

Supplemental Figure Legends

S1 (figure) **Domain organization of class I/II/IV HDACs from *C. elegans* (a), *Drosophila* (b) and *Danio rerio* (c).**

Deacetylase (DAC) domains, zinc fingers and other motifs are depicted as in Figure 1. GenBank accession numbers and genetic loci are listed in brackets at right. These deacetylases have not been as well characterized as their counterparts in yeast and mammals. While the five *D. melanogaster* proteins can be easily grouped according to their mammalian homologs, the eight *C. elegans* proteins are more complicated. ceHda-2 and ceHda-3 are more homologous to HDAC1 and HDAC2 than to HDAC3. Like ceHda-6 and ceHda-8, ceHda-4 and ceHda-5 may belong to class IIb since both are highly similar to the deacetylase domains of HDAC6 and HDAC10. For zebrafish, the HDAC7 sequence needs to be verified about the binding motifs for MEF2 and 14-3-3. The two clones listed for zebrafish HDAC9 could also be from separate genes, so further analysis is needed to address this. HDAC3l, HDAC3-like protein.

S2 (figure) **Sequence comparison of selective human HDACs with orthologues in sea urchin and zebrafish.**

a. Sequence alignment of human HDAC8 (hHDAC8) with its ortholog from the sea urchin *Strongylocentrotus purpuratus* (sHDAC8; GenBank accession number, XP_791175.1). The conserved PKA site is underlined and the serine residues for phosphorylation are highlighted in red. **b.** Sequence comparison of human HDAC4 with a putative orthologue from the sea urchin *S. purpuratus* (GenBank accession number, XP_797761.2). sHDAC4 refers to the protein from the latter organism. 14-3-3 and MEF2

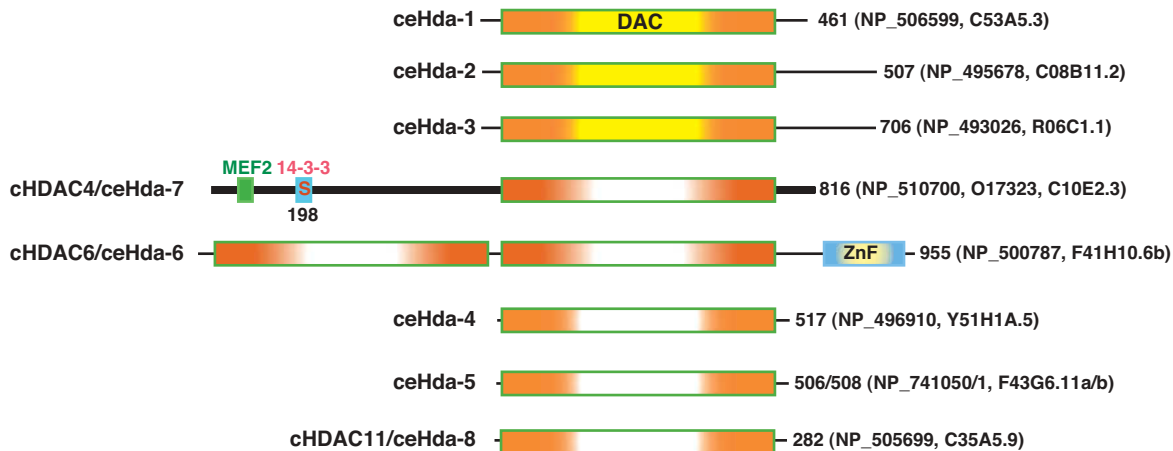
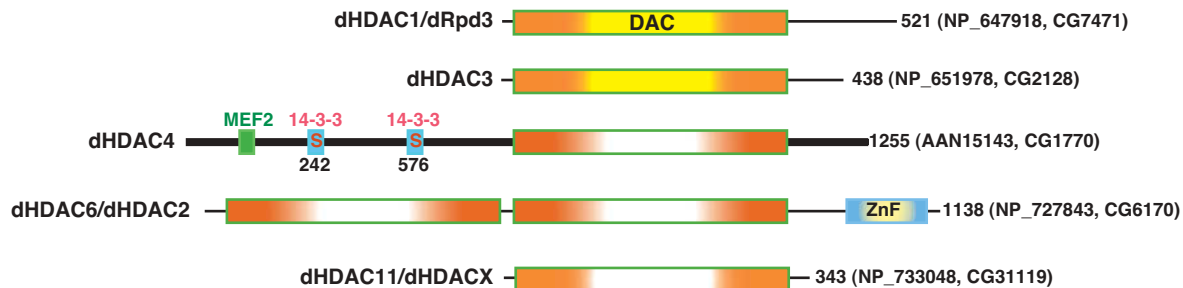
binding sites are underlined with key residues highlighted in color. Also underlined are a Q-rich domain, important for dimerization, and a nuclear localization signal (NLS). The SP box is present in HDAC5 and HDAC9, but not in HDAC7. It is also conserved in class IIa HDACs from *C. elegans* and *D. melanogaster*. The leucine and isoleucine residues in the box resemble a nuclear export sequence, but expression of an HDAC4 fragment encompassing revealed that the box might not possess nuclear export activity¹, suggesting that it may have another function. The arrow denotes the substitution of a catalytically important tyrosine residue by histidine in the human protein. This substitution occurs in zebrafish, but not in *C. elegans* or *D. melanogaster*, so it appears to be vertebrate-specific². Note that an HDAC4-like protein from the sea squirt *Ciona intestinalis* (an invertebrate chordate) has a phenylalanine at the equivalent position². **c** Sequence comparison of human HDAC10 (GenBank accession number, NP_114408) with a putative ortholog from the zebrafish *D. rerio* (zHDAC10; GenBank accession number, NP_956069.1). Two conserved motifs in the C-terminal extension are underlined and labeled with a hydrophobic (H) box and a question mark to denote their potential functional importance.

