Supplementary Material



**Figure S1.** Total ion chromatogram of *Astragalus sarcocolla* leaf extract recorded in positive ionization mode.

|  |  |  |
| --- | --- | --- |
| C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\acacetin.png | C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\cinnamic acid 2d.png | C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\luteolin.png |
| **Acacetin** | **Cinnamic acid** | **Luteolin** |
| C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\kaempferol.png | C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\apigenin 2d.png |  |
| **Kaempferol** | **Apigenin** |  |

**Figure S2.** Molecular docking of compounds with MMP-9

|  |  |  |
| --- | --- | --- |
| C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\acacetin.png | C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\cinnamic acid.png | C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\luteolin.png |
| **Acacetin** | **Cinnamic acid** | **Luteolin** |
| C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\kaempferol.png | C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\apigenin.png |  |
| **Kaempferol** | **Apigenin** |  |

**Figure S3.** Molecular docking of compounds with PTGS2

|  |  |  |
| --- | --- | --- |
| C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\acacetin.png | C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\cinnamic acid-.png | C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\luteolin.png |
| **Acacetin** | **Cinnamic acid** | **Luteolin** |
| C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\kaempferol.png | C:\Users\اكسترا\AppData\Local\Microsoft\Windows\INetCache\Content.Word\apigenin.png |  |
| **Kaempferol** | **Apigenin** |  |

**Figure S4.** Molecular docking of compounds with EGFR

**Table S1.** OB and DL values of identified compounds

|  |  |  |
| --- | --- | --- |
| **Compound** | **DL** | **OB** |
| 7,3',4',5'-Tetrahydroxyflavone | 0.51 | 1 |
| Acacetin | 0.76 | 0.99 |
| Apigenin | 0.63 | 0.99 |
| Aromadendrin | 0.63 | 0.99 |
| Caffeic acid | 0.47 | 0.99 |
| Cinnamic acid | 0.65 | 0.49 |
| Ellagic acid | 0.22 | 0.99 |
| Ethyl ferulate | 0.61 | 0.9 |
| Gallic acid | 0.46 | 0.99 |
| Hyperin | 0.23 | 0.99 |
| Isofraxidin | 0.78 | 0.45 |
| Isoliquiritigenin | 0.58 | 0.78 |
| Kaempferol | 0.55 | 0.99 |
| Licochalcone A | 0.46 | 0.008 |
| Licochalcone B | 0.46 | 0.57 |
| Luteolin | 0.51 | 1 |
| Luteolin-5-O-β-glucoside | 0.51 | 1 |
| Morin | 0.46 | 0.99 |
| Myricetin | 0.37 | 0.99 |
| Naringin | 0.2 | 0.99 |
| Quercetin | 0.43 | 0.99 |
| Rosmarinic acid | 0.3 | 0.98 |
| Scoparone | 0.7 | 0.98 |
| Scopoletin | 0.7 | 0.99 |
| Sinapic acid | 0.76 | 0.7 |
| Syringic acid | 0.76 | 0.067 |
| Xanthoxylin | 0.75 | 0.047 |

