

Electronic Supplementary Information

Synthesis and SAR assessment of novel Tubathian analogs in the pursuit of potent and selective HDAC6 inhibitors

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Enzyme inhibition assay performed by Cerep

% inhibition of control values with regard to HDAC6 inhibitory activity^{a,b}

Compound	% inhibition HDAC6	Compound	% inhibition HDAC6	Compound	% inhibition HDAC6
3a	34	3b	53	3c	65
3d	65	3e	74	3f	51
3g	40	3h	54	3i	99
3j	100	3k	100	3l	99
3m	100				

^a Test concentration: 10 μ M; ^b Mean value of two screening sessions

Assay	Compound	Test Concentration (M)	% of Control Values		
			1st	2nd	Mean
HDAC2 (h)	3l	3.0E-09	108.0	112.2	110.1
HDAC2 (h)	3l	3.0E-08	107.3	109.2	108.2
HDAC2 (h)	3l	3.0E-07	110.1	108.7	109.4
HDAC2 (h)	3l	3.0E-06	97.3	104.0	100.6
HDAC2 (h)	3l	3.0E-05	68.9	61.7	65.3
HDAC2 (h)	3j	3.0E-10	118.3	117.8	118.1
HDAC2 (h)	3j	3.0E-09	120.4	119.5	119.9
HDAC2 (h)	3j	3.0E-08	113.4	115.4	114.4
HDAC2 (h)	3j	3.0E-07	114.7	112.7	113.7
HDAC2 (h)	3j	3.0E-06	101.4	98.5	100.0
HDAC2 (h)	3j	3.0E-05	60.1	64.2	62.1
HDAC2 (h)	2c	3.0E-10	84.3	97.7	91.0
HDAC2 (h)	2c	3.0E-09	80.6	81.1	80.9
HDAC2 (h)	2c	3.0E-08	83.2	90.0	86.6
HDAC2 (h)	2c	3.0E-07	95.2	91.0	93.1
HDAC2 (h)	2c	3.0E-06	82.2	85.4	83.8
HDAC2 (h)	2c	3.0E-05	43.7	43.0	43.4
HDAC2 (h)	2a	3.0E-10	103.2	106.9	105.1
HDAC2 (h)	2a	3.0E-09	108.7	111.0	109.9
HDAC2 (h)	2a	3.0E-08	94.8	95.8	95.3
HDAC2 (h)	2a	3.0E-07	99.9	95.2	97.5
HDAC2 (h)	2a	3.0E-06	87.9	86.4	87.1
HDAC2 (h)	2a	3.0E-05	52.8	44.8	48.8
HDAC1 (h)	3l	3.0E-10	101.3	100.4	100.9
HDAC1 (h)	3l	3.0E-09	93.9	95.1	94.5
HDAC1 (h)	3l	3.0E-08	91.6	93.7	92.6
HDAC1 (h)	3l	3.0E-07	96.4	92.8	94.6
HDAC1 (h)	3l	3.0E-06	76.4	77.9	77.1
HDAC1 (h)	3l	3.0E-05	26.4	26.8	26.6
HDAC1 (h)	3j	3.0E-10	100.4	99.7	100.0
HDAC1 (h)	3j	3.0E-09	101.8	100.7	101.3

Assay	Compound	Test Concentration (M)	% of Control Values		
			1st	2nd	Mean
HDAC1 (h)	3j	3.0E-08	96.7	95.8	96.3
HDAC1 (h)	3j	3.0E-07	95.7	96.2	96.0
HDAC1 (h)	3j	3.0E-06	73.1	75.9	74.5
HDAC1 (h)	3j	3.0E-05	22.0	27.1	24.5
HDAC3 (h)	3l	3.0E-10	107.3	103.6	105.4
HDAC3 (h)	3l	3.0E-09	108.8	106.1	107.4
HDAC3 (h)	3l	3.0E-08	106.7	99.6	103.1
HDAC3 (h)	3l	3.0E-07	103.2	104.6	103.9
HDAC3 (h)	3l	3.0E-06	102.8	106.1	104.5
HDAC3 (h)	3l	3.0E-05	92.2	78.3	85.2
HDAC3 (h)	3j	3.0E-10	105.3	107.8	106.6
HDAC3 (h)	3j	3.0E-09	109.1	107.5	108.3
HDAC3 (h)	3j	3.0E-08	107.4	104.5	106.0
HDAC3 (h)	3j	3.0E-07	98.8	104.9	101.9
HDAC3 (h)	3j	3.0E-06	84.0	92.6	88.3
HDAC3 (h)	3j	3.0E-05	56.5	41.0	48.7
HDAC3 (h)	2c	3.0E-10	100.9	105.2	103.0
HDAC3 (h)	2c	3.0E-09	101.3	100.7	101.0
HDAC3 (h)	2c	3.0E-08	105.9	107.2	106.5
HDAC3 (h)	2c	3.0E-07	110.5	109.2	109.8
HDAC3 (h)	2c	3.0E-06	92.9	94.4	93.7
HDAC3 (h)	2c	3.0E-05	43.9	53.2	48.5
HDAC3 (h)	2a	3.0E-10	100.5	102.4	101.4
HDAC3 (h)	2a	3.0E-09	101.7	99.7	100.7
HDAC3 (h)	2a	3.0E-08	103.3	98.1	100.7
HDAC3 (h)	2a	3.0E-07	102.5	98.0	100.2
HDAC3 (h)	2a	3.0E-06	94.9	97.7	96.3
HDAC3 (h)	2a	3.0E-05	50.2	47.7	49.0
HDAC4 (h)	3l	3.0E-10	121.2	96.8	109.0
HDAC4 (h)	3l	3.0E-09	101.1	104.5	102.8
HDAC4 (h)	3l	3.0E-08	101.0	92.2	96.6
HDAC4 (h)	3l	3.0E-07	59.2	69.9	64.6
HDAC4 (h)	3l	3.0E-06	21.1	24.5	22.8
HDAC4 (h)	3l	3.0E-05	2.0	1.8	1.9
HDAC4 (h)	3j	3.0E-10	103.4	106.2	104.8
HDAC4 (h)	3j	3.0E-09	101.9	102.4	102.1
HDAC4 (h)	3j	3.0E-08	101.8	98.8	100.3
HDAC4 (h)	3j	3.0E-07	75.9	81.2	78.5
HDAC4 (h)	3j	3.0E-06	25.9	36.0	30.9
HDAC4 (h)	3j	3.0E-05	3.5	5.5	4.5
HDAC5 (h)	3l	3.0E-10	123.3	126.0	124.7
HDAC5 (h)	3l	3.0E-09	124.9	119.5	122.2
HDAC5 (h)	3l	3.0E-08	118.1	118.2	118.2

