New PPARα/γ/δ Optimal Activator Rationally Designed by Computational Methods

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Table S1. Molecules and physicochemical properties

| Name  | MW    | MV   | Polarizability | AlogP98 | NHBD | NHBA | DM  | SA   | Ki  |
|-------|-------|------|----------------|---------|------|------|-----|------|-----|
| 1RDT  | 550.66| 413.70| 23655.62       | 5.70    | 4.00 | 6.00 | 2.66| 489.06| 1.10|
| 18944089 | 432.48| 320.30| 18027.82       | 5.20    | 1.00 | 6.00 | 0.84| 358.64| 0.40|
| 446642 | 510.60| 387.20| 21846.00       | 5.22    | 2.00 | 6.00 | 5.78| 461.11| 1.00|
| 9843045| 384.44| 289.40| 15171.62       | 3.78    | 1.00 | 6.00 | 1.86| 365.29| 2.50|
| 10578809| 561.60| 414.40| 23793.06       | 6.00    | 2.00 | 7.00 | 2.38| 477.37| 5.10|
| 77999  | 357.44| 266.40| 14855.22       | 3.46    | 1.00 | 5.00 | 3.57| 318.34| 10.00|
| 10433070| 434.61| 351.90| 16866.92       | 5.52    | 1.00 | 5.00 | 1.59| 437.27| 20.00|
| 44383664| 487.60| 382.40| 20160.84       | 7.63    | 1.00 | 6.00 | 5.47| 465.15| 26.00|
| 10004390| 459.55| 335.10| 19134.32       | 6.75    | 1.00 | 6.00 | 4.92| 437.39| 30.00|
| 44385396| 503.60| 389.00| 20505.64       | 7.35    | 1.00 | 7.00 | 7.98| 476.19| 41.00|
| 10068664| 385.47| 294.50| 17132.64       | 6.01    | 2.00 | 3.00 | 1.79| 333.89| 50.00|
| 9827261| 477.59| 359.20| 20328.46       | 6.60    | 1.00 | 7.00 | 13.85| 394.74| 60.00|
| 44419783| 396.45| 298.30| 15771.82       | 2.91    | 1.00 | 7.00 | 1.68| 380.02| 73.00|
| 11464352| 422.49| 320.50| 16657.58       | 3.84    | 1.00 | 7.00 | 2.03| 379.79| 81.00|
| 447458 | 419.48| 321.80| 17507.60       | 5.04    | 1.00 | 5.00 | 2.42| 387.21| 90.00|
| 44345164| 404.21| 265.00| 17214.48       | 4.49    | 2.00 | 9.00 | 2.14| 319.65| 100.00|

MW: molecular weight; MV: molecular volume; NHBD: number of hydrogen bond donors, NHBA: number of hydrogen bond acceptors; DM: dipole magnitude; SA: surface area; Ki: affinity constant.

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Table S2. GOLD Score of candidates, crystallographic molecule 1RDT and PPARγ ligands docked with PPARγ receptor

| Fitness | S(bb_ext) | S(vdw_ext) | S(int) | File name  |
|---------|-----------|------------|--------|------------|
| 91.46   | 10.75     | 62.92      | −5.81  | candidate 1 |
| 70.00   | 0.38      | 55.12      | −6.17  | candidate 2 |
| 68.41   | 6.74      | 49.09      | −5.83  | candidate 3 |
| 62.91   | 6.00      | 50.43      | −12.43 | candidate 4 |
| 64.06   | 0.35      | 46.73      | −0.54  | candidate 5 |
| 67.01   | 0.00      | 56.04      | −10.04 | candidate 6 |
| 96.19   | 3.91      | 82.19      | −20.73 | candidate 7 |
| 68.00   | 5.66      | 49.69      | −5.99  | ‘9843045’  |
| 85.61   | 3.05      | 73.34      | −18.28 | ‘1RDT’     |
| 65.04   | 0.06      | 49.45      | −3.02  | ‘77999’    |
| 84.47   | 3.97      | 72.86      | −19.68 | ‘446642’   |
| 72.06   | 4.93      | 55.79      | −9.57  | ‘447458’   |
| 81.73   | 1.04      | 66.29      | −10.47 | ‘9827261’  |
| 79.15   | 0.47      | 64.02      | −9.35  | ‘10004390’ |
| 68.28   | 5.98      | 49.24      | −5.41  | ‘10068664’ |
| 72.14   | 2.02      | 59.36      | −11.49 | ‘10433070’ |
| 81.13   | 3.46      | 65.11      | −11.86 | ‘10578809’ |
| 71.91   | 3.55      | 52.63      | −3.99  | ‘11464352’ |
| 80.90   | 3.64      | 58.46      | −3.13  | ‘18944089’ |
| 57.78   | 2.59      | 47.71      | −10.41 | ‘5289162’  |
| 72.09   | 1.53      | 62.25      | −15.03 | ‘44383664’ |
| 75.14   | 1.37      | 66.57      | −17.77 | ‘44385396’ |
| 71.97   | 4.24      | 52.19      | −4.04  | ‘44419783’ |

Table S3. Binding affinity of candidates 1, 2 and 7 and specific PPAR ligands. The binding affinity of ligands was assessed with AutoDock/Vina software

| Entry       | Alpha | Delta | Gamma |
|-------------|-------|-------|-------|
| Candidate 1 | −9.7  | −10.8 | −12.9 |
| Candidate 2 | −9.2  | −9.0  | −9.5  |
| Candidate 7 | −7.6  | −8.1  | −12.1 |
| Rosiglitazone (gamma) | −8.7  | −8.4  | −8.4  |
| Tesaglitazar (alpha/gamma) | −8.5  | −7.9  | −8.1  |