**Table S2.** Target genes of each compound

|  |  |
| --- | --- |
| Name | Genes |
| 7,3',4',5'-Tetrahydroxyflavone | ESR2 |
| 7,3',4',5'-Tetrahydroxyflavone | MMP3 |
| 7,3',4',5'-Tetrahydroxyflavone | MMP9 |
| 7,3',4',5'-Tetrahydroxyflavone | CYP1B1 |
| 7,3',4',5'-Tetrahydroxyflavone | PTGS2 |
| 7,3',4',5'-Tetrahydroxyflavone | CFTR |
| 7,3',4',5'-Tetrahydroxyflavone | TERT |
| 7,3',4',5'-Tetrahydroxyflavone | MMP2 |
| 7,3',4',5'-Tetrahydroxyflavone | EGFR |
| 7,3',4',5'-Tetrahydroxyflavone | MMP13 |
| 7,3',4',5'-Tetrahydroxyflavone | MMP12 |
| 7,3',4',5'-Tetrahydroxyflavone | IGF1R |
| 7,3',4',5'-Tetrahydroxyflavone | MPO |
| 7,3',4',5'-Tetrahydroxyflavone | XDH |
| 7,3',4',5'-Tetrahydroxyflavone | AHR |
| 7,3',4',5'-Tetrahydroxyflavone | TYR |
| 7,3',4',5'-Tetrahydroxyflavone | ESR1 |
| 7,3',4',5'-Tetrahydroxyflavone | SRC |
| 7,3',4',5'-Tetrahydroxyflavone | APP |
| 7,3',4',5'-Tetrahydroxyflavone | PTK2 |
| 7,3',4',5'-Tetrahydroxyflavone | GLO1 |
| 7,3',4',5'-Tetrahydroxyflavone | HSD17B2 |
| 7,3',4',5'-Tetrahydroxyflavone | NUAK1 |
| Acacetin | ESR2 |
| Acacetin | MMP3 |
| Acacetin | MMP9 |
| Acacetin | CYP1B1 |
| Acacetin | PTGS2 |
| Acacetin | CFTR |
| Acacetin | TERT |
| Acacetin | MMP2 |
| Acacetin | EGFR |
| Acacetin | MMP13 |
| Acacetin | MMP12 |
| Acacetin | IGF1R |
| Acacetin | MPO |
| Acacetin | AR |
| Acacetin | NOS2 |
| Acacetin | XDH |
| Acacetin | AHR |
| Acacetin | TYR |
| Acacetin | ESR1 |
| Acacetin | SRC |
| Acacetin | APP |
| Acacetin | PTK2 |
| Acacetin | GLO1 |
| Acacetin | HSD17B2 |
| Acacetin | PFKFB3 |
| Apigenin | ESR2 |
| Apigenin | MMP3 |
| Apigenin | MMP9 |
| Apigenin | CYP1B1 |
| Apigenin | PTGS2 |
| Apigenin | CFTR |
| Apigenin | TERT |
| Apigenin | MMP2 |
| Apigenin | EGFR |
| Apigenin | MMP13 |
| Apigenin | MMP12 |
| Apigenin | IGF1R |
| Apigenin | MPO |
| Apigenin | AR |
| Apigenin | XDH |
| Apigenin | AHR |
| Apigenin | TYR |
| Apigenin | ESR1 |
| Apigenin | SRC |
| Apigenin | APP |
| Apigenin | PTK2 |
| Apigenin | GLO1 |
| Apigenin | HSD17B2 |
| Apigenin | PFKFB3 |
| Caffeic acid | MMP1 |
| Caffeic acid | ESR2 |
| Caffeic acid | MMP9 |
| Caffeic acid | NFE2L2 |
| Caffeic acid | ELANE |
| Caffeic acid | MMP2 |
| Caffeic acid | HSD11B1 |
| Caffeic acid | EGFR |
| Caffeic acid | PIK3CA |
| Caffeic acid | MIF |
| Caffeic acid | ERBB2 |
| Caffeic acid | ESR1 |
| Caffeic acid | TLR4 |
| Caffeic acid | APP |
| Cinnamic acid | EGFR2 |
| Cinnamic acid | CA6 |
| Cinnamic acid | KMO |
| Cinnamic acid | IDO1 |
| Cinnamic acid | FOLH1 |
| Cinnamic acid | RNPEP |
| Cinnamic acid | MAOB |
| Cinnamic acid | AHR |
| Cinnamic acid | CHRNA7 |
| Cinnamic acid | AKR1C1 |
| Cinnamic acid | AKR1B10 |
| Cinnamic acid | ESR2 |
| Cinnamic acid | DAO |
| Cinnamic acid | CAPN1 |
| Cinnamic acid | CAPN2 |
| Cinnamic acid | PTPN1 |
| Cinnamic acid | MMP2 |
| Cinnamic acid | MMP1 |
| Cinnamic acid | MMP9 |
| Cinnamic acid | ALOX5 |
| Cinnamic acid | TRPA1 |
| Cinnamic acid | CA4 |
| Cinnamic acid | CA12 |
| Cinnamic acid | CA3 |
| Cinnamic acid | CA5A |
| Cinnamic acid | CA5B |
| Cinnamic acid | CA9 |
| Cinnamic acid | CA14 |
| Cinnamic acid | CA7 |
| Cinnamic acid | TLR4 |
| Cinnamic acid | SLC16A1 |
| Cinnamic acid | AKR1B1 |
| Cinnamic acid | CA1 |
| Cinnamic acid | CA2 |
| Cinnamic acid | HCAR2 |
| Ellagic acid | ESR2 |
| Ellagic acid | PTGS2 |
| Ellagic acid | EGFR |
| Ellagic acid | IGF1R |
| Ellagic acid | XDH |
| Ellagic acid | PDGFRB |
| Ellagic acid | GSR |
| Ellagic acid | ERBB2 |
| Ellagic acid | ESR1 |
| Ellagic acid | SRC |
| Ellagic acid | PTK2 |
| Ellagic acid | NUAK1 |
| Ethyl ferulate | MMP1 |
| Ethyl ferulate | ESR2 |
| Ethyl ferulate | MMP9 |
| Ethyl ferulate | CYP1B1 |
| Ethyl ferulate | NFE2L2 |
| Ethyl ferulate | ELANE |
| Ethyl ferulate | FADS1 |
| Ethyl ferulate | MMP2 |
| Ethyl ferulate | HSD11B1 |
| Ethyl ferulate | EGFR |
| Ethyl ferulate | SIRT1 |
| Ethyl ferulate | ERBB2 |
| Ethyl ferulate | ESR1 |
| Ethyl ferulate | TLR4 |
| Ethyl ferulate | APP |
| Ethyl ferulate | HSD17B2 |
| Gallic acid | ESR2 |
| Gallic acid | IGF1R |
| Hyperin | PTGS2 |
| Hyperin | TERT |
| Hyperin | XDH |
| Hyperin | TNF |
| Isofraxidin | ELANE |
| Isofraxidin | TERT |
| Isofraxidin | EGFR |
| Isofraxidin | GSR |
| Isofraxidin | SRC |
| Isofraxidin | PTK2 |
| Isofraxidin | NUAK1 |
| Isoliquiritigenin | EGFR |
| Isoliquiritigenin | TERT |
