**Table S2.** The potential targets of DHA are predicted by molecular docking.

|  |  |  |  |
| --- | --- | --- | --- |
| Predicted proteins | PDBID | Docking score（kcal/mol） | Experimental activities of natural ligands |
| Nature | DHA |
| hiv-1 reverse transcriptase/ribonuclease h | 3M8P | -13.63 | -9.86 | IC50 = 2.1 nM |
| muscarinic acetylcholine receptor m2 redesigned apo | 5YC8 | -13.75 | -9.75 | Kd = 6.4 nM |
| retinol-binding protein 2 | 4GKC | -8.47 | -9.71 | Kd = 150 nM |
| odorant-binding protein | 1DZM | -8.42 | -9.61 | IC50 = 3.9 uM |
| hth-type transcriptional repressor kstr | 5CW8 | -12.67 | -9.6 | Kd = 60 nM |
| estrogen receptor | 2FAI | -9.66 | -9.51 | Ki = 570 nM |
| odorant-binding protein | 1HN2 | -8.88 | -9.5 | Kd = 1.0 uM |
| orphan nuclear receptor pxr | 2O9I | -11.12 | -9.5 | IC50 = 40 nM |
| antibody fab fragment mor03268 heavy chain | 2JB6 | -15.52 | -9.45 | Kd = 11 pM |
| histamine n-methyltransferase | 1JQD | -9.77 | -9.42 | Ki = 6.9 μM |
| oxysterols receptor lxr-alpha | 3IPU | -13.46 | -9.36 | Ki = 48 nM |
| retinaldehyde-binding protein 1 | 4CIZ | -7.22 | -9.32 | Kd ~ 51 nM |
| beta-glucosidase | 1E55 | -9.81 | -9.28 | Ki = 76 μM |
| vitamin d3 receptor a | 6FOB | -12.13 | -9.26 | IC50 = 23.5 nM |
| estrogen receptor beta | 2Z4B | -10.89 | -9.24 | Ki = 0.44 nM |
| bile acid receptor | 5Q11 | -8.68 | -9.24 | IC50 = 7.19 μM |
| envelope glycoprotein gp160 | 5U7O | -13.12 | -9.18 | Kd = 73 nM |
| mineralocorticoid receptor | 5L7G | -11.9 | -9.17 | Ki = 16 nM |
| vitamin d3 receptor | 3VTB | -14.45 | -9.16 | IC50 = 0.5 nM |
| pheromone-binding protein asp1 | 3D78 | -7.84 | -9.14 | Kd = 23 nM |
| sex hormone-binding globulin | 1LHU | -11.179 | -9.12421 | Kd = 1.48 nM |
| estrogen-related receptor gamma | 2EWP | -15.197 | -9.10081 | IC50 = 0.079 μM |
| reverse transcriptase/ribonuclease h | 5VQQ | -14.9779 | -9.05644 | IC50 = 5.3 μM |
| oxysterols receptor lxr-beta | 5KYA | -12.5777 | -9.0046 | Ki = 6 nM |
| abc transporter substrate-binding protein | 4PFU | -11.5754 | -8.98646 | Kd = 0.67 μM |
| nicotinamide riboside transporter pnuc | 4QTN | -9.82228 | -8.96369 | Kd = 142 nM |
| igg1-kappa db3 fab (light chain) | 2DBL | -8.09274 | -8.91324 | IC50 = 2 nM |
| acarbose/maltose binding protein gach | 3K00 | -17.564 | -8.90126 | Kd = 1.7 μM |
| scytalone dehydratase | 3STD | -12.6381 | -8.89449 | Ki = 7.7 pM |
| estrogen receptor beta | 2J7X | -11.0952 | -8.87677 | IC50 = 1.7 nM |
| antibody fab fragment | 1C12 | -9.33097 | -8.8282 | Kd = 1.9 nM |
