**Table S10.** Prediction result for literature-reported MBIs using NNC model II.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Chemical | PubChem ID | 1A2 | 2C9 | 2C19 | 2D6 | 3A4 | Reference | PIS | Predicted |
| (-)-Clusin | 44575398 | - | - | - | - | MBI | 16248836 | 0.478  | Inhibitor |
| (-)-Dihydroclusin | 332806 | - | - | - | - | MBI | 16248836 | 0.450  | Inhibitor |
| (-)-Dihydrocubebin | 193042 | - | - | - | - | MBI | 16248836 | 0.391  | Inhibitor |
| (-)-Hinokinin | 442879 | - | - | - | - | MBI | 16248836 | 0.504  | Inhibitor |
| (-)-Yatein | 442835 | - | - | - | - | MBI | 16248836 | 0.533  | Inhibitor |
| 17-alpha-Ethynyl estradiol | 5991 | - | - | - | - | MBI | 16248836 | 0.559  | Inhibitor |
| 1-aminobenzotriazole | 1367 | - | - | - | - | MBI | 21722087 | 0.194  | Inhibitor |
| 1-propynyl pyrene | 57396178 | MBI | - | - | - | - | 16248836 | 0.889  | Inhibitor |
| 2-ethynyl naphtalene | 115017 | MBI | - | - | - | - | 16248836 | 0.371  | Inhibitor |
| 2-propynyl phenanthrene | 10059170 | MBI | - | - | - | - | 16248836 | 0.700  | Inhibitor |
| 3-(3'',4''-dimethoxybenzyl)-2-(3',4'-methylenedioxybenzyl)butyrolactone | - | - | - | - | - | MBI | 18563665 | 0.543  | Inhibitor |
| 3,5-Diethoxycarbonyl-1,4-dihydro-2,6-dimethyl-4-ethylpyridine(DDEP) | 70857 | MBI | MBI | - | - | MBI | 16248836 | 0.156  | Non-inhibitor |
| 3-[2-(2,4,6-trimethylphenyl)thioethyl]-4-methylsydnone(TTMS) | 124145 | MBI | - | - | - | MBI | 16248836 | 0.522  | Inhibitor |
| 4-(1-propynyl)biphenyl | 12136078 | MBI | - | - | - | - | 16248836 | 0.767  | Inhibitor |
| 4-Hydroxypropranolol | 91565 | - | - | - | MBI | - | 17584015 | 0.335  | Inhibitor |
| 4-Ipomeanol | 36284 | - | - | - | - | MBI | 16248836 | 0.125  | Non-inhibitor |
| 4-propynyl biphenyl | 23267244 | MBI | - | - | - | - | 16248836 | 0.797  | Inhibitor |
| 5'-hydroxy-5-hydroxymethyl-4'',5''-methylenedioxy-1,2,3,4-dibenzo-1,3,5-cycloheptatriene | - | - | - | - | - | MBI | 18985859 | 0.593  | Inhibitor |
| 5-hydroxygraveroline | - | - | - | - | MBI | - | 22465502 | 0.499  | Inhibitor |
| 5-Hydroxythiabendazole | 108227 | MBI | - | - | - | - | 19754423 | 0.410  | Inhibitor |
| 5-methoxypsoralen | 2355 | - | - | - | - | MBI | 17988092 | 0.482  | Inhibitor |
| 5-Methylchrysene | 19427 | MBI | - | - | - | - | 19754423 | 0.668  | Inhibitor |
| 6',7'-DihydroxyBergamottin | 12082365 | - | - | - | - | MBI | 16248836 | 0.535  | Inhibitor |
| 7-(4-trifluoromethyl)coumarin propargyl ether | - | - | - | - | - | MBI | 18653744 | 0.572  | Inhibitor |
| 7-coumarin propargyl ether | - | - | - | - | - | MBI | 18653744 | 0.492  | Inhibitor |
| 7-Ethynyl-3,4,8-trimethylcoumarin | - | MBI | - | - | - | - | 22443586 | 0.601  | Inhibitor |
| 7-Ethynyl-3-phenylcoumarin | - | MBI | - | - | - | - | 22443586 | 0.687  | Inhibitor |
| 7-Ethynyl-4-(trifluoromethyl)coumarin | - | MBI | - | - | - | - | 22443586 | 0.562  | Inhibitor |
| 7-Ethynyl-4-methyl-3-phenylcoumarin | - | MBI | - | - | - | - | 22443586 | 0.746  | Inhibitor |
| 7-Ethynyl-4-methylcoumarin | - | MBI | - | - | - | - | 22443586 | 0.532  | Inhibitor |