Assay	Compound	Test Concentration (M)	% of Control Values		
			1st	2nd	Mean
HDAC5 (h)	3l	3.0E-07	75.8	67.3	71.5
HDAC5 (h)	3l	3.0E-06	18.2	20.3	19.2
HDAC5 (h)	3l	3.0E-05	2.8	4.7	3.7
HDAC5 (h)	3j	3.0E-10	92.9	103.6	98.2
HDAC5 (h)	3j	3.0E-09	101.1	102.3	101.7
HDAC5 (h)	3j	3.0E-08	106.6	102.8	104.7
HDAC5 (h)	3j	3.0E-07	77.4	85.8	81.6
HDAC5 (h)	3j	3.0E-06	31.3	34.5	32.9
HDAC5 (h)	3j	3.0E-05	6.3	7.0	6.7
HDAC5 (h)	2c	3.0E-10	111.7	111.2	111.4
HDAC5 (h)	2c	3.0E-09	111.7	115.3	113.5
HDAC5 (h)	2c	3.0E-08	110.4	107.6	109.0
HDAC5 (h)	2c	3.0E-07	72.8	74.1	73.4
HDAC5 (h)	2c	3.0E-06	16.3	14.5	15.4
HDAC5 (h)	2c	3.0E-05	3.7	2.9	3.3
HDAC5 (h)	2a	3.0E-10	105.4	105.8	105.6
HDAC5 (h)	2a	3.0E-09	103.7	102.6	103.1
HDAC5 (h)	2a	3.0E-08	98.0	97.2	97.6
HDAC5 (h)	2a	3.0E-07	61.9	63.5	62.7
HDAC5 (h)	2a	3.0E-06	18.6	17.0	17.8
HDAC5 (h)	2a	3.0E-05	8.4	5.2	6.8
HDAC6 (h)	3l	1.0E-05	-0.1	2.1	1.0
HDAC6 (h)	3l	3.0E-10	101.4	100.8	101.1
HDAC6 (h)	3l	3.0E-09	81.9	73.0	77.4
HDAC6 (h)	3l	3.0E-08	25.7	21.6	23.6
HDAC6 (h)	3l	3.0E-07	7.6	6.0	6.8
HDAC6 (h)	3l	3.0E-06	1.5	1.0	1.3
HDAC6 (h)	3l	3.0E-05	1.2	1.1	1.2
HDAC6 (h)	3m	1.0E-05	0.8	-0.7	0.1
HDAC6 (h)	3m	3.0E-10	101.6	98.7	100.2
HDAC6 (h)	3m	3.0E-09	89.7	81.2	85.4
HDAC6 (h)	3m	3.0E-08	38.9	37.3	38.1
HDAC6 (h)	3m	3.0E-07	9.9	7.6	8.8
HDAC6 (h)	3m	3.0E-06	3.8	2.6	3.2
HDAC6 (h)	3m	3.0E-05	-0.2	1.0	0.4
HDAC6 (h)	3i	1.0E-05	1.7	-0.1	0.8
HDAC6 (h)	3i	3.0E-10	95.0	101.9	98.5
HDAC6 (h)	3i	3.0E-09	80.7	81.4	81.1
HDAC6 (h)	3i	3.0E-08	32.2	36.5	34.3
HDAC6 (h)	3i	3.0E-07	6.4	5.9	6.2
HDAC6 (h)	3i	3.0E-06	1.0	1.9	1.5
HDAC6 (h)	3i	3.0E-05	1.2	1.0	1.1
HDAC6 (h)	3j	1.0E-05	-0.2	0.1	0.0