| thyroid hormone receptor beta-1 | 1NQ0 | -13.8889 | -8.82757 | IC50 = 0.048 nM |
| estrogen receptor beta | 1YYE | -11.2789 | -8.8164 | IC50 = 2.7 nM |
| nuclear receptor ror-gamma | 6CN6 | -7.53786 | -8.75438 | IC50 = 5.0 nM |
| epoxide hydrolase 2 | 5ALT | -7.07148 | -8.74159 | IC50 = 13.1 μM |
| progesterone receptor | 1ZUC | -9.185 | -8.73387 | IC50 = 1.7 nM |
| nr1h4 protein | 3FXV | -14.8428 | -8.71985 | IC50 = 0.094 μM |
| bilin-binding protein diga16 | 1LKE | -11.3113 | -8.70372 | Kd = 30.2 nM |
| retinal rod rhodopsin-sensitive cgmp 3'5'-cyclic | 5E80 | -12.335 | -8.67848 | Kd = 5 nM |
| constitutive androstane receptor | 1XNX | -9.56901 | -8.67185 | Ki = 416 nM |
| deoxycytidine kinase | 4JLN | -8.8473 | -8.64079 | IC50 = 16.7 nM |
| glucocorticoid receptor | 3K23 | -13.9739 | -8.62887 | IC50 = 6.3 nM |
| alpha-2u-globulin | 2A2G | -7.00648 | -8.61645 | Kd = 0.1 uM |
| heat shock protein hsp90-alpha | 6EYB | -8.5265 | -8.58907 | Kd = 4.22 μM |
| squalene-hopene cyclase | 1O79 | -14.2183 | -8.50709 | IC50 = 406 nM |
| retinoic acid receptor rxr-alpha | 3FAL | -12.4172 | -8.45199 | IC50 = 165 nM |
| multidrug resistance protein 1a | 4XWK | -9.05193 | -8.4455 | IC50 = 23.2 μM |
| lactonase for protein | 5XO7 | -12.2569 | -8.39083 | Kd = 0.44 μM |
| antibody fab fragment 4-4-20 | 1FLR | -10.2523 | -8.30142 | Kd = 0.1 nM |
| nuclear receptor ror-beta | 1N4H | -9.23805 | -8.29379 | Ki = 0.28 μM |
| isoprenyl transferase | 4Q9O | -10.2606 | -8.29187 | Kd = 1.7 μM |
| dir1 protein | 2RKN | -11.0867 | -8.28344 | Kd = 0.06 μM |
| n-acylethanolamine-hydrolyzing acid amidase subunit alpha | 6DXX | -10.8158 | -8.23113 | IC50 = 230 nM |
| androgen receptor | 2HVC | -9.92414 | -8.21805 | Ki = 1.5 nM |
| acetylcholine receptor | 2XYS | -15.4927 | -8.21757 | Ki = 38 nM |
| listeriolysin positive regulatory factor a | 6EXM | -9.98743 | -8.19623 | IC50 = 3.0 μM |
| vitamin d3 receptor | 1IE9 | -15.5874 | -8.19226 | Kd = 0.065 nM |
| maltose binding protein | 1URG | -10.444 | -8.18923 | Kd = 1.5 μM |
| 78-dihydro-8-oxoguanine triphosphatase | 6F1X | -8.42149 | -8.18707 | IC50 = 0.02 μM |
| choline kinase alpha | 5AFV | -8.72281 | -8.13349 | Kd = 2.6 μM |
| retinol binding protein | 1ERB | -9.93572 | -8.01155 | Kd = 8 nM |
| spermidine synthase putative | 4YV1 | -7.51742 | -8.01093 | IC50 = 830 μM |
| estradiol 17-beta-dehydrogenase 1 | 3HB4 | -10.6953 | -7.96833 | Ki = 0.9 nM |
| receptor-interacting serine/threonine-protein kinase 1 | 4ITI | -10.9142 | -7.9584 | IC50 = 439.5 nM |
