIRC5, BAX, CYP1B1, RASSF1, ODC1, INSR, TP63, GSTM1, NR3C2

Figure S1 Seventy-five common targets shared by the FAA compound targets and the breast cancer-related targets.

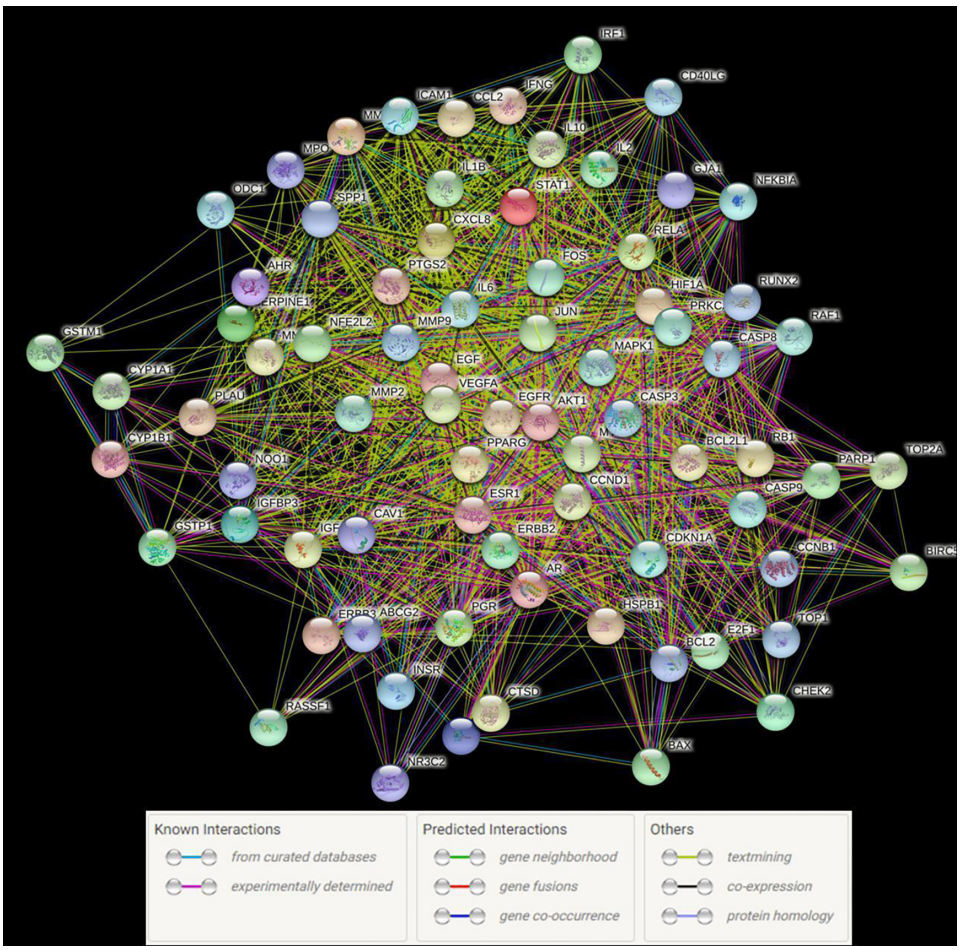

Figure S2 PPI network of FAA compound targets against breast cancer from the STRING database. PPI, protein-protein interaction; FAA, folium Artemisia argyi; STRING, Search Tool for the Retrieval of Interacting Genes.

https://dx.doi.org/10.21037/atm-22-5769

Table S1 All FAA compounds before screening

Molecule ID	Molecule name	OB (%)	DL
MOL001015	ZINC00388662	67.05	0.08
MOL001040	(2R)-5,7-dihydroxy-2-(4-hydroxyphenyl)chroman-4-one	42.36	0.21
MOL001121	19894-97-4	49.98	0.06
MOL001129	l-Verbenone	50.66	0.06
MOL000118	(L)-alpha-Terpineol	48.8	0.03
MOL000119	ZINC02040970	40.43	0.06
MOL001217	()-Bornyl acetate	65.55	0.08
MOL001242	dl-Thujone	63.88	0.05
MOL001245	(1S,5R)-7,7-dimethyl-4-bicyclo[3.1.1]hept-3-enecarboxaldehyde	41.25	0.06
MOL000125	(-)-alpha-Pinene	46.25	0.05
MOL001254	(S)-p-Mentha-1,8-dien-7-al	39	0.03
MOL000126	(-)-nopinene	44.84	0.05
MOL000128	NERYLACETATE	25.94	0.04
MOL000130	CAM	67.17	0.05
MOL001303	(1R,2R,4S)-2,4-diisopropenyl-1-methyl-1-vinylcyclohexane	5.58	0.06
MOL000131	EIC	41.9	0.14
MOL001388	(+)-Ledol	16.96	0.12
MOL001442	phytol	33.82	0.13
MOL001494	Mandenol	42	0.19
MOL001600	copaene	29.47	0.12
MOL001640	NON	26.74	0.03
MOL000018	(+/-)-Isoborneol	86.98	0.05
MOL001871	simiarenol	11.86	0.77
MOL001899	ZINC02169908	23.3	0.1
MOL000019	D-Camphene	34.98	0.04
MOL000197	Myrcene	24.96	0.02
MOL001999	scoparone	74.75	0.09
MOL000200	(S)-(+)-alpha-Phellandrene	27.9	0.02
MOL002002	cis-Carveol	45.61	0.03
MOL002021	4-Vinyl-m-xylene	36.82	0.02
MOL000207	Methyleugenol	73.36	0.04
MOL000208	()-Aromadendrene	55.74	0.1
MOL002160	1-terpineol	49.83	0.03
MOL002185	7-oxabicyclo-2.2.1-heptane,1-methyl-4-[1-methylethyl]-	60.92	0.04
MOL000223	caffeic acid	25.76	0.05