References

1. Wang, A. H. & Yang, X. J. Histone deacetylase 4 possesses intrinsic nuclear import and export signals. *Mol. Cell. Biol.* **21**, 5992-6005 (2001).
2. Lamb, N. et al. Unraveling the hidden catalytic activity of vertebrate class IIa histone deacetylases. *Proc. Natl. Acad. Sci. USA* **104**, 17355-17340 (2007).

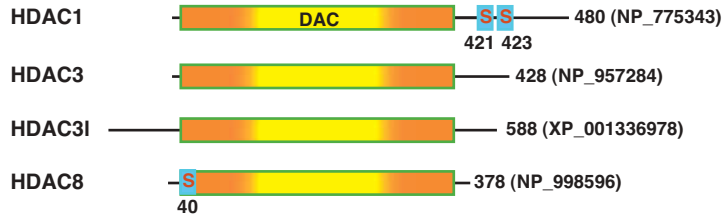
S3 (figure) **Crystal structures of the deacetylase domains of HDAC7 and HDAC8.**

a Ribbon diagram of the crystal structure of the HDAC7 deacetylase domain complexed with the inhibitor SAHA (suberoylanilide hydroxamic acid), with α -helices and β -strands coloured in red and yellow, respectively. **b** Ribbon diagram of overall structure of the HDAC8 deacetylase domain with bound SAHA, with α -helices and β -strands coloured in cyan and purple, respectively. **c** Ribbon diagram showing superposition of the HDAC7 HDAC8 structures. The PDB codes for the HDAC7 structure are 2NVR and 2PQO (Schuetz, A., Min, J.R., Allali-Hassani, A., Loppnau, P., Kwiatkowski, N.P., Mazitschek, R., Edwards, A.M., Arrowsmith, C.H., Vedadi, M., Bochkarev, A., and Plotnikov, A.N., data to be published), whereas the code for HDAC8 is 1T69. This figure was kindly provided by Drs. Xueyong Zhu and Ian A. Wilson (Scripps Research Institute).

a *C. elegans***b** *Drosophila*

C *Danio rerio*

Class I



Class II



Class IV



Supplementary S2a (figure)