| beta-mannosidase/beta-glucosidase | 4RE3 | -7.19358 | -7.95572 | Ki = 2.7 nM |
| aristolochene synthase | 3CKE | -8.41089 | -7.94623 | Ki = 0.8 μM |
| sulfotransferase 1a1 | 2D06 | -9.32247 | -7.94079 | Ki = 83.2 μM |
| thymidine kinase | 1E2K | -8.04201 | -7.9397 | Ki = 11.4 μM |
| fatty-acid amide hydrolase 1 | 3QK5 | -12.0598 | -7.9331 | IC50 = 18 nM |
| ectonucleotide pyrophosphatase/phosphodiesterase | 4ZG7 | -9.81115 | -7.89714 | IC50 = 0.002 μM |
| acetylcholinesterase | 1QTI | -10.5037 | -7.81359 | IC50 = 0.36 μM |
| retinal dehydrogenase 1 | 5L2M | -9.14852 | -7.81174 | IC50 = 0.13 μM |
| retinol-binding protein 4 | 1RBP | -11.9652 | -7.80567 | Kd = 0.19 μM |
| acetylcholinesterase | 4M0F | -12.657 | -7.78715 | Ki = 1.7 nM |
| pheromone binding protein | 1OW4 | -8.05757 | -7.77585 | Kd = 2.1 μM |
| retinoic acid receptor alpha | 5K13 | -13.6528 | -7.75875 | Ki = 1.8 nM |
| retinol-binding protein 1 | 5HBS | -9.9486 | -7.75602 | Kd = 18.5 nM |
| estrogen-related receptor gamma | 1VJB | -12.7746 | -7.75223 | IC50 = 0.013 μM |
| transcriptional enhancer factor tef-4 | 5DQ8 | -10.5892 | -7.72417 | Kd = 73 μM |
| sec14-like protein 2 | 4OMK | -8.34077 | -7.71812 | Kd = 40.10 μM |
| listeriolysin regulatory protein | 6EV0 | -9.85061 | -7.68538 | IC50 = 1.8 μM |
| folate receptor beta | 4KN0 | -10.8195 | -7.65984 | Kd = 40 nM |
| acetylcholinesterase | 5DTJ | -8.68847 | -7.6597 | Kd = 34 μM |
| ketosteroid isomerase | 5AI1 | -8.08759 | -7.64411 | Kd = 0.34 μM |
| maltose/maltodextrin-binding protein | 2GH9 | -13.4676 | -7.62515 | Kd = 1 μM |
| dual specificity protein kinase clk3 | 2WU7 | -8.5202 | -7.59416 | IC50 = 530 nM |
| cyclin-dependent kinase 8 | 5IDN | -12.1298 | -7.53783 | IC50 = 2.6 nM |
| alkanal monooxygenase alpha chain | 3FGC | -13.1749 | -7.53503 | Kd = 120 μM |
| camp-dependent protein kinase regulatory subunit | 5T3N | -8.65318 | -7.50616 | Kd = 9.1 nM |
| maltose binding periplasmic protein | 3JYR | -12.9634 | -7.50602 | Kd = 2.9 μM |
| ces1 protein | 1YA4 | -8.0953 | -7.48307 | Ki = 15.2 μM |
| cyclin-dependent kinase 2 | 4EOS | -9.89181 | -7.46651 | Ki = 0.89 μM |
| farnesyltransferase/geranylgeranyltransfera | 4GTR | -11.3454 | -7.45351 | IC50 < 5 nM |
| adenosylmethionine-8-amino-7-oxononanoate aminotran | 4MQP | -8.00185 | -7.4474 | Ki = 10.4 μM |
| sigma non-opioid intracellular receptor 1 | 5HK2 | -9.63519 | -7.40543 | Ki = 2.6 nM |
| methionyl-trna synthetase | 4MWC | -7.5791 | -7.39319 | IC50 = 1360 nM |
| ectonucleotide pyrophosphatase/phosphodiesterase | 5DLV | -11.3793 | -7.38376 | IC50 = 10.4 μM |