| 7-Ethynyl-6-methoxycoumarin | - | MBI | - | - | - | - | 22443586 | 0.564  | Inhibitor |
| 7-Ethynylcoumarin | - | MBI | - | - | - | - | 22443586 | 0.528  | Inhibitor |
| a reactive intermediate of dihydralazine  | - | MBI | - | - | - | - | 17584015 | 0.620  | Inhibitor |
| Acetylene | 6326 | MBI | - | - | - | - | 16248836 | 0.078  | Non-inhibitor |
| alpha-Naphtoflavone | 11790 | - | - | - | - | MBI | 16248836 | 0.725  | Inhibitor |
| Amprenavir | 65016 | - | - | - | - | MBI | 16248836 | 0.338  | Inhibitor |
| Antofloxacin | 24806573 | MBI | - | - | - | - | 19754423 | 0.093  | Non-inhibitor |
| Azamulin | 3086060 | - | - | - | - | MBI | 16248836 | 0.147  | Non-inhibitor |
| B[a]P | 2336 | MBI | - | - | - | - | 19754423 | 0.526  | Inhibitor |
| benz[a]anthracene | 5954 | MBI | - | - | - | - | 19754423 | 0.568  | Inhibitor |
| benzo[b]fluoranthene | 9153 | MBI | - | - | - | - | 19754423 | 0.534  | Inhibitor |
| benzo[j]fluoranthene | 9152 | MBI | - | - | - | - | 19754423 | 0.526  | Inhibitor |
| Bergamottin | 5471349 | - | - | - | - | MBI | 16248836 | 0.643  | Inhibitor |
| Carbamazepine | 2554 | MBI | - | - | - | - | 19754423 | 0.589  | Inhibitor |
| chalepensin | 128834 | - | - | - | - | MBI | 23257392 | 0.662  | Inhibitor |
| Chrysene | 9171 | MBI | - | - | - | - | 19754423 | 0.571  | Inhibitor |
| Cimetidine | 2756 | - | MBI | MBI | MBI | - | 16248836 | 0.117  | Non-inhibitor |
| Clarithromycin | 84029 | - | - | - | - | MBI | 16248836 | 0.227  | Inhibitor |
| Clopidogrel | 60606 | - | - | MBI | - | - | 16248836 | 0.631  | Inhibitor |
| Clorgyline | 4380 | MBI | - | - | - | MBI | 19754423, 24016115 | 0.452  | Inhibitor |
| Compound 15 | - | - | - | - | MBI | - | 16808005 | 0.394  | Inhibitor |
| Compound 17 | - | - | - | - | MBI | - | 16808005 | 0.420  | Inhibitor |
| Cyclohexylline | 54584617 | MBI | - | - | - | - | 16248836 | 0.051  | Non-inhibitor |
| D617 (Verapamil metabolite) | 53886 | - | - | - | - | MBI | 16248836 | 0.441  | Inhibitor |
| Delavirdine | 5625 | - | - | - | - | MBI | 16248836 | 0.543  | Inhibitor |
| Desethylamiodarone | 104774 | MBI | - | - | - | - | 19754423 | 0.660  | Inhibitor |
| Desmethyl tamoxifen | 3036172 | - | - | - | - | MBI | 16248836 | 0.730  | Inhibitor |
| dibenz[a,j]acridine | 9177 | MBI | - | - | - | - | 19754423 | 0.484  | Inhibitor |
| Diclofenac | 3033 | - | - | - | - | MBI | 16248836 | 0.538  | Inhibitor |
| Dihydralazine | 10230 | MBI | - | - | - | MBI | 16248836 | 0.098  | Non-inhibitor |
| Diltiazem | 39186 | - | - | - | - | MBI | 16248836 | 0.324  | Inhibitor |
| DMBA | 6001 | MBI | - | - | - | - | 19754423 | 0.720  | Inhibitor |
| DMP777 | 177992 | - | - | - | - | MBI | 16248836 | 0.383  | Inhibitor |
| DPC-681 | 3083536 | - | - | - | - | MBI | 16248836 | 0.468  | Inhibitor |
| EMTPP | 2813098 | - | - | - | MBI | MBI | 25273356 | 0.554  | Inhibitor |
| Enoxacin  | 3229 | MBI | - | - | - | - | 17584015 | 0.065  | Non-inhibitor |
| Erythromycin | 12560 | - | - | - | - | MBI | 16248836 | 0.203  | Inhibitor |
| Fluoxetine | 3386 | - | - | MBI | - | MBI | 24016115 | 0.467  | Inhibitor |