| Isoliquiritigenin | APP |
| Isoliquiritigenin | NOS2 |
| Isoliquiritigenin | PTGS2 |
| Isoliquiritigenin | PDPK1 |
| Isoliquiritigenin | ESR1 |
| Isoliquiritigenin | ESR2 |
| Isoliquiritigenin | HSD17B2 |
| Isoliquiritigenin | IGF1R |
| Isoliquiritigenin | XDH |
| Isoliquiritigenin | CFTR |
| Isoliquiritigenin | CYP1B1 |
| Isoliquiritigenin | TYR |
| Isoliquiritigenin | AHR |
| Isoliquiritigenin | GLO1 |
| Isoliquiritigenin | MMP12 |
| Kaempferol | XDH |
| Kaempferol | TYR |
| Kaempferol | HSD17B2 |
| Kaempferol | AHR |
| Kaempferol | CYP1B1 |
| Kaempferol | GLO1 |
| Kaempferol | MMP9 |
| Kaempferol | MMP2 |
| Kaempferol | ESR2 |
| Kaempferol | EGFR |
| Kaempferol | IGF1R |
| Kaempferol | MPO |
| Kaempferol | SRC |
| Kaempferol | PTK2 |
| Kaempferol | MMP13 |
| Kaempferol | MMP3 |
| Kaempferol | NUAK1 |
| Kaempferol | APP |
| Kaempferol | MMP12 |
| Kaempferol | ESR1 |
| Kaempferol | PTGS2 |
| Kaempferol | CFTR |
| Kaempferol | PFKFB3 |
| Kaempferol | TERT |
| Licochalcone B | ESR2 |
| Licochalcone B | CYP1B1 |
| Licochalcone B | PTGS2 |
| Licochalcone B | TERT |
| Licochalcone B | MMP2 |
| Licochalcone B | HSD11B1 |
| Licochalcone B | EGFR |
| Licochalcone B | MMP12 |
| Licochalcone B | IGF1R |
| Licochalcone B | NOS2 |
| Licochalcone B | ODC1 |
| Licochalcone B | PDGFRB |
| Licochalcone B | PIK3CA |
| Licochalcone B | CHEK1 |
| Licochalcone B | TYR |
| Licochalcone B | ESR1 |
| Licochalcone B | SRC |
| Licochalcone B | APP |
| Licochalcone B | PDPK1 |
| Luteolin | ESR2 |
| Luteolin | MMP3 |
| Luteolin | MMP9 |
| Luteolin | CYP1B1 |
| Luteolin | PTGS2 |
| Luteolin | CFTR |
| Luteolin | TERT |
| Luteolin | MMP2 |
| Luteolin | EGFR |
| Luteolin | MMP13 |
| Luteolin | MMP12 |
| Luteolin | IGF1R |
| Luteolin | MPO |
| Luteolin | AR |
| Luteolin | XDH |
| Luteolin | AHR |
| Luteolin | TYR |
| Luteolin | ESR1 |
| Luteolin | SRC |
| Luteolin | APP |
| Luteolin | PTK2 |
| Luteolin | GLO1 |
| Luteolin | HSD17B2 |
| Luteolin | NUAK1 |
| Luteolin | PFKFB3 |
| Morin | ESR2 |
| Morin | MMP3 |
| Morin | MMP9 |
| Morin | CYP1B1 |
| Morin | PTGS2 |
| Morin | CFTR |
| Morin | TERT |
| Morin | MMP2 |
| Morin | EGFR |
| Morin | MMP13 |
| Morin | IGF1R |
| Morin | MPO |
| Morin | AR |
| Morin | XDH |
| Morin | AHR |
| Morin | TYR |
| Morin | ESR1 |
| Morin | SRC |
| Morin | PTK2 |
| Morin | GLO1 |
| Morin | HSD17B2 |
| Morin | APEX1 |
| Morin | PFKFB3 |
| Myricetin | ESR2 |
| Myricetin | MMP3 |
| Myricetin | MMP9 |
| Myricetin | CYP1B1 |
| Myricetin | MMP2 |
| Myricetin | MMP13 |
| Myricetin | MMP12 |
| Myricetin | IGF1R |
| Myricetin | MPO |
| Myricetin | XDH |
| Myricetin | AHR |
| Myricetin | TYR |
| Myricetin | SRC |
| Myricetin | APP |
| Myricetin | PTK2 |
| Myricetin | GLO1 |
| Myricetin | HSD17B2 |
| Myricetin | NUAK1 |
| Myricetin | APEX1 |
| Naringin | MMP1 |
| Naringin | CYP1B1 |
| Naringin | MMP7 |
| Naringin | MMP13 |
| Naringin | MMP12 |
| Naringin | TYR |
| Naringin | MMP8 |
| Quercetin | ESR2 |
| Quercetin | MMP3 |
| Quercetin | MMP9 |
| Quercetin | CYP1B1 |
| Quercetin | TERT |
| Quercetin | MMP2 |
| Quercetin | EGFR |
| Quercetin | MMP13 |
| Quercetin | MMP12 |
| Quercetin | IGF1R |
| Quercetin | MPO |
| Quercetin | XDH |
| Quercetin | AHR |
| Quercetin | TYR |
| Quercetin | SRC |
| Quercetin | APP |
| Quercetin | PTK2 |
| Quercetin | GLO1 |
| Quercetin | HSD17B2 |
| Quercetin | NUAK1 |
| Quercetin | APEX1 |
| Rosmarinic acid | MMP1 |
| Rosmarinic acid | MME |
| Rosmarinic acid | MMP3 |
| Rosmarinic acid | MMP9 |
| Rosmarinic acid | MMP2 |
| Rosmarinic acid | EGFR |
| Rosmarinic acid | MMP13 |
| Rosmarinic acid | MMP12 |
| Rosmarinic acid | SELP |
| Rosmarinic acid | TYR |
| Rosmarinic acid | ERBB2 |
| Rosmarinic acid | ESR1 |
| Rosmarinic acid | MMP14 |
| Rosmarinic acid | MMP8 |
| Scoparone | ESR2 |
| Scoparone | PTGS2 |
| Scoparone | MAPK10 |
| Scoparone | EGFR |
| Scoparone | IGF1R |
| Scoparone | MPO |
| Scoparone | PTPRC |
| Scoparone | XDH |
| Scoparone | PDGFRB |
| Scoparone | MAPK14 |
| Scoparone | CTSK |
| Scoparone | CTSS |
| Scoparone | MAPK8 |
| Scoparone | ERBB2 |
| Scoparone | SRC |
| Scoparone | NUAK1 |
| Scoparone | JAK1 |
| Scoparone | APEX1 |
| Scopoletin | ESR2 |
| Scopoletin | PTGS2 |
| Scopoletin | EGFR |
| Scopoletin | XDH |
| Scopoletin | GSR |
| Scopoletin | ERBB2 |
| Scopoletin | ESR1 |
| Scopoletin | SRC |
| Scopoletin | PTK2 |
| Scopoletin | NUAK1 |