		PKA ↓		
hHDAC8	18	YIYSPEYVSMCDSLAKIPKRAS	MVHSLIEAYALHKQMRIVKPKVASMEEMATFH	TDAYLQ 77
		Y+++ + + +CD + KIPKRAS	MVH+LIEAY L + V P+ A+ +E+ TFH+ Y++	
sHDAC8	293	YVFNQKLLQLCDQVPKIPKRAS	MVHTLIEAYDLLDHVTPVSP	EFATKDELLTFHSQEQEYIE 352
		<u>Conservation motif</u>		
hHDAC8	78	HLQKVSQEGDDDDHPDSI--EYGLGYDC	PATEGIFDYAAAIGGATITAAQCLIDGMCKVAI	135
		L++V+ E D + + + ++GLGYDCP+ ++D+ + GA+++ A+ LI C++AI		
sHDAC8	353	FLERNVLEEDSEKDEELKQQFGLGYDC	PSLPLVYDFVRLVAGASLS	CAKALIQQKCRIAI 412
hHDAC8	136	NWSGGWHHAKKDEASGFCYLNDAV	LGLRLRRKFERILYVDL	DLHHDGVEDAFSFTSKV 195
		NW+GGWHHA++DEA+GFCY+ND VL IL+L+ F R+LYVDL	DLHHDG V+DAF FT KV	
sHDAC8	413	NWNGGWHHARDEAAGFCYVNDIVL	LAILKLKEHFNRLYVDL	DLHHDGAVDDAFIFTPKV 472
hHDAC8	196	MTVSLHKFSPGFFPGTGDVSDV	GLGKGRYYSVNVIQDGIQDEKYYQICESV	LKEVYQAF 255
		MTVSLHKFSPGFFPGTG ++ VG G+G++Y+++VP++DGI+DE+Y + V+++V F		
sHDAC8	473	MTVSLHKFSPGFFPGTGS	LNVRVGGGRGKFYTISVPLKDG	IKDEQYSDLFTRVIEQVRVKF 532
hHDAC8	256	NPKAVVLQLGADTIAGDPMCSFN	NMTPVGIGKCLKYILQWQLATLILGGGGYN	LANTARCW 315
		P VV+Q GADT++ DPM SFN+TP+G+G+C+ +L W+L TL+LGGGGYN+ANTARCW		
sHDAC8	533	QPSVVVVQCGADTLSSDPMQSF	NLTPLVGQGCVSRVLSWKLPTLLLGGGGYN	MANTARCW 592
hHDAC8	316	TYLTGVILGKTLSSIEIPDHEFF	TAYGPDYVLEITPSCR	PDRNEPHRIQQILNYIKGNLKH 375
		+YLTG++LG+ L SEIPDHEFF YGP Y LE+ P+ + N ++ + I NL++		
sHDAC8	593	SYLTGLVLGQKLPSEIPDHEFF	LEYGPGYQLEVCPAHY	TNYNTVEYMETVAKAITKNLEN 652
hHDAC8	376	V 376		
		V		
sHDAC8	653	V 653		

Supplementary S2b (figure)