Assay	Compound	Test Concentration (M)	% of Control Values		
			1st	2nd	Mean
HDAC6 (h)	3j	3.0E-10	97.3	99.6	98.5
HDAC6 (h)	3j	3.0E-09	75.8	76.2	76.0
HDAC6 (h)	3j	3.0E-08	26.8	26.6	26.7
HDAC6 (h)	3j	3.0E-07	3.2	4.6	3.9
HDAC6 (h)	3j	3.0E-06	1.3	1.4	1.3
HDAC6 (h)	3j	3.0E-05	0.3	1.2	0.7
HDAC6 (h)	3k	1.0E-05	-1.0	-1.3	-1.1
HDAC6 (h)	3k	3.0E-10	117.0	98.6	107.8
HDAC6 (h)	3k	3.0E-09	65.6	61.4	63.5
HDAC6 (h)	3k	3.0E-08	14.4	16.8	15.6
HDAC6 (h)	3k	3.0E-07	2.6	2.2	2.4
HDAC6 (h)	3k	3.0E-06	-0.4	-0.2	-0.3
HDAC6 (h)	3k	3.0E-05	1.3	0.0	0.7
HDAC7 (h)	3l	3.0E-10	104.5	106.2	105.3
HDAC7 (h)	3l	3.0E-09	101.5	99.9	100.7
HDAC7 (h)	3l	3.0E-08	87.5	78.5	83.0
HDAC7 (h)	3l	3.0E-07	35.8	37.9	36.8
HDAC7 (h)	3l	3.0E-06	8.4	8.7	8.5
HDAC7 (h)	3l	3.0E-05	1.0	0.6	0.8
HDAC7 (h)	3j	3.0E-10	103.1	105.1	104.1
HDAC7 (h)	3j	3.0E-09	105.2	99.7	102.5
HDAC7 (h)	3j	3.0E-08	84.6	84.8	84.7
HDAC7 (h)	3j	3.0E-07	41.0	42.9	41.9
HDAC7 (h)	3j	3.0E-06	12.7	8.4	10.5
HDAC7 (h)	3j	3.0E-05	1.3	1.5	1.4
HDAC7 (h)	2c	3.0E-10	99.9	104.1	102.0
HDAC7 (h)	2c	3.0E-09	99.1	98.2	98.7
HDAC7 (h)	2c	3.0E-08	77.8	78.5	78.1
HDAC7 (h)	2c	3.0E-07	25.8	26.1	26.0
HDAC7 (h)	2c	3.0E-06	5.0	5.2	5.1
HDAC7 (h)	2c	3.0E-05	0.4	0.1	0.2
HDAC7 (h)	2a	3.0E-10	102.7	107.5	105.1
HDAC7 (h)	2a	3.0E-09	98.2	102.1	100.2
HDAC7 (h)	2a	3.0E-08	77.7	88.0	82.9
HDAC7 (h)	2a	3.0E-07	36.2	28.8	32.5
HDAC7 (h)	2a	3.0E-06	4.8	5.0	4.9
HDAC7 (h)	2a	3.0E-05	0.8	1.0	0.9
HDAC8 (h)	3l	3.0E-10	91.9	95.2	93.5
HDAC8 (h)	3l	3.0E-09	94.6	107.1	100.8
HDAC8 (h)	3l	3.0E-08	93.6	92.1	92.9
HDAC8 (h)	3l	3.0E-07	79.0	87.6	83.3
HDAC8 (h)	3l	3.0E-06	32.8	43.5	38.2
HDAC8 (h)	3l	3.0E-05	8.2	4.7	6.5

Assay	Compound	Test Concentration (M)	% of Control Values		
			1st	2nd	Mean
HDAC8 (h)	3j	3.0E-10	105.2	107.0	106.1
HDAC8 (h)	3j	3.0E-09	104.3	107.2	105.8
HDAC8 (h)	3j	3.0E-08	99.7	103.0	101.4
HDAC8 (h)	3j	3.0E-07	89.4	86.4	87.9
HDAC8 (h)	3j	3.0E-06	53.6	45.6	49.6
HDAC8 (h)	3j	3.0E-05	7.1	7.1	7.1
HDAC9 (h)	3l	3.0E-10	112.2	107.8	110.0
HDAC9 (h)	3l	3.0E-09	96.3	105.2	100.7
HDAC9 (h)	3l	3.0E-08	91.9	77.4	84.7
HDAC9 (h)	3l	3.0E-07	52.1	43.8	48.0
HDAC9 (h)	3l	3.0E-06	11.4	13.4	12.4
HDAC9 (h)	3l	3.0E-05	-2.0	3.0	0.5
HDAC9 (h)	3j	3.0E-10	109.4	104.0	106.7
HDAC9 (h)	3j	3.0E-09	105.6	112.2	108.9
HDAC9 (h)	3j	3.0E-08	85.7	89.2	87.4
HDAC9 (h)	3j	3.0E-07	65.1	69.5	67.3
HDAC9 (h)	3j	3.0E-06	25.5	22.7	24.1
HDAC9 (h)	3j	3.0E-05	6.9	10.1	8.5
HDAC9 (h)	2c	3.0E-10	76.2	100.5	88.4
HDAC9 (h)	2c	3.0E-09	101.7	99.9	100.8
HDAC9 (h)	2c	3.0E-08	92.7	87.4	90.0
HDAC9 (h)	2c	3.0E-07	58.8	112.7	58.8
HDAC9 (h)	2c	3.0E-06	13.8	8.5	11.1
HDAC9 (h)	2c	3.0E-05	-3.2	-1.4	-2.3
HDAC9 (h)	2a	3.0E-10	114.9	94.3	104.6
HDAC9 (h)	2a	3.0E-09	93.4	96.8	95.1
HDAC9 (h)	2a	3.0E-08	95.7	95.9	95.8
HDAC9 (h)	2a	3.0E-07	50.9	56.2	53.6
HDAC9 (h)	2a	3.0E-06	14.5	14.6	14.6
HDAC9 (h)	2a	3.0E-05	6.2	3.0	4.6
HDAC10 (h)	3l	3.0E-10	100.5	99.9	100.2
HDAC10 (h)	3l	3.0E-09	98.9	95.0	97.0
HDAC10 (h)	3l	3.0E-08	98.2	97.7	98.0
HDAC10 (h)	3l	3.0E-07	96.8	87.5	92.2
HDAC10 (h)	3l	3.0E-06	72.8	76.8	74.8
HDAC10 (h)	3l	3.0E-05	35.9	29.8	32.8
HDAC10 (h)	3j	3.0E-10	98.9	97.2	98.0
HDAC10 (h)	3j	3.0E-09	95.2	101.8	98.5
HDAC10 (h)	3j	3.0E-08	98.6	102.4	100.5
HDAC10 (h)	3j	3.0E-07	100.9	96.2	98.5
HDAC10 (h)	3j	3.0E-06	65.1	68.5	66.8
HDAC10 (h)	3j	3.0E-05	20.7	16.2	18.5
HDAC10 (h)	2c	3.0E-10	95.1	98.0	96.6