Table S1 (*continued*)

https://dx.doi.org/10.21037/atm-22-5769

Table S1 (*continued*)

Molecule ID	Molecule name	OB (%)	DL
MOL000234	L-Limonen	38.09	0.02
MOL002351	3-Hexenol	62.74	0.01
MOL000024	alpha-humulene	22.98	0.06
MOL002453	(-)-Comphene	34.98	0.04
MOL000252	farnesol	28.44	0.06
MOL002558	Skimmetin	27.37	0.05
MOL000259	o-Thymol	43.28	0.03
MOL000262	(1R,4S)-1,7,7-trimethylbicyclo[2.2.1]hept-2-ene	39.62	0.04
MOL000264	Tereben	29.62	0.02
MOL000266	beta-Cubebene	32.81	0.11
MOL000267	beta-Citronellol	38.89	0.02
MOL002675	Hexenal	46.01	0.01
MOL000268	(1S,5S)-1-isopropyl-4-methylenebicyclo[3.1.0]hexane	46.21	0.04
MOL000027	alpha-Curcumene	4.68	0.06
MOL000271	l-carvone	49.47	0.03
MOL002883	Ethyl oleate (NF)	32.4	0.19
MOL003047	[(1S)-endo]-(-)-Borneol	83.54	0.05
MOL003180	widdrene	53.81	0.12
MOL000034	2-[(1R,3S,4S)-3-isopropenyl-4-methyl-4-vinylcyclohexyl]propan-2-ol	19.03	0.07
MOL003521	Isohomogenol	32.61	0.04
MOL003574	α-gurjunene	52.57	0.1
MOL000358	beta-sitosterol	36.91	0.75
MOL000361	Amyrin	17.6	0.76
MOL003837	esculetin	22.97	0.07
MOL003937	Naphthalene, 1,2,3,4,4a,5,6,8a-octahydro-7-methyl-4-methylene-1-(1-methylethyl)-, (1alpha,4abeta,8aalpha)-	20.21	0.08
MOL000040	Scopoletol	27.77	0.08
MOL000415	rutin	3.2	0.68
MOL000431	coumarin	29.17	0.04
MOL000441	LUPENONE	11.66	0.78
MOL004480	acetic acid	47.87	0
MOL000449	Stigmasterol	43.83	0.76
MOL000459	CHEBI:39932	32.79	0.01
MOL004617	Ayapanin	41.55	0.06
MOL004741	(7aR)-4,4,7a-trimethyl-6,7-dihydro-5H-benzofuran-2-one	40.48	0.07

Table S1 (*continued*)

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Table S1 (*continued*)

Molecule ID	Molecule name	OB (%)	DL
MOL000478	Eucarvone	53.14	0.03
MOL000479	Farnesene	17.42	0.05
MOL000508	Friedelin	29.16	0.76
MOL002003	(-)-Caryophyllene oxide	32.67	0.13
MOL000520	alpha-amyrin	10.28	0.76
MOL005386	Vulgarin	29.21	0.2
MOL005705	Eicosanol	12.1	0.16
MOL005711	vinyl 2,2-dimethyl-3-phenyl-propionate	27.55	0.06
MOL005712	3-methyl-6-(1-methylethylidene)-cyclohexene	29.14	0.02
MOL005713	2,6,6-Trimethylcyclohexa-2,4-dienone	75.49	0.03
MOL005714	cirsilneol	81.96	0.01
MOL005715	3,4-DIMETHYLBIPHENYL	27.29	0.06
MOL001878	4,5-Di-O-caffeoylquinic acid	1.78	0.69
MOL005717	6,6-dimethyl-3-methylene bicyclo[3.1.1]-heptane	49.35	0.05
MOL005718	6-Methoxy-7,8-methylenedioxy coumarin	28.61	0.13
MOL005719	12-Tricosanol	12.42	0.23
MOL005720	24-methylenecyloartanone	41.11	0.79
MOL005721	cycloart-25-en-3β,24-diol	20.92	0.8
MOL005722	ZINC00395662	51.92	0.01
MOL005723	Phytodolor	52.32	0.1
MOL005724	Amylene	41.4	0
MOL005725	(-)-isoperitenone	56.98	0.03
MOL005726	Artemisia ketone	74.44	0.02
MOL005727	MIPK	74.51	0.01
MOL005728	Ayanin	14.96	0.37
MOL005729	1-octen-3-ol	15.22	0.4
MOL005730	3-NONANONE	22.89	0.02
MOL005731	Methylenecyclopentane	51.11	0.01
MOL005732	Pentadecanal	10.38	0.06
MOL005733	(2S)-6-methyl-2-[(2S,5R)-5-methyl-5-vinyl-2-tetrahydrofuranyl]hept-5-en-3-one	23.29	0.08
MOL005734	eupatilin	29.39	0.38
MOL005735	dammaradienyl acetate	44.83	0.83
MOL005736	cyperene	51.87	0.11
MOL005737	vulgarole	49.04	0.14
MOL005738	2-benzylidenesuccinic acid	70.7	0.06

