Histone acetylation and deacetylation play essential roles in modifying chromatin structure and regulating gene expression in eukaryotes. Histone deacetylases (HDACs) catalyze the deacetylation of lysine residues in the histone N-terminal tails and are found in large multi-protein complexes with transcriptional co-repressors. Human HDACs are grouped into three classes based on their similarity to known yeast factors: class I HDACs are similar to the yeast transcriptional repressor yRPD3, class II HDACs to yHDA1 and class III HDACs to ySIR2. In this review, we focus on the biology of class II HDACs. These newly discovered enzymes have been implicated as global regulators of gene expression during cell differentiation and development. We discuss their emerging biological functions and the molecular mechanisms by which they are regulated.

The DNA of eukaryotic cells in chromatin is tightly wrapped around octamers of histone proteins, restricting its accessibility to factors involved in DNA replication and transcription. Local or extended structural changes in chromatin play an important role in the control of gene expression and are governed by complexes that remodel chromatin and by enzymes that posttranslationally modify histones (reviewed in Ref. [1]).

All core histone proteins are reversibly and dynamically acetylated at multiple sites in their N-terminal tails. Hyperacetylated histones are generally found in transcriptionally active genes and hypoacetylated histones in transcriptionally silent regions, such as heterochromatin. The level of histone acetylation at a particular locus in chromatin reflects the competing activities of histone acetyltransferases and histone deacetylases (HDACs). The identification and characterization of numerous transcriptional regulators possessing histone acetyltransferase or HDAC activities has validated the prediction that histone acetylation plays a critical role in transcriptional regulatory mechanisms (for general reviews see Ref. [2]).

Eighteen distinct human HDACs are grouped into three classes based on their primary homology to three *Saccharomyces cerevisiae* HDACs. Class I HDACs (HDAC1, -2, -3, -8 and -11) are homologous to yRPD3, share a compact structure, and are predominantly nuclear proteins expressed in most tissues and cell lines (Fig. 1a) (reviewed in Ref. [3]). Class II HDACs, the subject of this review, are homologous to yHDA1 and are subdivided into two subclasses, Iia (HDAC4, -5, -7 and -9 and its splice variant MITR) and Iib (HDAC6 and HDAC10), based on sequence homology and domain organization (Fig. 1a,b) [4–12]. Whereas class I and II HDACs and their...
The class IIa HDACs: HDAC4, -5, -7 and -9

HDAC4, -5, -7 and -9 contain a highly conserved C-terminal catalytic domain (~420 amino acids) homologous to yHDA1 and an N-terminal domain with no similarity to other proteins (Fig. 1b) [4–7,13]. MITR, a splice variant of HDAC9, consists of only its N-terminus without an HDAC domain. The activity of the class IIa HDACs is regulated at several levels, including tissue-specific gene expression, recruitment of distinct cofactors and nucleocytoplasmic shuttling.

Tissue-specific expression

Whereas most class I HDACs are ubiquitously expressed, the class IIa HDACs are expressed in a restricted number of cell types. Three of the class IIa HDACs, HDAC4, -5 and -9, show highest expression in heart, skeletal muscle and brain, where their biological activities might be partially redundant [4,5,7,13–15]. In contrast to initial reports describing highest HDAC7 expression in heart and lung tissues [16,17], we have recently observed that HDAC7 is most highly expressed in CD4/CD8 double-negative thymocytes (F. Dequiedt et al., unpublished).

Interaction partners

HDACs represent the catalytic components of large multi-protein complexes. They do not bind directly to DNA and are thought to be recruited to specific promoters through their interaction with DNA sequence-specific transcription factors (Fig. 2). The MEF2 family of transcription factors is one of the major targets of class IIa HDACs and will be discussed in detail below (see section on the biological role of HDACs). Other interactions occur with CtBP (E1A C-terminal binding protein), 14-3-3 proteins, calmodulin (CaM), transcriptional co-repressors, heterochromatin protein HP1α and SUMO.