**Table S3.** Skin anti-aging target genes

|  |  |  |  |
| --- | --- | --- | --- |
| **Gene Symbol** | PPIA | TGFB1 | DOCK8 |
| MMP1 | BSG | COL1A1 | HLA-A |
| SOD2-OT1 | MIR1248 | EIF2AK2 | NDUFS3 |
| ELN | BNC2 | CHRNA3 | RANBP2 |
| LINC01672 | HDAC4 | IRF4 | ALG1 |
| LOX | MME | LOXL1 | CHKB |
| MC1R | CAV1 | JUN | EMX2 |
| CERNA3 | ACTG1 | COL7A1 | HLA-C |
| TGFBR2 | TUBA1B | PTGS2 | OCA2 |
| FBN1 | MIR451A | AQP3 | P4HA2 |
| HNF1A-AS1 | MIR511 | DNMT1 | PGF |
| TRP-AGG2-5 | MIR3615 | CFTR | PLOD1 |
| SMAD2 | ITGB1 | ELANE | SEMA4D |
| SMAD7 | HAS2 | RARA | SLC22A4 |
| AFG2A | MIR23A | IVL | TRPS1 |
| CHKB-CPT1B | MMP3 | BMP6 | WNT10A |
| IGF1 | CD36 | DCN | ABCC5 |
| MIR663B | FANCA | MAPK10 | EFEMP1 |
| MIR125A | RUNX2 | HYAL3 | HMGA2 |
| KRT16 | PRDM1 | CASP8 | PLXNA1 |
| ESR2 | SLC45A2 | RHOA | PNPT1 |
| CSPG4 | ZBTB20 | TUBB3 | PSMA4 |
| CRABP2 | EN1 | CACNA1S | SLC39A8 |
| TRP-AGG2-6 | IST1 | EPHA4 | ACSF3 |
| SOX2 | AKAP12 | MAP3K1 | CDK10 |
| H19 | NUDT6 | PRKD1 | EIF2B2 |
| VIM | SPIRE2 | LIMK1 | FADS1 |
| AQP5 | TCF25 | PRLR | FADS2 |
| LINC-ROR | DEF8 | ARSA | FARSB |
| SPRY1 | MARVELD3 | FGF10 | ID2 |
| TIMP1 | ZNF821 | MAPK7 | KANK1 |
| PPARG | HSALNG0022515 | PTPRJ | KIDINS220 |
| KRT17 | CCN1 | TNNT2 | NAT2 |
| GPER1 | MMP9 | DLST | NDE1 |
| PAX3 | CYP1B1 | KITLG | PGC |
| PTEN | FGF2 | MYH11 | PREP |
| TNC | MFAP4 | PIK3C2A | QPCT |
| POSTN | TP53 | SLC22A5 | RASGRF1 |
| PAPPA-AS1 | TP63 | SPRY2 | SRD5A2 |
| NR1H3 | SERPINF1 | ATG5 | TWIST2 |
| EDAR | MMAA | TAX1BP1 | GSDMC |
| FOXL2 | MSI2 | TYW3 | HYKK |
| HTR5A | PIAS4 | ASB1 | KLHL6 |
| MMADHC | S1PR4 | CEP112 | REEP3 |
| MRPS22 | SBF2 | DOHH | SHC4 |
| RAD52 | SRPK2 | ELK4 | ZNF23 |
| RAPSN | TTLL5 | ERRFI1 | ZNF778 |
| SECISBP2 | ACYP1 | GCC2 | ADAT2 |
| AKAP1 | AKAP10 | HMG20B | FAM219B |
| CELF1 | CDC42EP3 | INAVA | FLACC1 |
| CRABP1 | CRELD2 | MFHAS1 | FRS3 |
| LHX1 | FMN1 | NDFIP2 | REC114 |
| MICB | INSIG1 | PCMTD1 | SEC14L5 |
| MTX2 | MKLN1 | PXDNL | SLC45A1 |
| PEX3 | NCAPH2 | RAB29 | ZC2HC1C |
| PKP1 | NUCB2 | RNF112 | ZHX3 |
| PRRX1 | PDLIM4 | SRFBP1 | C11orf58 |
| FZR1 | RAB11FIP2 | ZXDC | CCDC138 |
| HPR | RNLS | DXO | IGFN1 |
| MLH3 | SLC24A2 | ISLR | NCR3LG1 |
| MORF4L1 | UBN1 | KLHL24 | PKD1L3 |
| NFIC | B9D1 | MCF2L2 | PRRG2 |
| RND3 | BANK1 | MFSD12 | WASHC1 |
| RPA3 | CBX4 | MGRN1 | ZBTB12 |
| RPL13 | GLCCI1 | PSD3 | DTHD1 |
| SLC36A2 | LHX8 | TIPARP | PROX2 |
| SYNE2 | NOSIP | USP49 | SLC36A3 |
| TIGIT | PHLPP2 | ARL15 | TMEM45A |
| ADAMTS7 | SEPTIN12 | C1QTNF4 | LEKR1 |
| ANKRD11 | SUPT3H | GLYR1 | PRAG1 |
| AP1G1 | YEATS2 | HUS1B | ZNG1A |
| ARHGEF7 | CBX8 | MBOAT2 | MFSD4A |
| ATP11B | CNTLN | RPS6KL1 | OR6B2 |
| CCNL1 | INSIG2 | STOML1 | ZNF518B |