HDAC4	90	IAEFQRQHEQLSRQHEAQLHEHIKQQQEMLAMKHQQ--ELLEHQKLERHRQEQELEKQH	147
		+A+F+ + QL +QH+ KQQQE++ ++H Q +LLE QR LE +Q+Q+ ++Q	
sHDAC4	96	LAQFKERQAQLVKQHQ-----KQQQELIMVRHVQREQLLEQQRLLLEAQQQQQQ--QQQQ	147
		Q-rich domain	
HDAC4	148	REQKLQQLKNKEKGKESAVASTEVMKQLQEFVLNKKKALAHN---LNHCISSDPRYWYG	204
		++ + Q L+ K+SA ASTEVK KLQ+F+LN+++ + LNH S R+W	
sHDAC4	148	QQAQKQHLEQLLAKKQSANASTEVDKQLQKFLLNROQRTDYGGSGPLNH--SPPYRHW--	203
		MEF2 binding	
HDAC4	205	KTQHSSSLQSSPPQSGVSTSYNHPVLGM--YDAKDDFPLRKTASEPNLKLRSRLKQKVAE	262
		T SS+D SPP + VS ++H +G YD+ + FPLRKTAS+ NLK+RSRLK+KV E	
sHDAC4	204	-TPPSSMDHHSPPHN-VSPQFHHQPMGFQYDSSN-FPLRKTASDSNLKVRSLKKEKVTE	260
		14-3-3 binding 1	NLS
HDAC4	263	RRS--SPLLRRKDGPPVVTALKKRPLDVTDSACSSAPGSPSPNNSSGVSVAENGIAPAV	320
		RR+ SPLLRR++GP +LK++P+ T S + G ++G + NG+ +V	
sHDAC4	261	RRTHGSPLLRRREGP--NSLKRKPIIDTSSNSAPGSGPSSPLSAGAAGGGDSPNGL--SV	316
		NLS	
HDAC4	321	PSIPAETSLAHLVAREGSAAPL-PLYTSPSLPNITLGLPATGPSAGTAGQDTERLTLP	379
		++P E S A +++ ++ + LY+SPSLPNI++G+PA A P	
sHDAC4	317	AALPEEASSATKMMLKQRLYGVVNDLYSSPSLPNISIGIPA----ANNPQHSPLGQVKP	372
		SP box	
HDAC4	380	ALQQRSLFPGTHLTPYLSTSPLELDG-GAAHSPLLQHMVLEQPPAQAPLVTGLGALPL	438
		L S+ L PYL +PL G AH L M + AQ ++	
sHDAC4	373	GL-PTASMLGAAPLNPYLPGAPLSLAGINPAH---LACMTFQDFQQAQTAAMSA-----	422
HDAC4	439	HAQSLVGADRVSPSIHKLRQHRPLGRTO ^S APLPQN 473	
		+ +G + P + HRPL RT ^S APLP N	
sHDAC4	423	---AQIG---IHPKPIRPVTHRPLV ^R TH ^S APLPNN 451	
		14-3-3 binding 2	
HDAC4	621	FGGHRPL ^S RAQ ^S SPASATFP-VSVQPEP-----TKPRFTTGLVYDTLMLKHQCCTCGSSSS	674
		FGGHRPL R +SSPA+A P +S+ TK FTTGL YDTLMLKHQC CG++ +	
sHDAC4	585	FGGHRPL ^M RV ^R SSPAAAGIPSLSLNHHHHDHNRKHTFTTGLAYDTLMLKHQCQCQGNQON	644
		14-3-3 binding 3	
HDAC4	675	HPEHAGRIQSIWSRLQETGLRGKCECIRGRKATLEELQTVHSEHTLLYGTNPLNRQKLD	734
		HPEH GR+QSIW+RL E G+ +CE IR RKA+LEELQ+ HSE +TL +GT+ ++ KLD	
sHDAC4	645	HPEHPGRLQSIWARLHERGIVSRCEIRTRKASLEELQSCHSEGYTLFFGTSQTHKAKLD	704
HDAC4	735	SKKLLGSLASVVFVRLPCGGVGVDSDTIWNNEVHSAGAARLAVGCVVELVFKVATGELKNGF	794
		S+KL F L CGG+GVD+DT+W+++ S GA R+A G V+EL FKVATGELKNGF	
sHDAC4	705	SRKLALIPKLNFTWLSCGGLGVDTDVWHDIQSPGAVRIAAGAVIELAFKVATGELKNGF	764
HDAC4	795	AVVRPPGHHAESTPMGFICYFNSVAVAAKLLQQRLSVSKILIVDWDVHHGNGTQQAFYS	854
		A+VRPPGHHAES MGFC+FNS+A+AAK L+ +L ++KILI+DWDVHHGN TQ+ FY D	
sHDAC4	765	AIVRPPGHHAETSQAMGFCFFNSIAIAAKQLRLKLNKILIIDWDVHHGNSTQKIFYED	824
HDAC4	855	PSVLYMSLHRYDDGNFFPGSGAPDEVTGPGVGFNVNMAFTGGLDPPMGDAEYLAARFRTV	914
		P VLY+SLHR+D+GNFFPG+GAPDE G G G+G+NVN+AF GGL+PPMGDAEY+AAFR++	
sHDAC4	825	PHVLYISLHRHDNGNFFPGTAPDES ^G CGAGLGYNVNIAFHGGLNPPMGDAEYIAAFRSI	884
HDAC4	915	VMPIASEFAPDVVLVSSGFDAVEGHPTPLGGYNLSARCFGYLTKQLMGLAGGRIVLALEG	974
		V+PIA EF+PDVVLVSSGFDA GHP PLGGY ++ CF Y+T+++MGLA GR+VLALEG	
sHDAC4	885	VLPIAREFSPDVVLVSSGFDAANGHPNPLGGYKVT ^P ACFSYMRKVMGLANGRVVLALEG	944
HDAC4	975	G ^H DLTAICDASEACVSALLGNELDPLPEKVLQORPNANAVRSMEKVMIEHS 1025	
		G+DLTAICDASE C LLG++ PL E + PNANAV + + +EI S	
sHDAC4	945	G ^Y DLTAICDASEVCAQTLLGDDPSPLSEDAINGVPNANAVECLRRRTIEIQS 995	