Assay	Compound	Test Concentration (M)	% of Control Values		
			1st	2nd	Mean
HDAC10 (h)	2c	3.0E-09	100.3	100.9	100.6
HDAC10 (h)	2c	3.0E-08	92.9	93.9	93.4
HDAC10 (h)	2c	3.0E-07	90.6	89.6	90.1
HDAC10 (h)	2c	3.0E-06	63.0	63.0	63.0
HDAC10 (h)	2c	3.0E-05	19.1	17.8	18.4
HDAC10 (h)	2a	3.0E-10	96.1	102.6	99.4
HDAC10 (h)	2a	3.0E-09	94.8	100.6	97.7
HDAC10 (h)	2a	3.0E-08	98.2	105.3	101.8
HDAC10 (h)	2a	3.0E-07	92.7	97.4	95.0
HDAC10 (h)	2a	3.0E-06	70.4	66.6	68.5
HDAC10 (h)	2a	3.0E-05	28.2	20.1	24.2
HDAC11 (h)	3l	3.0E-10	85.8	103.5	94.7
HDAC11 (h)	3l	3.0E-09	88.3	90.4	89.4
HDAC11 (h)	3l	3.0E-08	96.4	86.3	91.3
HDAC11 (h)	3l	3.0E-07	89.9	84.1	87.0
HDAC11 (h)	3l	3.0E-06	79.9	74.2	77.0
HDAC11 (h)	3l	3.0E-05	34.5	32.6	33.5
HDAC11 (h)	3j	3.0E-10	106.1	111.4	108.8
HDAC11 (h)	3j	3.0E-09	100.2	100.6	100.4
HDAC11 (h)	3j	3.0E-08	86.5	86.7	86.6
HDAC11 (h)	3j	3.0E-07	57.9	67.2	62.5
HDAC11 (h)	3j	3.0E-06	34.3	37.2	35.8
HDAC11 (h)	3j	3.0E-05	9.7	8.2	9.0

Western Blots performed by Laboratory of Neurobiology and Vesalius Research Center, VIB

Western Blot screening at 1 μ M (normalized to Tubastatin A)

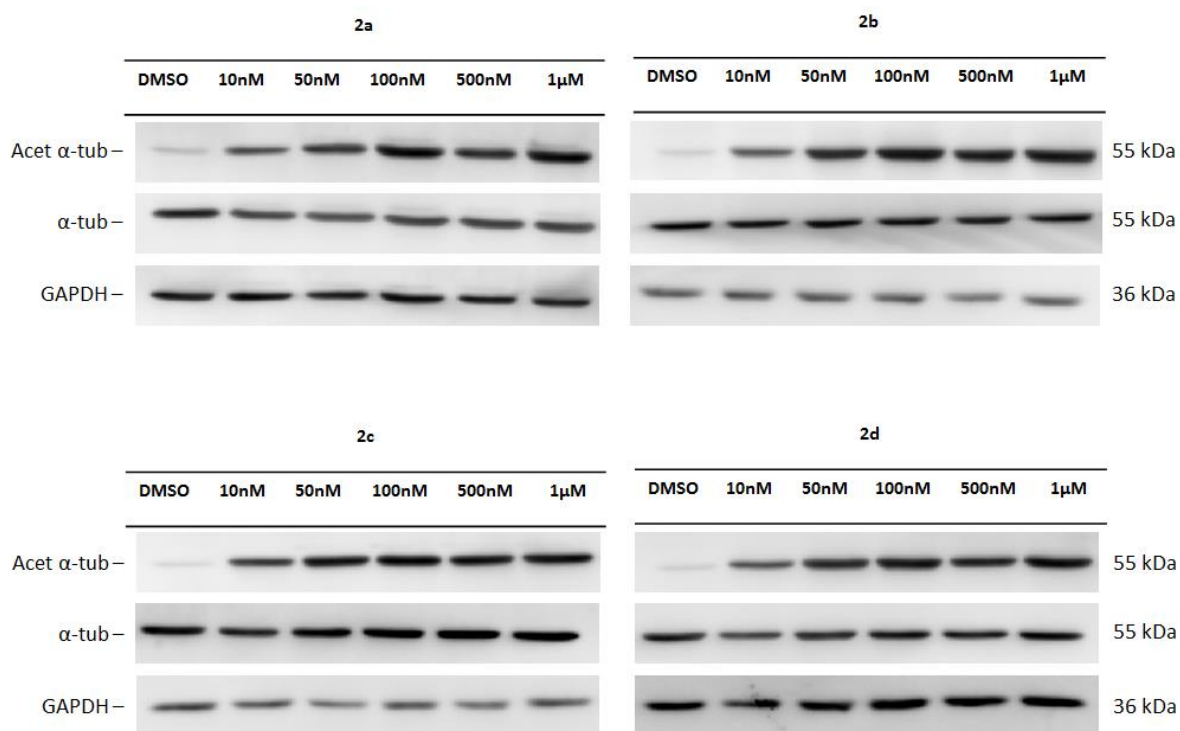
Experiment	Normalized ratio Acetyl α -Tubulin/ α -Tubulin						
	DMSO	Tub A	2a	2b	2c	2d	DMSO
1	19,84	100	88,31	105,29	85,29	89,26	6,25
2	7,04	100	189,75	158,82	93,39	84,89	5,8
3	5,01	100	75,86	75,36	83,74	81,23	7,96
Average	10,63	100	117,97	113,16	87,47	85,13	6,67