| CERS6 | LAD1 | ABI3BP | RBM43 |
| CLIC5 | LCORL | ARAP2 | ASCL5 |
| EDC3 | MARCO | ATXN1L | FOXL2NB |
| EPN2 | MEMO1 | B3GALT1 | CLEC18C |
| FUCA2 | PLXNB2 | CEP20 | MROH9 |
| GAS8 | PPARGC1B | CHCHD6 | SOX2-OT |
| GNA15 | RALY | CHST13 | CCDC26 |
| JAZF1 | ROGDI | DBNDD1 | DOCK8-AS1 |
| MLLT3 | SEM1 | FRYL | SMIM24 |
| TEKTIP1 | LINC01956 | LINC01956 | lnc-ZNF80-4 |
| PRR23C | LOC105377205 | LOC105377205 | CM034953-350 |
| SMIM22 | LOC439933 | LOC439933 | ENSG00000279599 |
| TEX41 | MAP1LC3BP1 | MAP1LC3BP1 | ENSG00000286748 |
| FAM106A | MFSD4A-AS1 | MFSD4A-AS1 | HSALNG0008386-002 |
| LINC00304 | SNORA63D | SNORA63D | LOC124900774 |
| LOXL1-AS1 | SNORA63E | SNORA63E | lnc-MC1R-1 |
| BNC2-AS1 | ENSG00000231424 | ENSG00000231424 | lnc-P4HA2-3 |
| C5orf67 | ENSG00000235979 | ENSG00000235979 | lnc-P4HA2-4 |
| UMAD1 | INSIG1-DT | INSIG1-DT | lnc-PAXIP1-23 |
| FOXO3B | LINC01427 | LINC01427 | lnc-SPIRE2-1 |
| JAZF1-AS1 | LINC01946 | LINC01946 | AB372682 |
| LINC01080 | LINC02438 | LINC02438 | CM034956-149 |
| MIR3936HG | LINC02674 | LINC02674 | CM034957-046 |
| ZBTB20-AS1 | LINC02836 | LINC02836 | CM034958-377 |
| LINC00977 | MFSD12-AS1 | MFSD12-AS1 | CM034959-006 |
| MIR124-2HG | ENSG00000229821 | ENSG00000229821 | ENSG00000267048 |
| LINC01432 | ENSG00000248975 | ENSG00000248975 | ENSG00000280053 |
| SNORD68 | ENSG00000253926 | ENSG00000253926 | ENSG00000290100 |
| BHLHE22-AS1 | ENSG00000261118 | ENSG00000261118 | HQ292159 |
| GLCCI1-DT | ENSG00000267077 | ENSG00000267077 | HSALNG0020226-409 |
| LINC00886 | ENSG00000271811 | ENSG00000271811 | HSALNG0020226-444 |
| LINC00976 | LIMS3-LOC440895 | LIMS3-LOC440895 | HSALNG0022519 |
| LINC01091 | ENSG00000198211 | ENSG00000198211 | HSALNG0028167 |
| SNORD14A | ENSG00000205653 | ENSG00000205653 | HSALNG0031044 |
| FAM138C | ENSG00000250934 | ENSG00000250934 | HSALNG0031045 |
| LINC00382 | ENSG00000255520 | ENSG00000255520 | HSALNG0061408 |
| LINC01714 | ENSG00000259006 | ENSG00000259006 | HSALNG0072602 |
| ZNF778-DT | ENSG00000260624 | ENSG00000260624 | HSALNG0123260 |
| LINC01931 | ENSG00000261762 | ENSG00000261762 | HSALNG0141989 |
| LINC01977 | LOC124909439 | LOC124909439 | HSALNG0147664 |
| LINC02458 | ENSG00000226992 | ENSG00000226992 | HSALNG0149400 |
| LINC02613 | ENSG00000236572 | ENSG00000236572 | HSALNG0149895 |
| MKLN1-AS | ENSG00000253092 | ENSG00000253092 | LOC124901232 |
| SNHG33 | ENSG00000266076 | ENSG00000266076 | LOC124903759 |
| ZBTB20-AS5 | ENSG00000268218 | ENSG00000268218 | MN298114-190 |
| ERRFI1-DT | ENSG00000278206 | ENSG00000278206 | MN298114-255 |
| MMADHC-DT | ENSG00000286084 | ENSG00000286084 | NONHSAG020376.2 |
| RUNX2-AS1 | ENSG00000287865 | ENSG00000287865 | RF00003-002 |