| Furafylline | 3433 | MBI | - | - | - | - | 16248836 | 0.219  | Inhibitor |
| Furanocoumarin dimer (GF-I-1) | - | - | - | - | - | MBI | 16248836 | 0.332  | Inhibitor |
| Furanocoumarin dimer (GF-I-4) | - | - | - | - | - | MBI | 16248836 | 0.323  | Inhibitor |
| Gestodene | 3033968 | - | - | - | - | MBI | 16248836 | 0.491  | Inhibitor |
| Glabridin | 124052 | - | - | - | - | MBI | 16248836 | 0.621  | Inhibitor |
| Gomisin C | 151529 | - | - | - | - | MBI | 16248836 | 0.528  | Inhibitor |
| helioxanthin | 177023 | - | - | - | - | MBI | 18563665 | 0.596  | Inhibitor |
| Hydrastine | 197835 | - | MBI | - | MBI | MBI | 16248836 | 0.505  | Inhibitor |
| hypophyllanthin  | 358902 | - | - | - | - | MBI | 21178301 | 0.485  | Inhibitor |
| Imatinib | 5291 | - | - | - | - | MBI | 22014153 | 0.334  | Inhibitor |
| Indinavir | 5362440 | - | - | - | - | MBI | 16248836 | 0.378  | Inhibitor |
| Irinotecan | 60838 | - | - | - | - | MBI | 16248836 | 0.297  | Inhibitor |
| Isoniazid | 3767 | MBI | - | MBI | - | MBI | 16248836 | 0.040  | Non-inhibitor |
| K11002 | - | - | - | - | - | MBI | 16248836 | 0.601  | Inhibitor |
| L-754,394 | 5481990 | - | - | - | MBI | MBI | 16248836 | 0.521  | Inhibitor |
| lapatinib | 208908 | - | - | - | - | MBI | 20624855 | 0.868  | Inhibitor |
| Laromustine | 3081349 | MBI | - | - | - | - | 19754423 | 0.012  | Non-inhibitor |
| Lilopristone | 13490845 | - | - | - | - | MBI | 16248836 | 0.307  | Inhibitor |
| Limonin | 235284 | - | - | - | - | MBI | 16248836 | 0.142  | Non-inhibitor |
| Lopinavir | 92727 | - | - | - | - | MBI | 16248836 | 0.522  | Inhibitor |
| lunamarine | 442922 | - | - | - | MBI | - | 22465502 | 0.575  | Inhibitor |
| madecassoside | 45356919 | - | - | MBI | - | MBI | 21349323 | 0.130  | Non-inhibitor |
| Methimazole | 1349907 | - | MBI | MBI | - | MBI | 16248836 | 0.029  | Non-inhibitor |
| Methylenedioxy methamphetamine | 1615 | - | - | - | MBI | - | 16248836 | 0.251  | Inhibitor |
| Methylenedioxyphenylbenzothiazoline | 54587576 | - | - | - | - | MBI | 16248836 | 0.578  | Inhibitor |
| Metoclopramide | 4168 | - | - | - | MBI | - | 16248836 | 0.170  | Non-inhibitor |
| Mibefradil | 60663 | - | - | - | - | MBI | 16248836 | 0.537  | Inhibitor |
| midazolam | 4192 | - | - | - | - | MBI | 23282066 | 0.802  | Inhibitor |
| Mifepristone | 55245 | - | - | - | - | MBI | 16248836 | 0.467  | Inhibitor |
| MS-PPOH | 35025892 | - | MBI | - | - | - | 21460231 | 0.436  | Inhibitor |
| N-desmethyldiltiazem | 107891 | - | - | - | - | MBI | 16248836 | 0.334  | Inhibitor |
| N-Desmethyltamoxifen | 3032890 | - | - | - | - | MBI | 18473851 | 0.720  | Inhibitor |
| Nefazodone | 4449 | - | - | - | - | MBI | 16248836 | 0.333  | Inhibitor |
| Nelfinavir | 64143 | - | - | - | - | MBI | 16248836 | 0.415  | Inhibitor |
| Nicardipine | 4474 | - | - | - | - | MBI | 18473851 | 0.497  | Inhibitor |
| NNC55-0396 | 9957280 | - | - | - | - | MBI | 18411403 | 0.532  | Inhibitor |
| Oleuropein | 5281544 | - | - | - | - | MBI | 18473851 | 0.093  | Non-inhibitor |
| Oltipraz | 47318 | MBI | - | - | - | - | 16248836 | 0.429  | Inhibitor |
