**Sirtuins inhibitors for NAM binding site**

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| # | Structure | Name | Remarks | | Ref. |
| 1 |  | Nicotinamide | 54.1% inhibition of HST2 at 0.1 mM  95.0% inhibition of HST2 at 1.5 mM | | 1 |
| 2 |  | Nicotinic acid | 2.1% inhibition of HST2 at 1 mM  18.3% inhibition of HST2 at 15 mM | |
| 3 |  | Thionicotinamide | 16.2% inhibition of HST2 at 1 mM  58.3% inhibition of HST2 at 15 mM | |
| 4 |  | 2-Acetylpyridine | 7.1% inhibition of HST2 at 5 mM  16.8% inhibition of HST2 at 30 mM | |
| 5 |  | 3-Pyridine-carboxyaldehyde | <2% inhibition of HST2 at 5 mM  10.6% inhibition of HST2 at 30 mM | |
| 6 |  | 3-Fluoropyridine | <2% inhibition of HST2 at 30 mM | |
| 7 |  | 3-Chloropyridine | 4.0% inhibition of HST2 at 5 mM  9.0% inhibition of HST2 at 30 mM | |
| 8 |  | 3-Bromopyridine | 5.6% inhibition of HST2 at 5 mM  19.1% inhibition of HST2 at 30 mM | |
| 9 |  | 3-Pyridinemethanol | 9.3% inhibition of HST2 at 5 mM  22.5% inhibition of HST2 at 30 mM | |
| 10 |  | 3-Methoxypyridine | 5.3% inhibition of HST2 at 5 mM  10.8% inhibition of HST2 at 30 mM | |
| 11 |  | 3-Hyroxypyridine | 34.5% inhibition of HST2 at 1 mM  83.9% inhibition of HST2 at 15 mM | |
| 12 |  | Pyridine | <2% inhibition of HST2 at 5 mM  6.4% inhibition of HST2 at 30 mM | |
| 13 |  |  | 88% inhibition of SIRT1 at 1 mM  92% inhibition of SIRT2 at 1 mM  16% inhibition of SIRT3 at 1 mM | | 2 |
| 14 |  |  | 97% inhibition of SIRT1 at 1 mM  100% inhibition of SIRT2 at 1 mM  77% inhibition of SIRT3 at 1 mM | |
| 15 |  |  | 108% inhibition of SIRT1 at 1 mM  115% inhibition of SIRT2 at 1 mM  110% inhibition of SIRT3 at 1 mM | |
| 16 |  |  | 99% inhibition of SIRT1 at 1 mM  109% inhibition of SIRT2 at 1 mM  110% inhibition of SIRT3 at 1 mM | |
| 17 |  |  | 105% inhibition of SIRT1 at 1 mM  110% inhibition of SIRT2 at 1 mM  36% inhibition of SIRT3 at 1 mM | |
| 18 |  |  | 88% inhibition of SIRT1 at 1 mM  111% inhibition of SIRT2 at 1 mM  110% inhibition of SIRT3 at 1 mM | |
| 19 |  |  | 86% inhibition of SIRT1 at 1 mM  115% inhibition of SIRT2 at 1 mM  118% inhibition of SIRT3 at 1 mM | |
| 20 |  |  | 101% inhibition of SIRT1 at 1 mM  107% inhibition of SIRT2 at 1 mM  89% inhibition of SIRT3 at 1 mM | |
| 21 |  |  | 117% inhibition of SIRT1 at 1 mM  145% inhibition of SIRT2 at 1 mM  113% inhibition of SIRT3 at 1 mM | |
| 22 |  |  | 125% inhibition of SIRT1 at 1 mM  136% inhibition of SIRT2 at 1 mM  84% inhibition of SIRT3 at 1 mM | |
| 23 |  | Splitomicin | * In vivo cell based chemical screen * Inactive ySir2p | | 3 |
| 24 |  | Dehydrosplitomicin | * In vivo cell based chemical screen * Inactive ySir2p | |
| 25 |  |  | * In vivo cell based chemical screen * Inactive ySir2p | |
| 26 |  |  | * In vivo cell based chemical screen * Inactive ySir2p | |
| 27 |  |  | * In vivo cell based chemical screen * Inactive ySir2p | |
| 28 |  |  | * In vivo cell based chemical screen * Inactive ySir2p | |
| 29 |  |  | * In vivo cell based chemical screen * Inactive ySir2p | |
| 30 |  |  | * In vivo cell based chemical screen * Inactive ySir2p | |
| 31 |  |  | * In vivo cell based chemical screen * Inactive ySir2p | |
| 32 |  |  | * In vivo cell based chemical screen * Inactive ySir2p | |
| 33 |  |  | * In vivo cell based chemical screen * Inactive ySir2p | |
| 34 |  |  | * In vivo cell based chemical screen * Inactive ySir2p | |
| 35 |  | *meta*-sirtinol | IC50(ySir2)=72 uM  IC50(hSIRT1)=59 uM  IC50(hSIRT2)=35.7uM | | 4 |
| 36 |  | *para*-sirtinol | IC50(ySir2)=33 uM  IC50(hSIRT1)=13 uM  IC50(hSIRT2)=25.9uM | |
| 37 |  | *(R)*-sirtinol | IC50(ySir2)=62 uM  IC50(hSIRT1)=55 uM  IC50(hSIRT2)=49.3uM | |
| 38 |  | *(S)*-sirtinol | IC50(ySir2)=66 uM  IC50(hSIRT1)=67 uM  IC50(hSIRT2)=39.4uM | |
| 39 |  | Indoles | IC50(SIRT1) = 3.5 uM  IC50(SIRT2) = 0.8 uM  Adenine-binding pocket | | 5 |
