Table I: post-translational modifications of HATs

Enzyme	Modif[1]	Modifying enzyme	Molecular role of the modification	Signalling pathway	References
CBP	Phospho	Cyclin E/cdk2	Stimulation of HAT activity	Progression towards S phase	(Ait-Si-Ali et al., 1998)
CBP	Phospho	Non classical PKC	Recruitment to transcription factors	Growth factors	(Zanger et al., 2001)
CBP	Phospho	CaMKIV	Transcriptional activation	Neuronal activity	(Impey et al., 2002)
CBP	Phospho	Map kinases	Stimulation of HAT activity	neuronal differentiation	(Ait-Si-Ali et al., 1999 ; Janknecht and Nordheim, 1996 ; Liu et al., 1999)
CBP	Met	CARM1	Inhibition of CREB binding	Various pathways	(Xu et al., 2001)
			Transcriptional activation	Estrogen response	(Chevillard-Briet et al., 2002)
p300	Phospho	AMP kinase	Inhibition of nuclear receptor binding	?	(Yang et al., 2001)
p300	Phospho	PKCδ	Inhibition of HAT activity	Growth Suppression?	(Yuan and Gambee, 2000; Yuan et al., 2002)
p300	Phospho	?	Transcriptional activation	Various pathways	(Schwartz et al., 2003)
p300	Sumo-1	Ubc9	Transcriptional repression	?	(Girdwood et al., 2003)
P/CAF	Ac	P/CAF	Stabilization of the enzyme ?	?	(Herrera et al., 1997)
GCN5	phospho	DNA-PK	Decreased HAT activity	Response to double-strand breaks ?	(Barlev et al., 1998)
ACTR	Ac	p300	Reduced nuclear receptor binding	Hormone response	(Chen et al., 1999)
ATF-2	phospho	P38, JNK	Stimulation of HAT activity	Response to UV irradiation	(Kawasaki et al., 2000)
Tip60	Phospho	?	Stimulation of HAT activity	Cell cycle control ?	(Lemercier et al., 2003)
Tip60	Ubiq	Mdm2	Degradation	Response to UV irradiation	(Legube et al., 2002)

[1]Modifications : Phosphorylation (phospho), Acetylation (Ac), Methylation (Met) , Ubiquitylation (Ubiq).

References

Ait-Si-Ali, S., Carlisi, D., Ramirez, S., Upegui-Gonzalez, L.C., Duquet, A., Robin, P., Rudkin, B., Harel-Bellan, A. and Trouche, D. (1999) Phosphorylation by p44 MAP Kinase/ERK1 stimulates CBP histone acetyl transferase activity in vitro. *Biochem Biophys Res Commun*, **262**, 157-62.

Ait-Si-Ali, S., Ramirez, S., Barre, F.X., Dkhissi, F., Magnaghi-Jaulin, L., Girault, J.A., Robin, P., Knibiehler, M., Pritchard, L.L., Ducommun, B., Trouche, D. and Harel-Bellan, A. (1998) Histone acetyltransferase activity of CBP is controlled by cycle-dependent kinases and oncoprotein E1A. *Nature*, **396**, 184-6.

Barlev, N.A., Poltoratsky, V., Owen-Hughes, T., Ying, C., Liu, L., Workman, J.L. and Berger, S.L. (1998) Repression of GCN5 histone acetyltransferase activity via bromodomain- mediated binding and phosphorylation by the Ku-DNA-dependent protein kinase complex. *Mol Cell Biol*, **18**, 1349-58.

Chen, H., Lin, R.J., Xie, W., Wilpitz, D. and Evans, R.M. (1999) Regulation of hormone-induced histone hyperacetylation and gene activation via acetylation of an acetylase. *Cell*, **98**, 675-86.

Chevillard-Briet, M., Trouche, D. and Vandel, L. (2002) Control of CBP co-activating activity by arginine methylation. *Embo J*, **21**, 5457-66.

Girdwood, D., Bumpass, D., Vaughan, O.A., Thain, A., Anderson, L.A., Snowden, A.W., Garcia-Wilson, E., Perkins, N.D. and Hay, R.T. (2003) p300 Transcriptional Repression Is Mediated by SUMO Modification. *Mol. Cell*, **11**, 1043-1054.

Herrera, J.E., Bergel, M., Yang, X.J., Nakatani, Y. and Bustin, M. (1997) The histone acetyltransferase activity of human GCN5 and PCAF is stabilized by coenzymes. *J Biol Chem*, **272**, 27253-8.

Impey, S., Fong, A.L., Wang, Y., Cardinaux, J.R., Fass, D.M., Obrietan, K., Wayman, G.A., Storm, D.R., Soderling, T.R. and Goodman, R.H. (2002) Phosphorylation of CBP mediates transcriptional activation by neural activity and CaM kinase IV. *Neuron*, **34**, 235-44.

Janknecht, R. and Nordheim, A. (1996) MAP kinase-dependent transcriptional coactivation by Elk-1 and its cofactor CBP. *Biochem. Biophys. Res. Commun.*, **228**, 831-837.