Table S1 (*continued*)

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Table S1 (*continued*)

Molecule ID	Molecule name	OB (%)	DL
MOL005739	Neryl butyrate	51.55	0.06
MOL005740	artemisia alcohol	45.45	0.04
MOL005741	cycloartenol acetate	41.11	0.8
MOL005742	Chinova acid	17.44	0.72
MOL005743	Proximadiol	36.71	0.11
MOL005744	carvenone	62.99	0.06
MOL005745	fernenol	10.5	0.78
MOL005746	fernenone	18.25	0.76
MOL005747	[(Z)-hex-1-enyl] acetate	22.18	0.02
MOL005748	17020-04-1	9.53	0.74
MOL005749	isopulegone	64.31	0.03
MOL005750	isoamylcyclohexane	28.19	0.02
MOL005751	(6aS,6aS,6bR,8aR,12aR,14aR,14bS)-4,4,6a,6b,8a,11,11,14a-octamethyl-2,6,6a,7,8,9,10,12,12a,13,14,14b-dodecahydro-1H-picen-3-one	13.64	0.77
MOL005752	[(4R)-4-isopropenyl-1-cyclohexenyl]methanol	49.01	0.03
MOL000608	()-Terpinen-4-ol	81.41	0.03
MOL000611	beta-Bourbonene	16.98	0.11
MOL000612	(-)-alpha-cedrene	55.56	0.1
MOL000615	delta-amorphene	17.95	0.08
MOL000674	Farnesol acetate	21.97	0.11
MOL000676	DBP	64.54	0.13
MOL000709	(S)-Matsutake alcohol	40.11	0.01
MOL000714	Hyacinthin	38.65	0.02
MOL000775	EEE	45.02	0
MOL000777	(2S)-2-methylbutan-1-ol	81.23	0
MOL000890	(+)-alpha-Curcumene	26.56	0.06
MOL000911	Terpilene	33.95	0.02
MOL000913	tricyclene	36.11	0.07
MOL000968	beta-Bisabolene	29.59	0.06
MOL000971	Ethylpalmitate	18.99	0.14
MOL000974	cuminal	38.29	0.03
MOL000098	quercetin	46.43	0.28

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Table S2 Breast cancer-related gene results in Genecards

Gene Symbol	GeneCards Link
BRCA2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BRCA2
BRCA1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BRCA1
TP53	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TP53
PALB2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PALB2
CHEK2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CHEK2
CDH1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDH1
ATM	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ATM
BRIP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BRIP1
ERBB2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ERBB2
MSH6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MSH6
MSH2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MSH2
APC	https://www.genecards.org/cgi-bin/carddisp.pl?gene=APC
PTEN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PTEN
MLH1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MLH1
BARD1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BARD1
ESR1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ESR1
EGFR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EGFR
PIK3CA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PIK3CA
RAD51D	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAD51D
PMS2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PMS2
AKT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AKT1
CDKN2A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDKN2A
RAD51C	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAD51C
NBN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NBN
KRAS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KRAS
STK11	https://www.genecards.org/cgi-bin/carddisp.pl?gene=STK11
CCND1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CCND1
NF1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NF1
SMAD4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SMAD4
RAD50	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAD50
CTNNB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CTNNB1
AR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AR
VEGFA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=VEGFA
MYC	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MYC
BRAF	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BRAF

Table S2 (*continued*)

https://dx.doi.org/10.21037/atm-22-5769

Table S2 (*continued*)

Gene Symbol	GeneCards Link
POLE	https://www.genecards.org/cgi-bin/carddisp.pl?gene=POLE
CYP19A1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CYP19A1
MRE11	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MRE11
CDK4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDK4
RB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RB1
HRAS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HRAS
FGFR2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FGFR2
MDM2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MDM2
CDKN1B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDKN1B
CDKN1A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDKN1A
RAD51	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAD51
TERT	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TERT
TGFBR2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TGFBR2
TGFB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TGFB1
IL6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL6
EGF	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EGF
MET	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MET
STAT3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=STAT3
TNF	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TNF
CASP8	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CASP8
MTOR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MTOR
BAX	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BAX
ESR2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ESR2
NOTCH1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NOTCH1
FAS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FAS
IGF2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IGF2
MIR21	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR21
TP63	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TP63
PGR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PGR
FGFR1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FGFR1
CXCR4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CXCR4
AXIN2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AXIN2
KIT	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KIT
EP300	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EP300
RAD51L3-RFFL	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAD51L3-RFFL