Experiment	Normalized ratio Acetyl Histone 3/Histone 4					
	DMSO	Tub A	2a	2b	2c	2d
1	74,63	100	93,4	158,41	177,77	137,35
2	141,46	100	83,21	63,25	86,49	102,22
3	139,93	100	55,43	39,37	34,64	40,32
Average	118,67	100	77,35	87,01	99,63	93,3

Experiment	Normalized ratio Acetyl α -Tubulin/ α -Tubulin							
	DMSO	Tub A	3l	3m	3j	3i	3k	DMSO
1	4,56	100,00	93,08	69,54	94,35	90,38	115,33	4,90
2	12,71	100,00	85,30	69,21	113,09	97,43	161,61	12,09
3	4,62	100,00	70,63	39,58	61,05	68,31	72,62	4,08
Average	7,30	100,00	83,00	59,44	89,50	85,37	116,52	7,02

Experiment	Normalized ratio Acetyl Histone 3/Histone 4							
	DMSO	Tub A	3l	3m	3j	3i	3k	DMSO
1	101,81	100,00	83,08	112,22	111,19	109,74	105,65	107,52
2	149,33	100,00	296,84	272,27	296,72	305,06	270,18	161,10
3	105,94	100,00	104,13	67,68	66,00	50,75	59,14	51,86
Average	119,03	100,00	161,35	150,72	157,97	155,18	144,99	106,83

Western Blot dose-response 2a-d (normalized to 1 μ M of the tested compound)



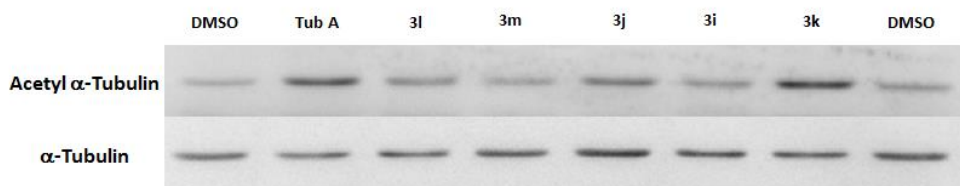
Exp.	Normalized ratio Acetyl α -Tubulin/ α -Tubulin											
	DMSO	Tub A 1 μ M	Tub A 500 nM	Tub A 100 nM	Tub A 50 nM	Tub A 10 nM	2a 1 μ M	2a 500 nM	2a 100 nM	2a 50 nM	2a 10 nM	DMSO
1	14,42	100,00	101,49	135,76	120,55	64,49	100,00	81,59	90,87	76,36	49,30	14,41
2	15,82	100,00	97,20	97,74	98,06	78,35	100,00	97,72	93,60	93,41	59,79	76,69
3	10,99	100,00	67,31	79,09	64,10	48,41	100,00	118,03	130,58	113,58	74,08	20,00
Average	13,47	100,00	99,67	104,20	94,25	63,75	100,00	97,45	104,99	94,45	61,06	37,03

Exp.	Normalized ratio Acetyl α -Tubulin/ α -Tubulin											
	DMSO	Tub A 1 μ M	Tub A 500 nM	Tub A 100 nM	Tub A 50 nM	Tub A 10 nM	2b 1 μ M	2b 500 nM	2b 100 nM	2b 50 nM	2b 10 nM	DMSO
1	5,48	100,00	74,51	101,26	79,74	47,14	100,00	94,37	96,25	65,08	44,58	7,06
2	16,13	100,00	97,20	97,74	98,06	78,35	100,00	103,14	143,57	92,15	53,01	13,89
3	10,80	100,00	88,99	79,95	76,70	46,51	100,00	71,52	86,80	80,82	58,80	12,16
Average	10,80	100,00	86,90	92,98	84,83	57,33	100,00	89,68	108,88	79,35	52,13	11,04

Exp.	Normalized ratio Acetyl α -Tubulin/ α -Tubulin											
	DMSO	Tub A 1 μ M	Tub A 500 nM	Tub A 100 nM	Tub A 50 nM	Tub A 10 nM	2c 1 μ M	2c 500 nM	2c 100 nM	2c 50 nM	2c 10 nM	DMSO
1	7,12	100,00	74,51	101,26	79,74	47,14	100,00	103,46	87,79	72,24	45,70	3,32
2	12,17	100,00	97,20	97,74	98,06	78,35	100,00	73,46	84,34	86,16	78,50	21,23
3	8,10	100,00	93,28	119,91	134,30	68,56	100,00	79,43	73,30	52,98	49,99	4,90
Average	9,31	100,00	88,33	106,31	104,03	64,68	100,00	85,45	81,81	70,46	58,06	9,82

Exp.	Normalized ratio Acetyl α -Tubulin/ α -Tubulin											
	DMSO	Tub A 1 μ M	Tub A 500 nM	Tub A 100 nM	Tub A 50 nM	Tub A 10 nM	2d 1 μ M	2d 500 nM	2d 100 nM	2d 50 nM	2d 10 nM	DMSO
1	6,89	100,00	74,51	101,26	79,74	47,14	100,00	83,66	86,44	99,55	44,45	5,11
2	15,05	100,00	101,49	135,76	120,55	64,49	100,00	106,99	110,37	85,59	53,44	5,05
3	30,41	100,00	97,20	97,74	98,06	78,35	100,00	88,49	81,69	81,36	47,53	11,55
4	19,67	100,00	69,71	83,97	78,50	50,20	100,00	94,52	111,27	115,32	74,35	17,26
Average	18,00	100,00	85,73	104,68	94,21	60,05	100,00	93,42	97,44	95,46	54,94	9,74