N-terminal extension

Deacetylase domain

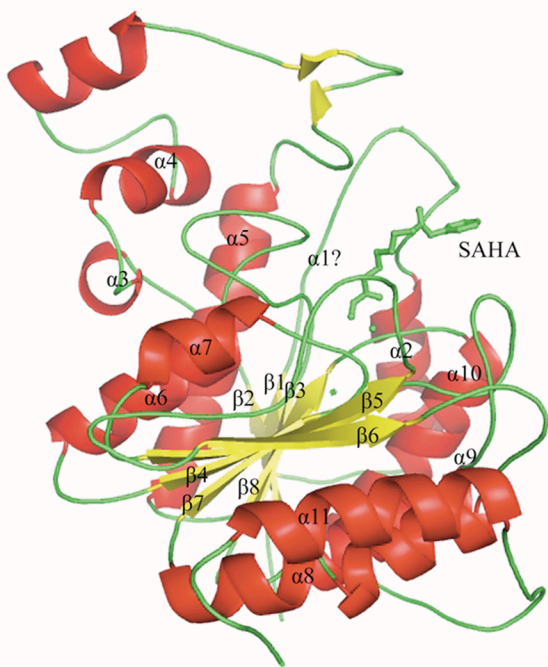
↑
Key tyrosine

Supplementary S2c (figure)

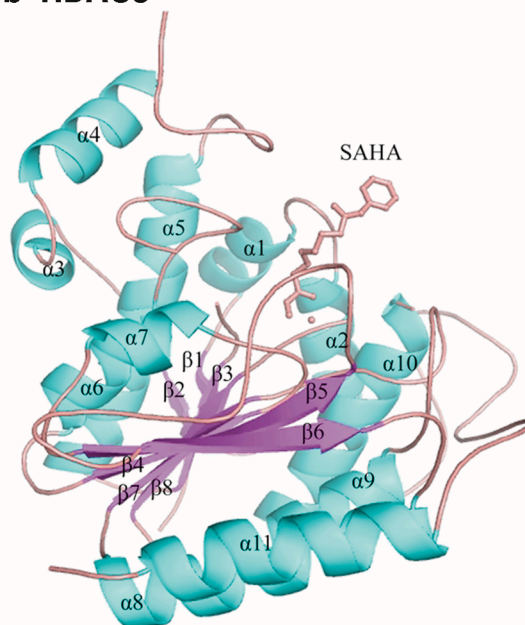
HDAC10	2	GTALVYHEDMTATRLLWDDPECEIERPERLTAALDRLRQRCLEQRCLRLSAREASEEELG	61	Deacetylase domain	
zHDAC10	4	G+AL++ E+M+ +LLW DP CEIE PERLT + + LR GL QRC + R+A+E+E+	63		
HDAC10	62	LVSPEYVSLVRETVLQVGLKEELQALSQGFDAIYFHPSTFHARLAAGAGLQLVDAVLTGA	121		
zHDAC10	64	L HS EY+ V++T + EEL A S +++ +YFH + +HCA+LAAGA LQLVD+V+	123		
HDAC10	122	VQNGLALVRPPGHGQRAAANGFCVFNVAIAAAHAKQKHGLHRILVVDVHGGQGIQY	181		
zHDAC10	124	V+NG+ALVRPPGHH QR+AAANGFCVFNVA AA +AK+ + L+RIL+VDVDVHGGQGIQY	183		
HDAC10	182	LFEDDPSVLYFSWHRYEHRFPFLRESADAVGRGQGLGFTVNLPNVQVGMGNADYVAA	241		
zHDAC10	184	FE+DPSVLYFSWHRYEH FWP L ESD +VG+G+G GF +NLPWN+VGM N+DY+AA	243		
HDAC10	242	FLHLLPLAFEDPELVLSAGFDSAIGDPEGQMQTPECF AHLTQLQLVLAGGRVCAVL	301		
zHDAC10	244	F H+LLP+A+EFDPPELV+VSAGFDSAIGDPEG+M A PE FAHLT LL LA G++C VL	303		
HDAC10	302	EGGYHLESLAESVCMTVQTLLGDPAPPLSGPMAPCSALESIQSARAAQAPHW---KSLQ	358		
zHDAC10	304	EGGY+L SL +SVC TV +LLGDP P +SG C SALESIQ+ R Q+ +W K L	363		
HDAC10	359	QQDVTAVPMSPSSHSPEGRPPPLPGGPVCKAAASAPSSLLDQPCPCPAPSVRTAVALTT	418		
zHDAC10	364	Q + P P + G P +A + +P SVRT V +	420		
HDAC10	419	PDITLVLPDVIQOEASALREETEAWARPHESLAREEALTALGKLLYLLDGMLDGQVNSG	478		C-terminal extension
zHDAC10	421	P + L LP + Q + + E T + + + ++	478		
HDAC10	479	IAATPASAAAATLDVAVRRGLSHG----AQRLLCVALGQLDRPPDLAHDGRSLWLNIRGK	534		
zHDAC10	479	+ L V+V+ L H A+R+L V +G + P +DG+ + I K	537		
HDAC10	535	EAAALSMFHVSTPL---PVMTGGFLSCILGLVLPLAYGFQPDVL-VALGPGHGLQGPHA	590		
zHDAC10	538	E + ++ L +T GF+ +LGL+LP+AY F P LVL + +	597		
HDAC10	591	ETEDKCVNRLTLCLREGESLTAGFMQALLGLILPVAYEFNPALVLGIVEETAAKTRLMRV	650		
zHDAC10	598	H box L + L + L + L+G + LGP PEDV+ +	657		
HDAC10	651	RGQLEPQWKMLQC 663			
zHDAC10	658	R +L+ +W +L+C RQRLQERWGLLRC 670			