| 40 |  | Indoles | 58.2% inhibition of SIRT1 at 50 uM  IC50(SIRT2) = 8.3 uM  Adenine-binding pocket | |
| 41 |  | **6-Chloro-2,3,4,9-tetrahydro-1H-Carbazole-1-carboxamide** | IC50 (SIRT1) = 38nM | |
| 42 |  | **2-Cyano-3-[5-(2,5-dichlorophenyl)-2-furanyl]-N-5-quinolinyl-2-propenamide** |  | Low-energy pose of AGK2 in SIRT2 generated by virtual ligand docking. Nicotinamide position is shown in wire for comparison. | 6 |
| 43 |  | 7-(1-naphthyl)-75-dibenzo phenazin-5-amine  7-(1-naphthyl)-75-dibenzo phenazin-7,9-diamine | National Cancer Institute (NCI) database  Inhibitor of SIRT2/SIRT3/SIRT5/SIRT6 | | 7 |
| 44 |  | N1,N4-di(9H-fluoren-9-ylidend)-1,4-benzenediamine | National Cancer Institute (NCI) database  Inhibitor of SIRT2 | |
| 45 |  | 4-methyl-6-(4-methyl-2-(4-morpholinyl)-6-quinoliny)methyl)-2-(4-morpholinyl)quinoline | National Cancer Institute (NCI) database  Inhibitor of SIRT2 | |
| 46 |  | 16,17-bis(9,10-dioxo-9,10-dihydro-1-anthracenyl)amino)anthra benzo pentaphene-5,10-dione | National Cancer Institute (NCI) database  Inhibitor of SIRT2/ SIRT6 | |
| 47 |  | N,N’-di(9H-fluoren-2-yl)thiourea | National Cancer Institute (NCI) database  Inhibitor of SIRT2 | |
| 48 |  | 3-hydroxyestra-1,3,5 (10)-trien-17-yl 3-phenylpropanoate | National Cancer Institute (NCI) database  Inhibitor of SIRT2 | |
| 49 |  | 3-(4-isopropylbenzylidene)-5-(2-naphthyl)-2(3H)-furanone | National Cancer Institute (NCI) database  Inhibitor of SIRT2  Activator of SIRT5 | |
| 50 |  | 2-(25-isoquinolin-2-yl)-1-(3-phenanthryl)ethanone | National Cancer Institute (NCI) database  Inhibitor of SIRT2/SIRT3/ SIRT6 | |
| 51 |  | 1,11a,13a-trimethyl-8-phenyl-2,3,3a,3b,4,5,5a,6,11,11a,11b,12,13,13a-tetradecahydro-1H-cyclopenta[5,6]naphtha[1,2-g]quinazolin-1-ol | National Cancer Institute (NCI) database  Inhibitor of SIRT2 | |
| 52 |  | 3,12-bis(hydroxyl(oxido)amino) anthrax[9,1,2-cde]benzo[rst] pentaphene -5,10-dione | National Cancer Institute (NCI) database  Inhibitor of SIRT2/ SIRT5 | |
| 53 |  | 5’-benzyl-12’-hydroxy-2’-methyl-3’,6’,18-trioxoergotaman | National Cancer Institute (NCI) database  Inhibitor of SIRT2 /SIRT5/SIRT6 | |
| 54 |  | (2-benzylphenyl)(2-naphthyl)methanimine | National Cancer Institute (NCI) database  Inhibitor of SIRT2 | |
| 55 |  | (3,5-dimethylphenyl)(2-(1-naphthy lmethyl)phenyl)methanimine | National Cancer Institute (NCI) database  Inhibitor of SIRT2 | |
| 56 |  | (4-methyl-1-naphthyl)(2-(1-naph thylmethyl)phenyl)methanimine | National Cancer Institute (NCI) database  Inhibitor of SIRT2 | |
| 57 |  | n.a. | National Cancer Institute (NCI) database  Inhibitor of SIRT2/ SIRT6 | |
| 58 |  | n.a. | National Cancer Institute (NCI) database  Inhibitor of SIRT2  Activator of SIRT6 | |
| 59 |  | 1-hydrosy-1,2-bis(7-methoxy-9H-fluoren-2-yl)-15-diazene | National Cancer Institute (NCI) database  Inhibitor of SIRT2 | |
| 60 |  | n.a. | National Cancer Institute (NCI) database  Activator of SIRT5/SIRT6 | |
| 61 |  | n.a. | National Cancer Institute (NCI) database  Inhibitor of SIRT2  Activator of SIRT6 | |
| 62 |  | 1-((3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)methyl)piperidine | National Cancer Institute (NCI) database  Inhibitor of SIRT2/SIRT3/SIRT5/SIRT6 | |
| 63 |  | 4-(3-pyridinyl)-5-((3-(trifluoromethyl)phenyl)sulfonyl)-4,5-dihydropyrrolo[1,2-1]quinoxaline | National Cancer Institute (NCI) database  Inhibitor of SIRT2  Activator of SIRT5/SIRT6 | |
| 64 |  | 2-anilino benzamide |  | | 8 |
| 65 |  | 2-(biphenyl)-3-ylamino)benzamide |  | | 9 |
| 66 |  | Thiobarbiturate | Virtual screening, free-energy calculation and biological testing | | 10 |
| 67 |  | 3-Pyridinemethanol |  | | PMC |
| 68 |  | Pyrazinecarboxamide |  | | PMC |
| 69 |  | 7,11b-  dihydroindeno[2,1-  c]chromene-  3,6a,9,10(6H)-tetrol |  | | PMC |
| 70 |  | Hematoxylin |  | | PMC |

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