Western Blot screening at 10 nM 3i-k (normalized to Tubastatin A)



Experiment	Normalized ratio Acetyl α -Tubulin/ α -Tubulin							
	DMSO	Tub A	3l	3m	3j	3i	3k	DMSO
1	41,80	100,00	52,56	41,59	42,63	86,69	163,65	78,80
2	74,05	100,00	67,91	85,33	77,46	67,26	128,30	92,14
3	27,92	100,00	49,97	35,71	38,87	36,43	101,18	34,01
Average	47,92	100,00	56,81	54,21	52,99	63,46	131,04	68,32

Ames Fluctuation Assay performed by Eurofins Cerep Panlabs

Bacterial cytotoxicity results 2c and 3l^{1,2}

Compound	Assay	Test Concentration (M)	Cytotoxicity (% of control)
2c	Bacterial cytotoxicity (TA98 - S9)	6.0E-07	108
2c	Bacterial cytotoxicity (TA98 - S9)	1.2E-06	102
2c	Bacterial cytotoxicity (TA98 - S9)	2.5E-06	95
2c	Bacterial cytotoxicity (TA98 - S9)	5.0E-06	101
2c	Bacterial cytotoxicity (TA98 - S9)	1.0E-05	97
2c	Bacterial cytotoxicity (TA98 - S9)	2.5E-05	96
2c	Bacterial cytotoxicity (TA98 - S9)	5.0E-05	95
2c	Bacterial cytotoxicity (TA98 - S9)	1.0E-04	92
3l	Bacterial cytotoxicity (TA98 - S9)	6.0E-07	105
3l	Bacterial cytotoxicity (TA98 - S9)	1.2E-06	103
3l	Bacterial cytotoxicity (TA98 - S9)	2.5E-06	93
3l	Bacterial cytotoxicity (TA98 - S9)	5.0E-06	96
3l	Bacterial cytotoxicity (TA98 - S9)	1.0E-05	90
3l	Bacterial cytotoxicity (TA98 - S9)	2.5E-05	95
3l	Bacterial cytotoxicity (TA98 - S9)	5.0E-05	97
3l	Bacterial cytotoxicity (TA98 - S9)	1.0E-04	99
2c	Bacterial cytotoxicity (TA100 - S9)	6.0E-07	95
2c	Bacterial cytotoxicity (TA100 - S9)	1.2E-06	95
2c	Bacterial cytotoxicity (TA100 - S9)	2.5E-06	102
2c	Bacterial cytotoxicity (TA100 - S9)	5.0E-06	100
2c	Bacterial cytotoxicity (TA100 - S9)	1.0E-05	99
2c	Bacterial cytotoxicity (TA100 - S9)	2.5E-05	110
2c	Bacterial cytotoxicity (TA100 - S9)	5.0E-05	98

Compound	Assay	Test Concentration (M)	Cytotoxicity (% of control)
2c	Bacterial cytotoxicity (TA100 - S9)	1.0E-04	109
3l	Bacterial cytotoxicity (TA100 - S9)	6.0E-07	110
3l	Bacterial cytotoxicity (TA100 - S9)	1.2E-06	115
3l	Bacterial cytotoxicity (TA100 - S9)	2.5E-06	115
3l	Bacterial cytotoxicity (TA100 - S9)	5.0E-06	100
3l	Bacterial cytotoxicity (TA100 - S9)	1.0E-05	93
3l	Bacterial cytotoxicity (TA100 - S9)	2.5E-05	95
3l	Bacterial cytotoxicity (TA100 - S9)	5.0E-05	110
3l	Bacterial cytotoxicity (TA100 - S9)	1.0E-04	118
2c	Bacterial cytotoxicity (TA1535 - S9)	6.0E-07	102
2c	Bacterial cytotoxicity (TA1535 - S9)	1.2E-06	101
2c	Bacterial cytotoxicity (TA1535 - S9)	2.5E-06	103
2c	Bacterial cytotoxicity (TA1535 - S9)	5.0E-06	102
2c	Bacterial cytotoxicity (TA1535 - S9)	1.0E-05	98
2c	Bacterial cytotoxicity (TA1535 - S9)	2.5E-05	97
2c	Bacterial cytotoxicity (TA1535 - S9)	5.0E-05	96
2c	Bacterial cytotoxicity (TA1535 - S9)	1.0E-04	94
3l	Bacterial cytotoxicity (TA1535 - S9)	6.0E-07	102
3l	Bacterial cytotoxicity (TA1535 - S9)	1.2E-06	104
3l	Bacterial cytotoxicity (TA1535 - S9)	2.5E-06	101
3l	Bacterial cytotoxicity (TA1535 - S9)	5.0E-06	101
3l	Bacterial cytotoxicity (TA1535 - S9)	1.0E-05	103
3l	Bacterial cytotoxicity (TA1535 - S9)	2.5E-05	100
3l	Bacterial cytotoxicity (TA1535 - S9)	5.0E-05	101
3l	Bacterial cytotoxicity (TA1535 - S9)	1.0E-04	98
2c	Bacterial cytotoxicity (TA1537 - S9)	6.0E-07	97
2c	Bacterial cytotoxicity (TA1537 - S9)	1.2E-06	95
2c	Bacterial cytotoxicity (TA1537 - S9)	2.5E-06	95