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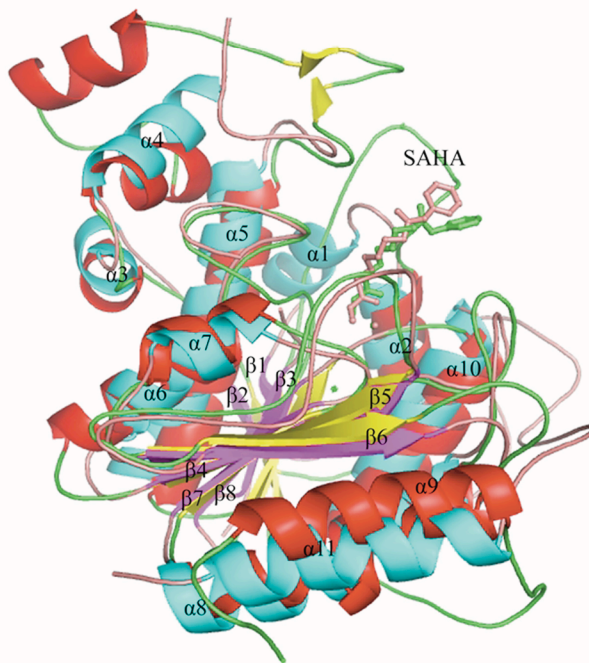
a HDAC7



b HDAC8



c Overlay



Supplementary S4 (table) Purification of class I/II HDAC complexes from yeast

<i>S. cerevisiae</i> Rpd3 complexes	Purification method	Conventional chromatography followed by tandem affinity with yeast cell extract expressing Rpd3- TAP or Sin3-TAP ^{1,2}	Conventional chromatography followed by tandem affinity with yeast cell extract expressing Rpd3- TAP or Sin3-TAP ²	Tandem affinity with yeast cell extract expressing Sin3-TAP, Rpd3- TAP, Ume1-TAP, Rco1-TAP, Eaf3- TAP, Rxt1-TAP, Pho23-TAP, or Sap30-TAP ³	Tandem affinity with yeast cell extract expressing Sin3- TAP, Rpd3-TAP, Ume1-TAP, Rco1- TAP, Eaf3-TAP, Rxt1-TAP, Pho23- TAP, or Sap30-TAP ³
	Proteins identified	Rpd3L: Rpd3, Sin3, Ume1, Pho23, Sap30, Sds3, Cti6, Rxt2, Rxt3, Dep1, Ume6, Ash1	Rpd3S: Rpd3, Sin3, Ume1, Rco1 , Eaf3	Rpd3C(L): Rpd3, Sin3, Ume1, Rxt1, Rxt2, Dep1, Sds3, Pho23 , Sap30	Rpd3C(S): Rpd3, Sin3, Ume1, Rco1 , Eaf3
<i>S. pombe</i> Clr6 complexes	Purification method	Anti-HA immunoaffinity with yeast cell extract expressing Clr6-HA or Pst1-HA followed by glycerol gradient ⁴	Anti-HA immunoaffinity with yeast cell extract expressing Clr6-HA or Pst1-HA followed by glycerol gradient ⁴		
	Proteins identified	Complex I: Pst1, Sds3, Clr6, Prw1 Complex I': Pst1, Sds3, Png2 , Clr6, Prw1	Complex II: Pst 2, Cph1 , Cph2 , Alp13, Clr6, Prw1		
<i>S. cerevisiae</i> Hda1 complex	Purification method	Conventional chromatography of yeast extract ⁵			
	Proteins identified	Hda1, Hda2, Hda3			
<i>S. pombe</i> Clr3 complex	Purification method	Anti-Flag immunoaffinity with yeast cell extract expressing Clr3- Flag ⁶			
	Proteins identified	Mit1 , Clr1, ccq1, Clr3, Clr2			
<i>S. cerevisiae</i> Hos2-Set3 complex	Purification method	Tandem affinity with yeast cell extract expressing Set3-TAP or Hos2- TAP ⁷			
	Proteins identified	Snt1, YIL112, Set3 , SIF2, Hos2, Hst1 , Cpr1,			

Note: The identified proteins in boldface denote subunits with domains (such as chromodomain and PHD finger) and enzymatic activities (such as ATPase, sirtuin and histone methyltransferase) for crosstalk with other chromatin-regulating processes.