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
EPCAM	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EPCAM
SRC	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SRC
AURKA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AURKA
XRCC3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=XRCC3
NRAS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NRAS
ERCC2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ERCC2
FGFR3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FGFR3
PLAU	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PLAU
EZH2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EZH2
ALK	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ALK
RET	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RET
BCL2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BCL2
SMARCA4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SMARCA4
TWIST1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TWIST1
MGMT	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MGMT
BAP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BAP1
NFKB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NFKB1
RAF1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAF1
PIK3R1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PIK3R1
TYMS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TYMS
PPARG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PPARG
IL10	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL10
FHIT	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FHIT
AKT2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AKT2
TOP2A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TOP2A
MUC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MUC1
MMP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MMP1
PRLR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PRLR
MTHFR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MTHFR
CXCL12	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CXCL12
DNMT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=DNMT1
PDGFRB	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PDGFRB
STAT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=STAT1
ATR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ATR
TGFBR1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TGFBR1

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
INS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=INS
MIR34A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR34A
TYMP	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TYMP
TSC2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TSC2
BMPR1A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BMPR1A
RELA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RELA
SMAD3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SMAD3
FLT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FLT1
H19	https://www.genecards.org/cgi-bin/carddisp.pl?gene=H19
MAP2K1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MAP2K1
MIR145	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR145
MUTYH	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MUTYH
WT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=WT1
ERBB4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ERBB4
PPM1D	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PPM1D
CHEK1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CHEK1
GLI1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GLI1
XIAP	https://www.genecards.org/cgi-bin/carddisp.pl?gene=XIAP
LEP	https://www.genecards.org/cgi-bin/carddisp.pl?gene=LEP
SPP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SPP1
MIR17	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR17
SNAI2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SNAI2
GNAS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GNAS
MIR146A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR146A
IDH1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IDH1
ERCC6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ERCC6
CYP1B1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CYP1B1
CYP17A1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CYP17A1
TNFRSF10B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TNFRSF10B
SLC2A1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SLC2A1
ERCC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ERCC1
MIR155	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR155
MIR27A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR27A
IGF1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IGF1
HSPB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HSPB1

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
VDR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=VDR
MIR221	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR221
XRCC2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=XRCC2
JAK2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=JAK2
CDKN3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDKN3
ZEB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ZEB1
PHB	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PHB
FGFR4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FGFR4
MIR143	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR143
PTGS2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PTGS2
C11orf65	https://www.genecards.org/cgi-bin/carddisp.pl?gene=C11orf65
KRT5	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KRT5
DICER1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=DICER1
SOX2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SOX2
PDGFRA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PDGFRA
TGFB2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TGFB2
CASP3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CASP3
MSH3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MSH3
MIR31	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR31
WWOX	https://www.genecards.org/cgi-bin/carddisp.pl?gene=WWOX
IRS1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IRS1
AKT3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AKT3
NF2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NF2
MIR125A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR125A
TCF7L2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TCF7L2
MIR200C	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR200C
TP73	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TP73
PTPN11	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PTPN11
MIR222	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR222
IGF1R	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IGF1R
FASLG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FASLG
MMP9	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MMP9
SMAD7	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SMAD7
MIR200A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR200A
ABCG2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ABCG2

Table S2 (*continued*)

https://dx.doi.org/10.21037/atm-22-5769

Table S2 (*continued*)

Gene Symbol	GeneCards Link
MMP2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MMP2
MAPK1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MAPK1
MIR126	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR126
MIR205	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR205
GNRH1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GNRH1
CREB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CREB1
DPYD	https://www.genecards.org/cgi-bin/carddisp.pl?gene=DPYD
TSC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TSC1
NTRK1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NTRK1
POLD1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=POLD1
FOXP3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FOXP3
MIR141	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR141
CCL2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CCL2
PDCD1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PDCD1
FH	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FH
HIF1A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HIF1A
GATA3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GATA3
MIR200B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR200B
GJA1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GJA1
AHR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AHR
NOS2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NOS2
MIR182	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR182
MIR10B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR10B
NKX2-1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NKX2-1
ODC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ODC1
WNT5A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=WNT5A
KRT14	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KRT14
COMT	https://www.genecards.org/cgi-bin/carddisp.pl?gene=COMT
RAD54L	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAD54L
KLLN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KLLN
ABCB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ABCB1
ABL1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ABL1
MIR20A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR20A
ABRAXAS1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ABRAXAS1
RARA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RARA

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
YAP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=YAP1
BMP2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BMP2
GSTP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GSTP1
FOXO1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FOXO1
JUN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=JUN
KLK3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KLK3
KISS1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KISS1
MIR335	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR335
CAT	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CAT
BIRC5	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BIRC5
MAP3K1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MAP3K1
MIR195	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR195
ERBB3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ERBB3
CTSD	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CTSD
GSTM1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GSTM1
PDGFB	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PDGFB
PIK3R2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PIK3R2
MIR203A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR203A
FGF8	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FGF8
WNT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=WNT1
BUB1B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BUB1B
MIR148A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR148A
MIR181A1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR181A1
SOS1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SOS1
MAD1L1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MAD1L1
CD44	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD44
TFF1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TFF1
MAP2K2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MAP2K2
SLC22A18	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SLC22A18
ETS1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ETS1
MIR210	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR210
CDKN2B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDKN2B
CYP2D6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CYP2D6
MEN1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MEN1
MIR183	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR183