| CDC42EP3-AS1 | MIR6074 | MIR6074 | RF00017-2204 |
| ENSG00000244255 | ENSG00000251730 | ENSG00000251730 | lnc-ZNF80-4 |
| LINC01818 | ENSG00000283549 | ENSG00000283549 | CM034953-350 |
| LINC01937 | ENSG00000285108 | ENSG00000285108 | ENSG00000279599 |
| RF00017-5465 | HSALNG0107483 | HSALNG0017752 | LORICRIN |
| RF00017-5469 | HSALNG0112528 | HSALNG0019549 | PYCR1 |
| RF00017-5751 | HSALNG0115121 | HSALNG0019550 | GLB1 |
| RF00017-6912 | HSALNG0115122 | HSALNG0031163 | CCN2 |
| RF02543-029 | HSALNG0119132 | HSALNG0036881 | MAPK1 |
| hsa-miR-5096-095 | HSALNG0119133 | HSALNG0070216 | TERT |
| lnc-AXIN2-3 | HSALNG0136225 | HSALNG0070217 | SIRT6 |
| lnc-C9orf92-5 | HSALNG0146188 | HSALNG0080934-002 | EGR1 |
| lnc-ENPP4-4 | HSALNG0147323 | HSALNG0080935 | MMP2 |
| lnc-FOXL2NB-8 | HSALNG0149214 | HSALNG0118222 | FOS |
| lnc-IGFN1-2 | HSALNG0150405 | HSALNG0148745 | CDKN2A |
| lnc-KBTBD4-4 | L13705-006 | HSALNG0149602 | SMAD3 |
| lnc-MFSD12-1 | LOC124901785 | LOC107985991 | IL6 |
| lnc-NCR3LG1-2 | LOC124901787 | LOC124902855 | HSD11B1 |
| lnc-PAXIP1-24 | LOC124901866 | LOC124904491 | IL1B |
| lnc-PAXIP1-25 | LOC124902106 | LOC124906290 | VCAN |
| lnc-PRDM1-2 | LOC124904071 | OP794609 | IL1A |
| lnc-PRDM1-7 | MN309336 | RF00017-2150 | SNX3 |
| lnc-TBXA2R-2 | NONHSAG024474.2 | RF00017-5931 | HMOX1 |
| lnc-ZNF821-5 | RF00017-027 | RF00017-6946 | CDKN1A |
| piR-46391-004 | RF00017-5930 | RF00994-412 | FABP5 |
| CM034952-579 | RF00026-100 | hsa-miR-5095-422 | MIR15B |
| CM034956-285 | lnc-B9D1-3 | lnc-C1QL2-3 | MIR30A |
| CM034958-378 | lnc-FOXD4-6 | lnc-MANBA-4 | VTRNA2-1 |
| HSALNG0008393-001 | lnc-HERC2-2 | lnc-PKD1L3-4 | EGFR |
| HSALNG0008393-002 | lnc-LIN28B-11 | piR-31199-094 | AGER |
| HSALNG0014260 | lnc-MBOAT2-5 | piR-33103-027 | COL3A1 |
| HSALNG0023466 | lnc-MBOAT2-7 | piR-38352-187 | EDA |
| HSALNG0028713 | lnc-PLXNA1-1 | piR-41405-062 | FBLN2 |
| HSALNG0028714 | lnc-PRDM1-9 | piR-41594-058 | SMAD4 |
| HSALNG0030067 | lnc-PREP-5 | piR-50444-396 | LMNA |
| HSALNG0044819 | lnc-PSD3-4 | piR-55194-280 | SPARC |
| HSALNG0047287 | lnc-TIPARP-1 | HSALNG0049100 | COL1A2 |
| HSALNG0047288 | piR-40452 | HSALNG0069516 | MMP7 |
| HSALNG0050329 | piR-44878-056 | LOC124904455 | HYAL2 |
| HSALNG0052405 | piR-45349-010 | RF00004-039 | MSRA |
| HSALNG0052458 | piR-46060-011 | RF00994-752 | MSRB1 |
| HSALNG0062559 | piR-50437-624 | piR-33804-100 | PCNA |
| HSALNG0070307 | piR-50443-147 | piR-36545-002 | PDYN |
| HSALNG0072600 | piR-54420 | piR-48369-006 | APOD |
| HSALNG0102477 | piR-57460-242 | SOD1 | MFAP2 |
| STRA6 | CM034954-232 | FLG | PAX6 |
| VSX2 | HSALNG0008398 | MIF | OTX2 |
| RAX | LAMB3 | PARK7 | PDPK1 |
| HGF | NR1H2 | YAP1 | FASLG |
