**Figure 2-source data 1.** **Classification of the 40 molecules selected using the computational approach.** The scoring function *S* and the free energy of binding DGbind from ABFE simulations used to identify potential hits are reported, along with the average pocket <CSP> from NMR and the average <mRNA enrichment slope> for MT bench assay. The structures of the molecules are illustrated in Figure 3 of the main text. Confirmed hits *in vitro* and/or *in vivo* are emphasized using a bold font and a color code: red for hits confirmed *in vitro* and *in vivo*, *black* for *in vitro* only, *green* for *in vivo* only and *blue* for a negative control that was found potent *in vivo* but not *in vitro*. Errors on the computed DGbind range from 0.34 to 0.97 kcal.mol-1.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | *In silico* | | | | *In vitro* | *In vivo* |
| Class | Subclass | Label | Traditional Name | Scoring Function *S* | Potential Hit | DGbind (kcal.mol-1) | Potential Hit | <CSP>pocket (ppm) | <mRNA enrichment slope> |
| *Flavonoids* | *Flavonols* | **F1** | *Quercetin* | 18.05 | YES | -9.68 | **YES** | **0.032** | 0.894 |
| **F2** | *Quercetagetin* | 21.21 | YES | -7.11 | **YES** | **0.039** | **0.840** |
| **F3** | *3-O-methylquercetin* | 6.15 | Possible | -10.82 | **YES** | **0.034** | **0.815** |
| **F4** | *Fisetin* | 11.85 | YES | -6.22 | **YES** | **0.028** | 1.102 |
| F5 | *Rutin* | -60.14 | NO | -10.08 | NO | 0.009 | 0.955 |
| F6 | *myricitrin* | -16.63 | NO | -4.86 | NO | **0.021** | 0.870 |
| **F7** | *Herbacetin* | 37.06 | YES | -9.98 | **YES** | **0.025** | 0.876 |
| **F8** | *Vincetoxicoside B* | 48.98 | YES | -8.06 | **YES** | **0.016** | 0.859 |
| *Flavones* | **F9** | *Scutellarien* | 18.94 | YES | -10.46 | **YES** | **0.020** | 0.998 |
| F10 | *Luteolin-7-methylether* | 41.75 | YES | -5.19 | YES | - | 0.960 |
| *Flavanones* | F11 | *Naringenin* | 17.95 | YES | -5.18 | NO | 0.004 | 0.966 |
| *Chalcones* | **C1** | *Butein* | 24.62 | YES | -7.60 | **YES** | **0.026** | **0.801** |
| **C2** | *Okanin* | 55.28 | YES | -6.96 | **YES** | **0.026** | **0.776** |
| **C3** | *Robtein* | 34.89 | YES | -7.57 | **YES** | **0.022** | **0.749** |
| C4 | *Chorilifol B* | 38.87 | YES | -6.02 | YES | - | 0.956 |
| C5 | *Bavachalcone* | 11.69 | YES | -5.61 | YES | - | 0.812 |
| **C6** | *homobutein* | -11.02 | NO | -2.23 | NO | 0.004 | **0.826** |
| C7 | *Cardamonin* | -6.40 | NO | -3.91 | NO | - | 0.981 |
| **C8** | *-* | 12.14 | YES | -7.34 | **YES** | **0.021** | **0.693** |
| C9 | *-* | 7.22 | Possible | -5.00 | NO | - | 0.914 |
| C10 | *-* | -21.68 | NO | -0.98 | NO | - | 0.906 |
| **C11** | *-* | 8.04 | Possible | -10.08 | **YES** | **0.010** | **0.793** |
| **C12** | *Lichochalcone B* | 7.77 | Possible | -7.37 | **YES** | **0.013** | **0.786** |
| *Flavonoids Analogs with unknown activity* | | A1 | *-* | -1.87 | Possible | -6.78 | Possible | - | 0.889 |
| A2 | *-* | -19.51 | NO | -5.90 | NO | - | 1.032 |
| **A3** | *-* | -59.37 | NO | -17.07 | **Possible** | - | **0.803** |
| A4 | *-* | -29.79 | NO | -8.73 | NO | - | 0.930 |
| A5 | *-* | -26.37 | NO | -6.77 | NO | - | 0.983 |
| A6 | *-* | -4.10 | NO | -4.04 | NO | - | 0.973 |
| A7 | *-* | -5.35 | NO | -6.31 | NO | - | 0.960 |
| A8 | *-* | -8.28 | NO | -3.47 | NO | - | 0.885 |
| *FDA approved drugs* | *PARP-1 inhibitors* | **P1** | *Niraparib* | 18.24 | YES | -7.24 | **YES** | **0.034** | **0.732** |
| P2 | *Olaparib* | -42.50 | NO | -1.66 | NO | 0.007 | 0.906 |
| P3 | *Talazoparib* | -14.08 | NO | -1.37 | NO | 0.009 | 0.927 |
| P4 | *Veliparib* | 33.59 | YES | -4.79 | NO | 0.006 | 0.950 |
| P5 | *Rucaparib* | 17.61 | YES | -5.76 | YES | 0.008 | 0.857 |
| *Drugs with cancer or viral indication* | D1 | *Nebivolol* | 19.89 | YES | -12.74 | YES | 0.005 | 1.131 |
| D2 | *Mefloquine* | 24.44 | YES | -3.49 | NO | 0.006 | 0.967 |
| D3 | *Icotinib* | 6.14 | Possible | -4.73 | NO | - | 0.975 |
| D4 | *Cabotegravir* | 12.46 | YES | -13.04 | YES | 0.003 | 0.907 |