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
CXCL8	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CXCL8
TFAP2A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TFAP2A
EDNRA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EDNRA
HMMR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HMMR
MKI67	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MKI67
RB1CC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RB1CC1
ABCC2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ABCC2
IL1B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL1B
MIR22	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR22
IGF2R	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IGF2R
PRKCD	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PRKCD
ETV6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ETV6
STAT5B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=STAT5B
MIR29C	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR29C
IFNG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IFNG
PARP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PARP1
HDAC4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HDAC4
ABCC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ABCC1
NOTCH3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NOTCH3
XRCC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=XRCC1
CD274	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD274
IGFBP3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IGFBP3
MIR127	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR127
MIR96	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR96
MIR204	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR204
KITLG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KITLG
CDK1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDK1
RUNX2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RUNX2
MIR373	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR373
MIR30E	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR30E
NTRK3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NTRK3
CDKN2C	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDKN2C
CYP1A1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CYP1A1
NCOA3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NCOA3
INSR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=INSR

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
ING1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ING1
MIR18A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR18A
MIR191	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR191
TGFA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TGFA
JAG1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=JAG1
CSF3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CSF3
CDK2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDK2
PRKACA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PRKACA
STS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=STS
ETV4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ETV4
CASP9	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CASP9
MIRLET7D	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIRLET7D
FGF2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FGF2
CTNNA1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CTNNA1
TNFSF10	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TNFSF10
MAPK8	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MAPK8
MIR146B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR146B
HFE	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HFE
KDR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KDR
GRN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GRN
BDNF	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BDNF
BCL2L1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BCL2L1
TACC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TACC1
BCAR3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BCAR3
SP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SP1
NOTCH2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NOTCH2
CAV1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CAV1
VEGFC	https://www.genecards.org/cgi-bin/carddisp.pl?gene=VEGFC
MIR199B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR199B
IL2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL2
MIR342	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR342
CDC6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDC6
SOX4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SOX4
KCNQ1OT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KCNQ1OT1
MAPK3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MAPK3

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
RRAS2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RRAS2
PTCH1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PTCH1
EPOR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EPOR
BCAR1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BCAR1
RASSF1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RASSF1
E2F1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=E2F1
PTK2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PTK2
FOXC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FOXC1
KRT19	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KRT19
NRG1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NRG1
VWF	https://www.genecards.org/cgi-bin/carddisp.pl?gene=VWF
REST	https://www.genecards.org/cgi-bin/carddisp.pl?gene=REST
NGF	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NGF
CEACAM5	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CEACAM5
HMGA1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HMGA1
MSR1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MSR1
PML	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PML
CDK6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDK6
LHCGR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=LHCGR
MIR451A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR451A
PLAUR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PLAUR
NQO1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NQO1
FANCD2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FANCD2
MMP14	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MMP14
MIR206	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR206
HGF	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HGF
SEMA3A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SEMA3A
MIAT	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIAT
MIR29B2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR29B2
DDR2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=DDR2
PSEN2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PSEN2
CBFB	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CBFB
MIR128-2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR128-2
MIR122	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR122
TLR4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TLR4

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
MYLK	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MYLK
PCNA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PCNA
SDHB	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SDHB
MIR193B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR193B
CCNE1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CCNE1
CCNA2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CCNA2
MIRLET7I	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIRLET7I
MIR152	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR152
RHOA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RHOA
MIR181B1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR181B1
CIB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CIB1
CCNB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CCNB1
MIR320A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR320A
BMP6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BMP6
NTRK2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NTRK2
CYCS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CYCS
ATF1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ATF1
RAD21	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAD21
PROM1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PROM1
FOS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FOS
PRKAR1A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PRKAR1A
KRT17	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KRT17
PTHLH	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PTHLH
GMNN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GMNN
VIM	https://www.genecards.org/cgi-bin/carddisp.pl?gene=VIM
NQO2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NQO2
SOD2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SOD2
MIR142	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR142
IRS2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IRS2
MIR429	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR429
PRKCA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PRKCA
SF3B1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SF3B1
HDAC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HDAC1
BRMS1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BRMS1
ENG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ENG

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
MAPK14	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MAPK14
SMAD2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SMAD2
LIMK1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=LIMK1
NAT2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NAT2
MIR499A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR499A
RRAS	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RRAS
DKC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=DKC1
HSP90AA1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HSP90AA1
MIRLET7A3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIRLET7A3
TIMP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TIMP1
FBXW7	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FBXW7
KRT7	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KRT7
MIR181A2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR181A2
MYH9	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MYH9
FN1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FN1
ABCC11	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ABCC11
CCND2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CCND2
SNAI1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SNAI1
RARB	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RARB
MTUS1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MTUS1
GSK3B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GSK3B
ICAM1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ICAM1
GREB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GREB1
LOC111589215	https://www.genecards.org/cgi-bin/carddisp.pl?gene=LOC111589215
RAC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAC1
MIR214	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR214
MIR196A2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR196A2
PLK1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PLK1
MIRLET7A1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIRLET7A1
WRN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=WRN
NUP214	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NUP214
RPS6KB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RPS6KB1
MCL1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MCL1
NME1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NME1
PIK3CG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PIK3CG