References

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Supplementary S5 (table) Purification of class I HDAC complexes from *Xenopus* and mammals

HDAC1/2	Sin3 complex	Purification method	Anti-mSin3 immunoaffinity with HeLa nuclear extract ^{1,2}	Anti-HDAC1 immunoaffinity followed by anti-mSin3A with U937 nuclear extract ³	Anti-SAP30 immunoaffinity with HeLa nuclear extract ⁴	Anti-mSin3A immunoaffinity with K562 nuclear extract ⁵	Anti-ING1 or TAP-ING2 immunoaffinity with HeLa nuclear extract or anti-Flag with nuclear extract from H1299 cells expressing Flag-p33 ^{ING1b} (refs. 6, 7)	Anti-Flag immunoaffinity with nuclear extract from H1299 cells expressing Flag-p33 ^{ING1b} or Flag-p40 (ref. 8)
		Proteins identified	mSin3, HDAC1/2, RbAp46/48, SAP30, SAP18	mSin3A, p72, HDAC1/2, RbAp48, p45, p33	Sin3, HDAC1/2, RbAp46/48, (p33), ING1, SAP30	SAP180/RBP1, Sin3A, SAP130, HDAC1/2, RbAp46/48, SDS3, SAP38/ING1, SAP30, SAP28	RBP1, RBP1-like (SAP180), SAP130, Sin3A, HDAC1/2, RbAp46/48, p42/SDS3, BRMS1 ING1/p33 ^{ING1b} , SAP30	RBP1, Sin3A, HDAC1/2, RbAp46/48, p40, p33 ^{ING1b} , SAP30
	NuRD/Mi-2 complex	Purification method	Anti-Mi2 immunoaffinity or conventional chromatography with HeLa nuclear extract ^{9,10}	Conventional chromatography with <i>Xenopus</i> egg extract ^{11,12}	Anti-CHD4 immunoaffinity with SW13 nuclear extract ¹³	Anti-HDAC2 immunoprecipitation with HeLa cell extract ¹⁴	Tandem affinity with extract from HEK293 cells expressing MBD2-TAP or MBD3-TAP ¹⁵	Conventional chromatography with HeLa nuclear extract ¹⁶
		Proteins identified	Mi2, MTA2, HDAC1/2, RbAP46/48, MBD3	Mi2, MTA-1 like, p66, xRPD3, RbAP46/48, MBD3	CHD4/CHD3, N190, N170, N160, N140, N135, N130, N85, N75, N70, N68, N66, HDAC1/2, N61, RbAP46/48 N38, N34	Mi2, p110, p70, HDAC1/2, RbAp48	Mi2, MTA1/2/3, p66, HDAC1/2, RbAP46/48, MBD2/3	Mi2, MTA2, p66/68, HDAC1/2, RbAP46/48, MBD2/3
	CoREST complex	Purification method	Anti-CoREST immunoaffinity with HeLa cell extract ¹⁷	Anti-Flag immunoaffinity followed by glycerol density gradient sedimentation with nuclear extract from HeLa cells expressing Flag-HDAC1 (ref. 18)	Anti-Flag immunoaffinity with nuclear extract from HEK293 cells expressing Flag-BHC110 (refs 19, 20)	Conventional chromatography with HeLa nuclear extract or anti-Flag immunoaffinity with nuclear extract from 293 cells expressing Flag-BRAF35 (ref. 21)	Anti-Flag/anti-HA immunoaffinity followed by glycerol density gradient sedimentation with nuclear extract from HeLa cells expressing Flag-HA-CtBP ²²	