Compound	Assay	Test Concentration (M)	Cytotoxicity (% of control)
2c	Bacterial cytotoxicity (TA1537 - S9)	5.0E-06	96
2c	Bacterial cytotoxicity (TA1537 - S9)	1.0E-05	93
2c	Bacterial cytotoxicity (TA1537 - S9)	2.5E-05	95
2c	Bacterial cytotoxicity (TA1537 - S9)	5.0E-05	96
2c	Bacterial cytotoxicity (TA1537 - S9)	1.0E-04	94
3l	Bacterial cytotoxicity (TA1537 - S9)	6.0E-07	98
3l	Bacterial cytotoxicity (TA1537 - S9)	1.2E-06	97
3l	Bacterial cytotoxicity (TA1537 - S9)	2.5E-06	94
3l	Bacterial cytotoxicity (TA1537 - S9)	5.0E-06	93
3l	Bacterial cytotoxicity (TA1537 - S9)	1.0E-05	95
3l	Bacterial cytotoxicity (TA1537 - S9)	2.5E-05	95
3l	Bacterial cytotoxicity (TA1537 - S9)	5.0E-05	98
3l	Bacterial cytotoxicity (TA1537 - S9)	1.0E-04	96

¹ Cytotoxicity is presented as % of control growth.

² A cytotoxicity value of less than 60 % is flagged, and the compound is considered as toxic at the respective concentration.

Ames results 2c and 3l

Compound	Assay	Test Concentration (M)	Count (# of wells)	Positive Significance (- to +++)	Fisher Exact Test (p-value)
2c	Ames fluctuation test (TA98 - S9)	5.0E-06	0	-	1.0000
2c	Ames fluctuation test (TA98 - S9)	1.0E-05	0	-	1.0000
2c	Ames fluctuation test (TA98 - S9)	5.0E-05	0	-	1.0000
2c	Ames fluctuation test (TA98 - S9)	1.0E-04	0	-	1.0000
3l	Ames fluctuation test (TA98 - S9)	5.0E-06	0	-	1.0000
3l	Ames fluctuation test (TA98 - S9)	1.0E-05	0	-	1.0000
3l	Ames fluctuation test (TA98 - S9)	5.0E-05	0	-	1.0000
3l	Ames fluctuation test (TA98 - S9)	1.0E-04	0	-	1.0000
2c	Ames fluctuation test (TA98 + S9)	5.0E-06	5	-	1.0000
2c	Ames fluctuation test (TA98 + S9)	1.0E-05	6	-	0.5000

Compound	Assay	Test Concentration (M)	Count (# of wells)	Positive Significance (- to +++)	Fisher Exact Test (p-value)
2c	Ames fluctuation test (TA98 + S9)	5.0E-05	2	-	0.2176
2c	Ames fluctuation test (TA98 + S9)	1.0E-04	2	-	0.2176
3l	Ames fluctuation test (TA98 + S9)	5.0E-06	5	-	1.0000
3l	Ames fluctuation test (TA98 + S9)	1.0E-05	5	-	1.0000
3l	Ames fluctuation test (TA98 + S9)	5.0E-05	1	-	0.1019
3l	Ames fluctuation test (TA98 + S9)	1.0E-04	1	-	0.1019
2c	Ames fluctuation test (TA100 - S9)	5.0E-06	2	-	1.0000
2c	Ames fluctuation test (TA100 - S9)	1.0E-05	0	-	0.2474
2c	Ames fluctuation test (TA100 - S9)	5.0E-05	1	-	0.5000
2c	Ames fluctuation test (TA100 - S9)	1.0E-04	0	-	0.2474
3l	Ames fluctuation test (TA100 - S9)	5.0E-06	1	-	0.5000
3l	Ames fluctuation test (TA100 - S9)	1.0E-05	0	-	0.2474
3l	Ames fluctuation test (TA100 - S9)	5.0E-05	1	-	0.5000
3l	Ames fluctuation test (TA100 - S9)	1.0E-04	3	-	0.5000
2c	Ames fluctuation test (TA100 + S9)	5.0E-06	9	-	0.3925
2c	Ames fluctuation test (TA100 + S9)	1.0E-05	7	-	1.0000
2c	Ames fluctuation test (TA100 + S9)	5.0E-05	5	-	0.3795
2c	Ames fluctuation test (TA100 + S9)	1.0E-04	6	-	0.5000
3l	Ames fluctuation test (TA100 + S9)	5.0E-06	10	-	0.2969
3l	Ames fluctuation test (TA100 + S9)	1.0E-05	17	+	0.0163
3l	Ames fluctuation test (TA100 + S9)	5.0E-05	14	-	0.0687
3l	Ames fluctuation test (TA100 + S9)	1.0E-04	2	-	0.0793
2c	Ames fluctuation test (TA1535 - S9)	5.0E-06	0	-	1.0000
2c	Ames fluctuation test (TA1535 - S9)	1.0E-05	0	-	1.0000
2c	Ames fluctuation test (TA1535 - S9)	5.0E-05	0	-	1.0000
2c	Ames fluctuation test (TA1535 - S9)	1.0E-04	0	-	1.0000
3l	Ames fluctuation test (TA1535 - S9)	5.0E-06	0	-	1.0000
3l	Ames fluctuation test (TA1535 - S9)	1.0E-05	0	-	1.0000