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
CSF2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CSF2
TIMP3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TIMP3
BAK1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BAK1
PRL	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PRL
GPER1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GPER1
KRT20	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KRT20
SERPINE1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SERPINE1
KRT18	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KRT18
TOP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TOP1
SNCG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SNCG
MIR98	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR98
MMP7	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MMP7
MIR223	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR223
PLCB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PLCB1
AREG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AREG
EHMT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EHMT1
NFE2L2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NFE2L2
ECM1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ECM1
PTPN3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PTPN3
RPS6KA3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RPS6KA3
DNMT3A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=DNMT3A
NR3C2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NR3C2
HOTAIR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HOTAIR
MACF1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MACF1
TIMP2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TIMP2
AXL	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AXL
MIR193A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR193A
ABCA3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ABCA3
MLH3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MLH3
ITGB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ITGB1
THBS1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=THBS1
RAP1A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAP1A
PRMT7	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PRMT7
FASN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FASN
SERPINB5	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SERPINB5

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
MIR128-1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR128-1
FLT4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FLT4
IFI27	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IFI27
BMI1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BMI1
GADD45A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GADD45A
EPHA4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EPHA4
KRT8	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KRT8
MIR328	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR328
SMAD6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SMAD6
VEGFD	https://www.genecards.org/cgi-bin/carddisp.pl?gene=VEGFD
OGG1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=OGG1
HSPB8	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HSPB8
SHBG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SHBG
SKP2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SKP2
PMS1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PMS1
DNMT3B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=DNMT3B
GRP	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GRP
CTLA4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CTLA4
MALAT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MALAT1
MIR140	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR140
GRB2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GRB2
MTA1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MTA1
HERC2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HERC2
FOXA1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FOXA1
PVT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PVT1
PIP	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PIP
BAD	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BAD
MIR106B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR106B
SIRT1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SIRT1
ALDH1A1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ALDH1A1
TERC	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TERC
MIR29A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR29A
MIR100	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR100
ANXA5	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ANXA5
MMP3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MMP3

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
ERCC4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ERCC4
CDC42	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDC42
E2F3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=E2F3
MIR9-3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR9-3
KLK10	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KLK10
BMP4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BMP4
FGF1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FGF1
PIK3CB	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PIK3CB
FOXO3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FOXO3
LGALS3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=LGALS3
HDAC9	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HDAC9
FOXM1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FOXM1
SHC1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SHC1
CDH2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDH2
POU5F1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=POU5F1
BCAS1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BCAS1
NFKBIA	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NFKBIA
TNFSF11	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TNFSF11
RAD51B	https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAD51B
PRKN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PRKN
MIR30A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR30A
CD24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD24
CA9	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CA9
HSPA5	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HSPA5
MIR150	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR150
TSG101	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TSG101
FLCN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FLCN
BECN1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BECN1
KEAP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KEAP1
SETD2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SETD2
ADIPOQ	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ADIPOQ
IL1RN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL1RN
BCAR4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BCAR4
UCA1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=UCA1
CCND3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CCND3

Table S2 (*continued*)

https://dx.doi.org/10.21037/atm-22-5769

Table S2 (*continued*)

Gene Symbol	GeneCards Link
HBEGF	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HBEGF
MIR34C	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR34C
ZEB2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ZEB2
BIRC3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BIRC3
IDH2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IDH2
CD40LG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD40LG
CASP7	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CASP7
EZR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EZR
ERCC5	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ERCC5
MIR502	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR502
SDHD	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SDHD
BSG	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BSG
MIR520C	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR520C
S100A4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=S100A4
JAK1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=JAK1
DIRC3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=DIRC3
HMGA2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HMGA2
GNRHR	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GNRHR
ST14	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ST14
MIR199A1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR199A1
NRP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NRP1
XBP1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=XBP1
CTSB	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CTSB
SMARCB1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SMARCB1
EPHA2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EPHA2
CREBBP	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CREBBP
CLU	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CLU
TOX3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TOX3
HSPA4	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HSPA4
BCL2L11	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BCL2L11
MYCN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MYCN
CSF1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CSF1
MIR25	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR25
HOXB13	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HOXB13
GAS5	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GAS5

Table S2 (*continued*)

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Table S2 (*continued*)

Gene Symbol	GeneCards Link
CD40	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD40
MMP11	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MMP11
NR1H2	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NR1H2
CDC25A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CDC25A
FGF3	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FGF3
MIR661	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR661
POSTN	https://www.genecards.org/cgi-bin/carddisp.pl?gene=POSTN
MIR483	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR483
YBX1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=YBX1
PAK1	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PAK1
MIR99A	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR99A
MUC16	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MUC16
TEK	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TEK