| MMP13 | SELP | CTSS | HIF1A |
| TRPV1 | BGN | TGM1 | MITF |
| LMNB1 | HBEGF | ATP6V1A | VDR |
| MMP12 | PPARA | FBN2 | ZEB1 |
| TGM5 | SHC1 | FERMT1 | DLL4 |
| RIN2 | GDF15 | MRC2 | F13A1 |
| PI3 | GDF11 | TIMP2 | KEAP1 |
| ACACA | SIRT4 | OPN1SW | KL |
| PPARGC1A | FABP12 | CTSV | MMP8 |
| KCND2 | DLEU2 | CXCL16 | OXTR |
| DIAPH2 | MIR146A | OPN3 | PTK2 |
| S100A8 | MIR146B | CFTR-AS1 | RHO |
| EDEM1 | MIR155 | SIRT1 | RPA1 |
| POLQ | MIR196A1 | MAPK8 | SOD2 |
| ENOX2 | MIR196A2 | XPC | ACAN |
| TRPC7 | MIR491 | FGFR2 | FANCD2 |
| FBXO40 | MIR542 | ERBB2 | FBLN5 |
| STXBP5L | SNORD24 | ESR1 | HSD17B4 |
| MT-TL1 | SNORD15A | MDM2 | KRT14 |
| HAS2-AS1 | PWAR1 | NTRK2 | MCM7 |
| MIR663A | SPRY4-IT1 | NFKB1 | TXN |
| LINC02605 | MIR135A2 | BAX | TYRP1 |
| IGF1R | RNF217-AS1 | CTSB | ANGPT1 |
| TGFBR1 | SNORD38B | NGF | ARNT |
| MPO | TRA-TGC7-1 | SRC | GLO1 |
| MYC | FGFR3 | TLR4 | PEPD |
| PTPRC | ATR | APP | PPARD |
| AR | PDGFRB | FN1 | RARG |
| ICAM1 | CTSD | IL6R | SFN |
| NOS2 | PIK3CA | JAG1 | SPP1 |
| ODC1 | TNF | MMP14 | THBS1 |
| RXRA | CHEK1 | PCSK9 | XPA |
| FOXO3 | MAPK14 | SCD | CSTA |
| HSPG2 | FAS | ABCA1 | CXCL10 |
| IL1R1 | GSR | BDNF | ECM1 |
| XDH | CTSK | CASP3 | F2RL1 |
| AHR | MYD88 | FASN | HMMR |
| HYAL1 | TYR | HSPA8 | KLK6 |
| KLF4 | VEGFA | IGF2 | PDGFA |
| VTN | CLU | ITGB4 | PPIF |
| CCL5 | GZMB | MAP2K1 | RARS1 |
| FGF7 | KANK4 | CCND1 | TERC |
| FOXM1 | H4C1 | JAK1 | OR51B5 |
| GDA | OPN5 | EP300 | MIR142 |
| KRT10 | STK40 | EZH2 | MIR191 |
| LAMA5 | MACROH2A2 | STAT1 | MIR34A |
| RPS27A | OR10A3 | EGF | MIR93 |
| TAGLN | DEFB103A | TGFB2 | MIR152 |
| ALG8 | MIR126 | EIF2AK3 | MIR20A |
| ATP6V0A2 | MIR34C | IRAK1 | MIRLET7B |
| FERMT3 | MIR409 | CD44 | MIR101-1 |
| HAGH | MT-RNR2 | CYCS | MIR17 |
| HSD17B2 | MT-RNR1 | COL4A1 | MIR381 |
| SULT1A1 | MT-TS1 | KCNJ5 | MIR15A |
| SULT1E1 | SLX1A-SULT1A3 | MAP2K4 | MIR520C |
| TFG | LOC654780 | NQO1 | SCARNA5 |
| COL10A1 | LINC00683 | OGG1 | MIR20B |
| CSF3 | MIR1246 | CNR1 | MIR101-2 |
| ERCC8 | MIR4535 | KCNA2 | TRE-TTC3-1 |
| IL11 | PTPRK | PRKAA1 | MIR526A2 |
| KLK7 | RPS3 | VEGFC | MIR378B |
| RECK | MIR377 | ABCC9 | WWTR1 |
| THBS4 | COL5A1 | APEX1 | CEMIP |
| CTRL | COL5A2 | ATF2 | HSD17B8 |
| MIP | CELA1 | EIF2S1 | SPRR1B |
| OPN4 | BDNF-AS | ERCC6 | NUAK1 |
| PIEZO1 | SNORD44 | HRH1 | MTNR1A |
| SLC27A1 | DNMT3A | KRT5 | LRG1 |
| TNS1 | STK11 | CRAT | BIVM-ERCC5 |
| CXCR6 | NR3C1 | H2AX | MIR217 |
| PSME4 | GPX4 | ORAI1 | MIR526B |
| SAA1 | PRKAB1 | S100B | PDPN |
| SLC27A6 | SERPINH1 | CRHR1 | NR2C2 |
| CALML5 | ERCC5 | IL15 | PSMC6 |
| DUSP16 | ACP1 | IL18R1 | TTF2 |
| FERMT2 | CRH | CRHR2 | ASIP |
| GREB1 | PFKFB3 | OLR1 |  |
| PSG1 | PTPRU | CRHBP |  |