Kawasaki, H., Schiltz, L., Chiu, R., Itakura, K., Taira, K., Nakatani, Y. and Yokoyama, K.K. (2000) ATF-2 has intrinsic histone acetyltransferase activity which is modulated by phosphorylation. *Nature*, **405**, 195-200.

Legube, G., Linares, L.K., Lemercier, C., Scheffner, M., Khochbin, S. and Trouche, D. (2002) Tip60 is targeted to proteasome-mediated degradation by Mdm2 and accumulates after UV irradiation. *Embo J*, **21**, 1704-1712.

Lemercier, C., Legube, G., Caron, C., Louwagie, M., Garin, J., Trouche, D. and Khochbin, S. (2003) Tip60 acetyltransferase activity is controlled by phosphorylation. *J Biol Chem*, **278**, 4713-8.

Liu, Y.Z., Thomas, N.S. and Latchman, D.S. (1999) CBP associates with the p42/p44 MAPK enzymes and is phosphorylated following NGF treatment. *Neuroreport*, **10**, 1239-43.

Schwartz, C., Beck, K., Mink, S., Schmolke, M., Budde, B., Wenning, D. and Klempnauer, K.H. (2003) Recruitment of p300 by C/EBPbeta triggers phosphorylation of p300 and modulates coactivator activity. *Embo J*, **22**, 882-92.

Xu, W., Chen, H., Du, K., Asahara, H., Tini, M., Emerson, B.M., Montminy, M. and Evans, R.M. (2001) A transcriptional switch mediated by cofactor methylation. *Science*, **294**, 2507-11.

Yang, W., Hong, Y.H., Shen, X.Q., Frankowski, C., Camp, H.S. and Leff, T. (2001) Regulation of transcription by AMP-activated protein kinase: phosphorylation of p300 blocks its interaction with nuclear receptors. *J Biol Chem*, **276**, 38341-4.

Yuan, L.W. and Gambee, J.E. (2000) Phosphorylation of p300 at serine 89 by protein kinase C. *J Biol Chem*, **275**, 40946-51.

Yuan, L.W., Soh, J.W. and Weinstein, I.B. (2002) Inhibition of histone acetyltransferase function of p300 by PKCdelta. *Biochim Biophys Acta*, **1592**, 205-11.

Zanger, K., Radovick, S. and Wondisford, F.E. (2001) CREB binding protein recruitment to the transcription complex requires growth factor-dependent phosphorylation of its GF box. *Mol Cell*, **7**, 551-8.

Table II: post-translational modifications of HDACs

Enzyme	**Modif**[1]	**Modifying enzyme**	**Molecular role of the modification**	**Signalling pathway**	**References**
Class II HDACs	Phospho	CaMkinases other	Nuclear export – Interaction with 14-3-3 proteins	Induction of muscle differentiation	See (McKinsey et al., 2001) and references therein
HDAC1/2	Phospho	CK2	Stimulation of HDAC activity	Cell cycle and apoptosis	(Pflum et al., 2001; Sun et al., 2002; Tsai and Seto, 2002)
HDAC1	Sumo-1	?	Increased transcriptional repression ?	?	(Colombo et al., 2002; David et al., 2002)
HDAC4	Sumo-1	RanBP2	Stimulation of HDAC activity	Control of muscle differentiation	(Kirsh et al., 2002)

[1]Modifications : Phosphorylation (phospho), Sumoylation by Sumo-1 (Sumo-1)

References

Colombo, R., Boggio, R., Seiser, C., Draetta, G.F. and Chiocca, S. (2002) The adenovirus protein Gam1 interferes with sumoylation of histone deacetylase 1. *EMBO Rep*, 3, 1062-8.

David, G., Neptune, M.A. and DePinho, R.A. (2002) SUMO-1 modification of histone deacetylase 1 (HDAC1) modulates its biological activities. *J Biol Chem*, 277, 23658-63.

Kirsh, O., Seeler, J.S., Pichler, A., Gast, A., Muller, S., Miska, E., Mathieu, M., Harel-Bellan, A., Kouzarides, T., Melchior, F. and Dejean, A. (2002) The SUMO E3 ligase RanBP2 promotes modification of the HDAC4 deacetylase. *Embo J*, 21, 2682-91.

McKinsey, T.A., Zhang, C.L. and Olson, E.N. (2001) Control of muscle development by dueling HATs and HDACs. *Curr Opin Genet Dev*, 11, 497-504.

Pflum, M.K., Tong, J.K., Lane, W.S. and Schreiber, S.L. (2001) Histone deacetylase 1 phosphorylation promotes enzymatic activity and complex formation. *J Biol Chem*, 276, 47733-41.

Sun, J.M., Chen, H.Y., Moniwa, M., Litchfield, D.W., Seto, E. and Davie, J.R. (2002) The transcriptional repressor Sp3 is associated with CK2-phosphorylated histone deacetylase 2. *J Biol Chem*, 277, 35783-6.

Tsai, S.C. and Seto, E. (2002) Regulation of histone deacetylase 2 by protein kinase CK2. *J Biol Chem*, 277, 31826-33.