		Proteins identified	p110b, Znf217, p80, CoREST, HDAC1/2, Sox-like	KIAA0601, CoREST, HDAC1, p37	X-FIM, FIM, ZnF516, KIAA0182, ZnF217, BHC110, BHC80, CoREST, HDAC1/2, CtBP, BRAF35	BHC110, BHC80, CoREST, HDAC1/2, BRAF35	CtBP1, CtBP2, EuHMT, G9a, ZEB1, HDAC1/2, LSD1 (NPAO/KIAA0601), CoREST	
HDAC3	N-CoR/SMRT complex	Purification method	Anti-HDAC3 immunoaffinity with HeLa cell extract ²³⁻²⁵	Anti-Flag immunoaffinity with nuclear extract from HeLa cells expressing Flag-HDAC3 (ref. 26)	Anti-SMRT immunoaffinity with HeLa nuclear extract or anti-Flag with nuclear extract from 293T cells expressing Flag-HDAC3 (refs. 27, 28)	Anti-N-CoR immunoaffinity with HeLa nuclear extract ^{25, 29, 30}		
		Proteins identified	N-CoR/SMRT, TFII-I, PP4 _{R1} , TBL1/TBLR1, HDAC3, GPS2, PP4 _C	N-CoR/SMRT, TBL1/TBLR1, HDAC3, GPS2	N-CoR/SMRT, AKAP95, HA95, TBL1, HDAC3, GPS2	N-CoR, TIF1 β , JMJD2A (KIAA0677), HsEg5, Kaiso, hsp70, IR10, TBL1/TBLR1, HDAC3, GPS2		

Note: In sub-stoichiometric amounts, HDAC1 and HDAC2 are also known to be present in many other complexes, e.g. SWI/SNF complexes^{31, 32}, PRP4 kinase complex³³, and the SMCx demethylase complex important for X-linked mental retardation³⁴. For clarity and simplicity, association of HDACs with numerous transcription factors is not listed and discussed here.

References

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Supplementary S6 (table) Roles of classical HDACs and associated subunits in worm and fly development

Mammal		<i>C. elegans</i>		<i>Drosophila</i>		
Deacetylase	Associated subunit	Protein name	Developmental role	Protein name	Developmental role	
HDAC1		Hda-1	One-fold stage ¹ Vuval development ³ Gonogenesis ⁵ Cell migration ^{7,8} Axon pathfinding ⁸	dRpd3/dHDAC1	Segmentation defects ² G2-M cell cycle progression ⁴ Essential for S2 cell viability ⁶ Euchromatic transcriptional repression ^{4,9} Activating SMRTER expression ^{4,9} Homeotic gene expression ¹⁰ and longevity ¹¹	
	RbAp46/48 RbAp46/48 Sin3	Rba-1 Rba-2/Lin-53 Sin-3	One-fold stage arrest ¹ Vulval development ^{3,12} Male sensory ray patterning ¹³	p55 p55 dSin3	Embryonic viability ¹⁴ Cell cycle progression ⁴ Activating SMRTER expression ⁴ Euchromatic transcriptional repression ^{4,9}	
	SAP18 Mi2	Let-48/Mi-2	Vulval development ^{3,15} Spatiotemporal cell differentiation ¹⁷	dSAP18 dMi2	Homeotic gene expression ¹⁰ Hox expression, larval and germ viability ¹⁶ Proneural gene expression ¹⁸	
	p66 MTA1 MTA1	? Egl-1/Lin-40 Egl-27	Vulval development ^{3,20} Vulval development ^{3,20} Cell polarity and migration ²¹ Hox gene expression ²²	dp66	Wnt signaling ¹⁹	
	CoREST	Spr-1	Inhibition of Notch signaling ²³ Vulval morphogenesis ²⁴ Gonal development ²⁴			
	LSD1	Spr-5	Presenilin expression ^{23,25}	Su(VAR)3-3	Position-effect variegation modifier ^{26,27} Initiation of heterochromatin formation ²⁶ Non-essential but important for viability ²⁷ Sterility control and ovary development ²⁷	
	HDAC3	N-CoR/SMRT	Hda-3	PolyQ toxicity ²⁸	dHDAC3 SMRTER	Non-essential for S2 cell viability ⁶ Non-essential for S2 cell viability ⁶
	HDAC4		Hda-4/-7	Non-essential ²⁹ Chemoreceptor signaling ³⁰	dHDAC4	Non-essential for S2 cell viability ⁶ Embryo segmentation ³¹
	HDAC6 HDAC11		Hda-6 Hda-8	? ?	dHDAC6 dHDACX	Non-essential for S2 cell viability ⁶ Non-essential for S2 cell viability ⁶

Note: Those subject to gene inactivation analysis are listed here. Some of the deacetylases have also been analyzed in zebrafish. For example, the HDAC1 ortholog has been shown to play a role in neurogenesis^{32,33}, oligodendrocyte differentiation³⁴, neuron migration³⁵, as well as formation of craniofacial cartilage and petoral fin³⁶.

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