Table S3 Breast cancer-related gene results in OMIM

Cytogenetic location	Gene/Locus	Gene/Locus MIM number
1p36.13	PLA2G2A, PLA2B, PLA2L, MOM1	172411
1p36.12	EPHB2, EPHT3, DRT, ERK, PCBC, CAPB, BDPLT22	600997
1p34.2	PTPRF, LAR, BNAH2	179590
1p34.1	MUTYH, MYH	604933
1p34.1	RAD54L, HR54, HRAD54	603615
1p22.1	BCAR3, SH2D3B, NSP2	604704
1p13.2	BCAS2, DAM1	605783
1p13.2	NRAS, ALPS4, NS6, CMNS, NCMS	164790
1q21.2	FALEC, FAL1	616092
1q24.3	FASLG, TNFSF6, APT1LG1, FASL, ALPS1B	134638
1q25.3	RNASEL, RNS4, PRCA1, HPC1	180435
1q32.1	BLACAT1, LINC00912	615480
1q42.2-q43	PCAP	602759
1q43	FH, HLRCC, MCUL1, FMRD	136850
1q43-q44	SDCCAG8, CCCAP, SLSN7, BBS16	613524
2p24.3	GACAT3, LINC01458	616132
2p21	EPCAM, ACSTD1, TROP1, M4S1, MIC18, DIAR5, HNPCC8	185535
2p21-p16	MSH2, COCA1, FCC1, HNPCC1	609309

Table S3 (*continued*)

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Table S3 (*continued*)

Cytogenetic location	Gene/Locus	Gene/Locus MIM number
2p16.3	MSH6, GTBP, HNPCC5	600678
2p15	EHBP1, KIAA0903, HPC12	609922
2q12.2	C2orf40, ECRG4	611752
2q13	BUB1	602452
2q14.1	IL1B	147720
2q14.1	IL1RN, MVCD4, DIRA	147679
2q31.3	SCHLAP1, PCAT114, LINC00913	615568
2q32.2	DIRC1	606423
2q33.1	CASP10, MCH4, ALPS2	601762
2q33.1	CASP8, MCH5, ALPS2B	601763
2q35	BARD1	601593
3p24.1	TGFBR2, HNPCC6, AAT3, MFS2, LDS2	190182
3p22.2	MLH1, COCA2, HNPCC2	120436
3p22.2	DLEC1, DLC1	604050
3p22.1	CTNNB1, NEDSDV, EVR7	116806
3q13.33	RABL3, PNCA5	618542
3q23	ATR, FRP1, SCKL1, FCTCS	601215
3q26.32	PIK3CA, CLOVE, MCAP, MCM, MCMTC, CWS5, CLAPO	171834
3q27.1	EIF4G1, EIF4G, PARK18	600495
4p16.3	FGFR3, ACH	134934
4q21.21	PCAT4, GDEP	609717
4q23	ADH1B, ADH2	103720
4q31.3	TLR2, TIL4	603028
4q32.3	PALLD, KIAA0992, PNCA1	608092
4q35.1	KMHN1	609488
5p13.2	PRLR, MFAB, HPRL	176761
5p13.1	DAB2, DOC2	601236
5q14.3	LUCAT1, SCAL1	618190
5q22.2	APC, GS, FPC, BTPS2, DESMD	611731
5q22.2	MCC	159350
5q31.1	IRF1, MAR	147575
5q34	HMMR	600936
5q35.2	FGFR4	134935
6p25.2	NQO2, NMOR2	160998
6p24.3	CTAG3, CAGE1	608304

Table S3 (*continued*)

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Table S3 (*continued*)

Cytogenetic location	Gene/Locus	Gene/Locus MIM number
6p24.3	HULC	612210
6p22.3	CASC15, LINC00340	616610
6q23.3	PBOV1, UROC28, UC28	605669
6q24.3-q25.1	SASH1, KIAA0790, CAPOK, DUH1	607955
6q25.1-q25.2	ESR1, ESR, ESTRR	133430
6q26	PRKN, PARK2, PDJ	602544
7p22.3	MAD1L1, TXBP181	602686
7p22.1	PMS2, PMSL2, HNPCC4	600259
7p21.1	MACC1	612646
7p11.2	EGFR, NISBD2	131550
7p11.2	VOPP1, ECOP, GASP	611915
7q11.23	PTPN12, PTPG1	600079
7q31.2	ST7, TSG7, RAY1, FAM4A1	600833
7q34	BRAF, NS7	164757
8p22	DLC1	604258
8p22	PDGFRL, PDGRL, PRLTS	604584
8q11.23	RB1CC1, CC1, KIAA0203	606837
8q22.1	RAD54B	604289
8q24.21	PCAT1	616043
8q24.21	PCAT2, PCA2, CARLO4	617678
8q24.21	PRNCR1, PCAT8	615452
8q24.21	CASC19, LINC01245, CARLO6	617703
8q24.21	CCAT1, CARLO5	617705
8q24.21	CASC21, LINC01244, CARLO2	617702
8q24.21	CASC8, LINC00860, CARLO1	617701
8q24.21	CASC11, LINC00990, CARLO7	617704
9p21.3	CDKN2A, MTS1, P16, MLM, CMM2	600160
9q21.2	PCA3, DD3	604845
9q22.33	FOXE1, FKHL15, TITF2, TTF2, NMTC4	602617
9q22.33	GALNT12, CRCS1	610290
9q33.1	DEC1	604767
10p15.2	KLF6, COPEB, BCD1, ZF9	602053
10p11.23	MAP3K8, COT, EST, TPL2	191195
10q11.22	MSMB, HPC13	157145
10q11.23	ERCC6, CKN2, COFS1, CSB, ARMD5, UVSS1, POF11	609413

Table S3 (*continued*)

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Table S3 (*continued*)