Compound	Assay	Test Concentration (M)	Count (# of wells)	Positive Significance (- to +++)	Fisher Exact Test (p-value)
3l	Ames fluctuation test (TA1535 - S9)	5.0E-05	0	-	1.0000
3l	Ames fluctuation test (TA1535 - S9)	1.0E-04	0	-	1.0000
2c	Ames fluctuation test (TA1535 + S9)	5.0E-06	3	-	0.5000
2c	Ames fluctuation test (TA1535 + S9)	1.0E-05	6	-	0.3700
2c	Ames fluctuation test (TA1535 + S9)	5.0E-05	1	-	0.1808
2c	Ames fluctuation test (TA1535 + S9)	1.0E-04	1	-	0.1808
3l	Ames fluctuation test (TA1535 + S9)	5.0E-06	2	-	0.3387
3l	Ames fluctuation test (TA1535 + S9)	1.0E-05	0	-	0.0586
3l	Ames fluctuation test (TA1535 + S9)	5.0E-05	1	-	0.1808
3l	Ames fluctuation test (TA1535 + S9)	1.0E-04	0	-	0.0586
2c	Ames fluctuation test (TA1537-S9)	5.0E-06	3	-	0.1211
2c	Ames fluctuation test (TA1537-S9)	1.0E-05	2	-	0.2474
2c	Ames fluctuation test (TA1537-S9)	5.0E-05	15	+++	0.0000
2c	Ames fluctuation test (TA1537-S9)	1.0E-04	17	+++	0.0000
3l	Ames fluctuation test (TA1537-S9)	5.0E-06	3	-	0.1211
3l	Ames fluctuation test (TA1537-S9)	1.0E-05	4	-	0.0586
3l	Ames fluctuation test (TA1537-S9)	5.0E-05	23	+++	0.0000
3l	Ames fluctuation test (TA1537-S9)	1.0E-04	31	+++	0.0000
2c	Ames fluctuation test (TA1537 + S9)	5.0E-06	6	-	0.1339
2c	Ames fluctuation test (TA1537 + S9)	1.0E-05	9	+	0.0253
2c	Ames fluctuation test (TA1537 + S9)	5.0E-05	15	+++	0.0004
2c	Ames fluctuation test (TA1537 + S9)	1.0E-04	23	+++	0.0000
3l	Ames fluctuation test (TA1537 + S9)	5.0E-06	7	-	0.0793
3l	Ames fluctuation test (TA1537 + S9)	1.0E-05	5	-	0.2176
3l	Ames fluctuation test (TA1537 + S9)	5.0E-05	18	+++	0.0000
3l	Ames fluctuation test (TA1537 + S9)	1.0E-04	30	+++	0.0000

Ames background results

Assay	Count(# of wells)
Ames fluctuation test (TA98 - S9)	1
Ames fluctuation test (TA98 + S9)	6
Ames fluctuation test (TA100 - S9)	3
Ames fluctuation test (TA100 + S9)	7
Ames fluctuation test (TA1535 - S9)	0
Ames fluctuation test (TA1535 + S9)	5
Ames fluctuation test (TA1537-S9)	0
Ames fluctuation test (TA1537 + S9)	3

Ames reference compounds results

Assay	Compound	Count (# of wells)	Positive Significance (- to +++)	Fisher Exact Test (p-value)
Ames fluctuation test (TA98 - S9)	Streptozotocin	1	-	0.5000
Ames fluctuation test (TA98 - S9)	9-Aminoacridine	0	-	1.0000
Ames fluctuation test (TA98 - S9)	2-Aminoanthracene	0	-	1.0000
Ames fluctuation test (TA98 - S9)	Quercetin	9	++	0.0013
Ames fluctuation test (TA98 + S9)	Streptozotocin	7	-	0.3795
Ames fluctuation test (TA98 + S9)	9-Aminoacridine	1	-	0.1019
Ames fluctuation test (TA98 + S9)	2-Aminoanthracene	48	+++	0.0000
Ames fluctuation test (TA98 + S9)	Quercetin	46	+++	0.0000
Ames fluctuation test (TA100 - S9)	Streptozotocin	27	+++	0.0000
Ames fluctuation test (TA100 - S9)	9-Aminoacridine	1	-	0.5000
Ames fluctuation test (TA100 - S9)	2-Aminoanthracene	2	-	1.0000
Ames fluctuation test (TA100 - S9)	Quercetin	1	-	0.5000
Ames fluctuation test (TA100 + S9)	Streptozotocin	39	+++	0.0000
Ames fluctuation test (TA100 + S9)	9-Aminoacridine	6	-	0.5000
Ames fluctuation test (TA100 + S9)	2-Aminoanthracene	36	+++	0.0000
Ames fluctuation test (TA100 + S9)	Quercetin	9	-	0.3925
Ames fluctuation test (TA1535 - S9)	Streptozotocin	47	+++	0.0000
Ames fluctuation test (TA1535 - S9)	9-Aminoacridine	0	-	1.0000
Ames fluctuation test (TA1535 - S9)	2-Aminoanthracene	0	-	1.0000

Assay	Compound	Count (# of wells)	Positive Significance (- to +++)	Fisher Exact Test (p-value)
Ames fluctuation test (TA1535 - S9)	Quercetin	0	-	1.0000
Ames fluctuation test (TA1535 + S9)	Streptozotocin	48	+++	0.0000
Ames fluctuation test (TA1535 + S9)	9-Aminoacridine	0	-	0.0586
Ames fluctuation test (TA1535 + S9)	2-Aminoanthracene	38	+++	0.0000
Ames fluctuation test (TA1535 + S9)	Quercetin	1	-	0.1808
Ames fluctuation test (TA1537-S9)	Streptozotocin	2	-	0.2474
Ames fluctuation test (TA1537-S9)	9-Aminoacridine	18	+++	0.0000
Ames fluctuation test (TA1537-S9)	2-Aminoanthracene	1	-	0.5000
Ames fluctuation test (TA1537-S9)	Quercetin	1	-	0.5000
Ames fluctuation test (TA1537 + S9)	Streptozotocin	6	-	0.1339
Ames fluctuation test (TA1537 + S9)	9-Aminoacridine	8	+	0.0455
Ames fluctuation test (TA1537 + S9)	2-Aminoanthracene	11	++	0.0072
Ames fluctuation test (TA1537 + S9)	Quercetin	4	-	0.3387