| histone-lysine n-methyltransferase suv420h1 | 5CPR | -8.78335 | -7.37902 | Kd = 27.5 nM |
| kes1 protein | 1ZHY | -10.446 | -7.3604 | Kd = 300 nM |
| glycine receptor subunit alpha-3 | 5CFB | -11.3634 | -7.35729 | Kd = 52 nM |
| integrin alpha-lglycine receptor | 3E2M | -12.194 | -7.35399 | IC50 = 0.4 nM |
| tankyrase-1 | 4LI6 | -12.7771 | -7.32769 | IC50 = 0.106 μM |
| gamma-aminobutyric acid receptor subunit beta-2gamma | 6D6U | -8.51338 | -7.32413 | Kd = 6.1 nM |
| endoplasmin | 6BAW | -9.71092 | -7.32007 | Kd = 4.2 μM |
| engineered digoxigenin binder protein dig10.2 | 4J8T | -11.1756 | -7.30427 | Kd = 168 nM |
| dual specificity tyrosine-phosphorylation-regulated kinase | 4AZE | -10.4331 | -7.29727 | Kd = 7.8 nM |
| s-adenosylmethionine synthase isoform type-2 | 5UGH | -9.40026 | -7.27447 | Kd = 170 nM |
| fatty acid-binding protein intestinal | 2MJI | -7.63185 | -7.26418 | Kd = 56.7 μM |
| camp-specific 3'5'-cyclic phosphodiesterase 4d | 4WCU | -8.52573 | -7.21836 | IC50 = 3 nM |
| transporter | 4M48 | -9.26239 | -7.20048 | Ki = 156 nM |
| maltose-binding periplasmic protein | 1N3W | -10.2181 | -7.18448 | Kd = 110 nM |
| rna-directed rna polymerase | 5PZN | -9.62232 | -7.17903 | IC50 = 0.041μM |
| beta-secretase 1 | 4XKX | -8.3875 | -7.16612 | IC50 = 0.9 nM |
| sugar transporter solute-binding protein | 4C1U | -12.4968 | -7.15956 | Kd = 81 nM |
| antibody kappa-chain | 1JGL | -12.1065 | -7.14871 | Kd = 2 nM |
| ubiquitin carboxyl-terminal hydrolase 7 | 5NGE | -7.63363 | -7.14314 | Kd = 65 nM |
| nad-dependent protein deacetylase sirtuin-2 | 5YQL | -11.0167 | -7.14085 | IC50 = 25.9 μM |
| gibberellin receptor gid1 | 3EBL | -9.58538 | -7.13701 | Kd = 0.5 μM |
| retinoic acid receptor rxr-alpha | 3NSQ | -7.27137 | -7.13409 | Kd = 6.2 μM |
| ectonucleotide pyrophosphatase/phosphodiesterase | 5OHI | -8.79278 | -7.12664 | IC50 = 3.4 nM |
| tankyrase-1 | 4N4T | -9.21881 | -7.12324 | IC50 = 49 nM |
| cgmp-specific 3'5'-cyclic phosphodiesterase | 6ACB | -11.019 | -7.12192 | IC50 = 0.39 nM |
| adp-dependent glucokinase | 5O0J | -12.5376 | -7.10782 | Kd = 16.85 μM |
| dimeric dihydrodiol dehydrogenase | 2POQ | -7.10967 | -7.10018 | IC50 = 38 μM |
| lanosterol synthase | 1W6J | -15.0589 | -7.03752 | IC50 = 6.5 nM |
| streptavidin | 1STR | -7.16723 | -7.03529 | Kd = 17 μM |
| camp-specific 3'5'-cyclic phosphodiesterase 4b | 1XLX | -9.0662 | -7.02917 | IC50 = 0.025 μM |

Note: PDB: Protein Data Bank; IC50: half-maximal inhibitory concentration; Kd: dissociation constant; Ki: inhibition constant.