**Table S4.** Intersecting genes between identified compounds and skin anti-aging gene

|  |  |  |  |
| --- | --- | --- | --- |
| **Genes** | | | |
| MMP1 | MMP13 | TYR | EP300 |
| ESR2 | MMP12 | MIF | APEX1 |
| HDAC4 | IGF1R | CTSS | PFKFB3 |
| MME | TGFBR1 | SIRT1 |  |
| ITGB1 | MPO | MAPK8 |  |
| MMP3 | PTPRC | ERBB2 |  |
| MMP9 | AR | ESR1 |  |
| CYP1B1 | ICAM11 | MDM2 |  |
| NFE2L2 | NOS2 | SRC |  |
| PTGS2 | ODC1 | TLR4 |  |
| CFTR | XDH | APP |  |
| ELANE | AHR | MMP14 |  |
| MAPK10 | SELP | FASN |  |
| TUBB3 | PDGFRB | PDPK1 |  |
| FADS1 | CTSD | MMP8 |  |
| MAPK10 | PIK3CA | PTK2 |  |
| TERT | TNF | GLO1 |  |
| MMP2 | CHEK1 | HSD17B2 |  |
| HSD11B1 | MAPK14 | NUAK1 |  |
| EGFR | GSR | CCND1 |  |
| MMP7 | CTSK | JAK1 |  |