| Onapristone | 5311505 | - | - | - | - | MBI | 16248836 | 0.313  | Inhibitor |
| OSI-930 | 9868037 | - | - | - | - | MBI | 21068193 | 0.720  | Inhibitor |
| Parathion | 991 | - | MBI | - | - | MBI | 16248836 | 0.375  | Inhibitor |
| Paroxetine | 43815 | - | - | - | MBI | MBI | 17584015 | 0.436  | Inhibitor |
| phyllanthin | 358901 | - | - | - | - | MBI | 21178301 | 0.527  | Inhibitor |
| PPOH | 53741002 | - | MBI | - | - | - | 21460231 | 0.439  | Inhibitor |
| R,S-Norverapamil | 104972 | - | - | - | - | MBI | 16248836 | 0.537  | Inhibitor |
| Raloxifene | 5035 | - | - | - | - | MBI | 16248836 | 0.680  | Inhibitor |
| resveratrol | 445154 | MBI | - | - | - | MBI | 17584015 | 0.520  | Inhibitor |
| Retrorsine | 5281743 | - | - | - | - | MBI | 19818743 | 0.021  | Non-inhibitor |
| Ritonavir | 392622 | - | - | - | - | MBI | 16248836 | 0.571  | Inhibitor |
| RO115-1954 | - | - | - | - | MBI | - | 16248836 | 0.330  | Inhibitor |
| Rofecoxib | 5090 | MBI | - | - | - | - | 17584015 | 0.539  | Inhibitor |
| Rutaecarpine | 65752 | - | - | - | - | MBI | 16248836 | 0.764  | Inhibitor |
| Saquinavir | 441243 | - | - | - | - | MBI | 16248836 | 0.262  | Inhibitor |
| savinin | 5281867 | - | - | - | - | MBI | 18563665 | 0.572  | Inhibitor |
| SCH-66712 | 54587574 | - | - | - | MBI | MBI | 25273356 | 0.413  | Inhibitor |
| sertraline | 68617 | - | - | - | - | MBI | 23929629 | 0.799  | Inhibitor |
| sesamin | 72307 | - | MBI | - | - | - | 20851877 | 0.443  | Inhibitor |
| Silybin | 5213 | - | MBI | - | - | MBI | 17584015 | 0.293  | Inhibitor |
| SN-38 | 104842 | - | - | - | - | MBI | 16248836 | 0.313  | Inhibitor |
| Suprofen | 5359 | - | MBI | - | - | - | 16248836 | 0.210  | Inhibitor |
| Sydnone | 198878 | MBI | - | - | - | MBI | 16248836 | 0.294  | Inhibitor |
| Tabimorelin | 9810101 | - | - | - | - | MBI | 18473851 | 0.504  | Inhibitor |
| Tacrine | 1935 | MBI | - | - | - | - | 16248836 | 0.520  | Inhibitor |
| Tadalafil | 110635 | - | - | - | MBI | MBI | 17584015 | 0.404  | Inhibitor |
| Tamoxifen | 2733526 | - | - | - | - | MBI | 16248836 | 0.702  | Inhibitor |
| Thiabendazole | 5430 | MBI | - | - | - | - | 19754423 | 0.432  | Inhibitor |
| ThioTEPA | 5453 | - | - | - | - | MBI | 18473851 | 0.081  | Non-inhibitor |
| thujopsene | 97829 | - | MBI | MBI | - | - | 25343299 | 0.144  | Non-inhibitor |
| Tiamulin | 656958 | - | - | - | - | MBI | 16248836 | 0.243  | Inhibitor |
| Ticlopidine | 5472 | - | - | MBI | - | - | 16248836 | 0.706  | Inhibitor |
| Tienilic acid | 38409 | - | MBI | - | - | - | 16248836 | 0.343  | Inhibitor |
| troglitazone | 5591 | - | - | - | - | MBI | 17584015 | 0.686  | Inhibitor |
| Troleandomycin | 202225 | - | - | - | - | MBI | 16248836 | 0.216  | Inhibitor |
| Verapamil | 2520 | - | - | - | - | MBI | 16248836 | 0.516  | Inhibitor |
| Zafirlukast | 5717 | - | - | - | - | MBI | 17584015 | 0.725  | Inhibitor |
| Zileuton | 10681296 | MBI | - | - | - | - | 16248836 | 0.298  | Inhibitor |
| Zolpidem | 5732 | - | - | - | - | MBI | 17598095 | 0.733  | Inhibitor |

-: not available; MBI: mechanism-based inhibitor; PIS: P450 inhibition score.