Cytogenetic location	Gene/Locus	Gene/Locus MIM number
10q23.2	SNCG, BCSG1	602998
10q23.31	PTEN, MMAC1, GLM2, CWS1	601728
10q25.2	MXI1	600020
10q25.3	HABP2, PHBP, HGFAL, FSAP, NMTC5	603924
10q26.11	CASC2	608598
10q26.13	FGFR2, BEK, CFD1, JWS, TK14, BBDS	176943
11p15.5	HRAS	190020
11p15.4	SLC22A1L, BWSCR1A, IMPT1	602631
11p11.2	PTPRJ, DEP1	600925
11q13.3	CCND1, PRAD1, BCL1	168461
11q13.3	ORAOV1, TAOS1	607224
11q13.3	CTTN, EMS1	164765
11q22.3	ATM, ATA, AT1	607585
11q23.1	COLCA1	615693
11q23.1	COLCA2	615694
11q23.1	PPP2R1B	603113
11q24.2	HEPN1	611641
11q25	OPCML	600632
12p12.1	CASC1, LAS1, PPP1R54	616906
12p12.1	KRAS, KRAS2, RASK2, NS, CFC2, RALD, OES	190070
12q13.13	ACVR1B, ACVRLK4, ALK4	601300
12q13.2	SBEM	610857
12q14.2	SRGAP1, KIAA1304, NMTC2	606523
12q24.12	ALDH2	100650
12q24.31	CDK2AP1, DOC1	602198
12q24.33	POLE, CRCS12, FILS, IMAGEI	174762
13q13.1	BRCA2, FANCD1, BROVCA2, GLM3, PNCA2	600185
13q14.2	RB1	614041
14q13.3	NKX2-1, TITF1, NKX2A, TTF1, NMTC1	600635
14q24.3	MLH3, HNPCC7	604395
14q32.33	XRCC3, CMM6	600675
14q32.33	AKT1, CWS6	164730
15q15.1	BUB1B, BUBR1, MVA1	602860
15q15.1	RAD51, RECA, MRMV2, FANCR	179617
15q23	PCAT29	616273

Table S3 (*continued*)

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Table S3 (*continued*)

Cytogenetic location	Gene/Locus	Gene/Locus MIM number
15q25.1	CHRNA5, LNCR2	118505
15q25.1	CHRNA3, LNCR2, PAOD2, BAIPRCK	118503
15q26.1	IQGAP1, SAR1	603379
16p13.13	BCAR4	613746
16p12.2	PALB2, FANCN, PNCA3	610355
16q22.1	CDH1, UVO, LCAM, ECAD, BCDS1	192090
16q22.1	NQO1, DIA4, NMOR1	125860
16q22.2-q22.3	ZFHX3, ATBF1	104155
16q23.1	BCAR1, CRKAS, CAS	602941
17p13.3	OVCA2	607896
17p13.3	HIC1	603825
17p13.1	TP53, P53, LFS1 , BCC7, BMFS5	191170
17p12	ELAC2, HPC2, COXPD17	605367
17p11.2	FLCN, BHD	607273
17q12	RAD51D, RAD51L3, BROVCA4	602954
17q12	ERBB2, NGL, NEU, HER2	164870
17q21.31	BRCA1, PSCP, BROVCA1, PNCA4, FANCS	113705
17q21.32	HOXB13, HPC9	604607
17q21.33	PHB	176705
17q22	MPO	606989
17q22	RNF43, RNF124, SSPCS	612482
17q22	RAD51C, FANCO, BROVCA3	602774
17q23.2	PPM1D, WIP1, JDVS	605100
17q23.2	BRIP1, BACH1, FANCJ	605882
17q24.1	AXIN2, ODCRCS	604025
17q25.1	RHBDF2, IRHOM2, TOC	614404
18p11.22	GACAT2, MTCL1AS1	616131
18q11.2	PCAT18, LINC01092	617647
18q21.1	SMAD7, MADH7, CRCS3	602932
18q21.2	SMAD4, MADH4, DPC4, JIP, MYHRS	600993
18q21.2	DCC, MRMV1, HGPPS2	120470
19p13.3	STK11, PJS, LKB1	602216
19p13.12	UCA1, LINC00178, CUDR	617500
19q13.2	CYP2A6, CYP2A3, CYP2A, P450C2A	122720
19q13.2	PCAT19, LINC01190	618192

Table S3 (*continued*)

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Table S3 (*continued*)

Cytogenetic location	Gene/Locus	Gene/Locus MIM number
19q13.33	BAX	600040
19q13.33	POLD1, CRCS10, MDPL	174761
20q11.21	BASE	607627
20q11.23	SRC, ASV, SRC1, THC6	190090
20q11.23	BLCAP, BC10	613110
20q13.12	NCOA3, AIB1, TNRC14	601937
20q13.13	BCAS4	607471
20q13.2	BCAS1, NABC1	602968
20q13.2	AURKA, STK15, AURORA2, BTAK, ARK1, STK6, AIK	603072
21q22.3	TFF1, BCEI	113710
22q11.21	HIC2, HRG22, KIAA1020	607712
22q12.1	CHEK2, RAD53, CHK2, CDS1, LFS2	604373

https://dx.doi.org/10.21037/atm-22-5769