CTBP1 was originally identified as an adenovirus E1A interacting protein and later found to interact with several Drosophila DNA-binding proteins, including Hairy, Snail, Krüppel and mammalian basic Krüppel-like factor 3 (BKLF/KLF3) (reviewed in Ref. [18]). CTBP associates with each of these proteins, as well as with HDAC4 and -5 and MITR, through a PXDLS motif, and acts as a transcriptional repressor [19]. However, since CTBP can still repress transcription in the absence of HDAC activity, the precise mechanism of CTBP-mediated transcriptional repression remains unclear [18].

The class IIa HDACs all interact with 14-3-3 proteins [20–24]. This interaction plays a critical role in the nucleocytoplasmic shuttling of class II HDACs (see section on dynamic subcellular localization for an in depth discussion of the role of 14-3-3 proteins).

The MEF2-binding domain of HDAC4 shares some features with known CaM-binding domains [25]. HDAC4 binds to CaM in vitro, and binding of CaM disrupts the MEF2–HDAC4 interaction. This mechanism could contribute to the Ca2+-dependent activation of MEF2 [26]; however, the significance of these observations for the biology of class IIa HDACs remains to be assessed.

Class II HDACs interact with two closely related co-repressors, SMRT (silencing mediator for retinoid and thyroid receptors) and N-CoR (nuclear receptor co-repressor). This interaction is critical for the enzymatic activity of class IIa HDACs and is discussed separately below. In addition, the N-terminal BTB/POZ domain of BCL6, a sequence-specific transcriptional repressor with Krüppel-like zinc-finger motifs that is involved in the pathogenesis of non-Hodgkin’s B-cell lymphomas [27,28], can bind either to SMRT, leading to the recruitment of the SMRT/N-CoR co-repressor complex [29–31], or to B-CoR, another co-repressor protein [32]. Therefore, class IIa HDACs might modulate the transcriptional repression of BCL6 and participate in its role in B-cell activation and differentiation, inflammation, and cell-cycle regulation [33]. BCL6 also interacts directly with a conserved region in the N-terminal domain of class IIa HDACs [34] (Fig. 2).
Thus, class IIa HDACs can be recruited to Bcl-6-regulated promoters by two mechanisms: direct interaction with BCL6 or indirect recruitment through co-repressors such as SMRT/N-CoR and B-CoR. It is not clear why B-CoR and BCL6 interact with such a disparate array of class I and class II HDACs. Further experiments are needed to assess the biological relevance of these observations.

HDAC4 and -5 and MTRT interact with HP1α. The interaction is mediated by an N-terminal domain that is distinct from other interacting sites on class II HDACs (Fig. 2). HP1 contains a chromodomain involved in the specific recognition of methylated lysine 9 of histone. HP1 also interacts with the histone methyltransferase SUV39H1. Since histone H3 must be deacetylated before it can be methylated, these observations suggest that the class II HDAC–HP1 interaction could be important in the establishment and maintenance of heterochromatin [35].

Finally, HDAC4, MITR and HDAC6 associate with and become modified by SUMO-1, a ubiquitin-like protein [36,37]. The biological significance of this modification has not been established.

Dynamic subcellular localization

All class IIa HDACs shuttle between the nucleus and the cytoplasm [6,20,21,23,26,38–40]. Class IIa HDACs bind to 14-3-3 proteins, a family of highly conserved acidic proteins (reviewed in Ref. [41]). This binding is dependent on the phosphorylation of two or three conserved N-terminal serine residues in class IIA HDACs and mediates their cytoplasmic sequestration (Fig. 1b) [20,21,23]; mutation of these sites prevents the export of class IIa HDACs from the nucleus to the cytoplasm [20–24,44] . Recent experiments in cardiomyocytes indicate that an unidentified HDAC kinase targets the same phosphorylation sites in class IIa HDACs in response to hypertrophic signals [45].

It is thought that 14-3-3 proteins modify the subcellular localization of targets by interfering with nuclear import and export signals. A nuclear import signal containing an arginine/lysine-rich motif has been mapped in HDAC4 (amino acids 251–272) and -5 (amino acids 264–285) [26,46], and appears to be conserved in HDAC7 and MITR/HDAC9. Phosphorylation-dependent binding of 14-3-3 proteins to the N-termini of class II HDACs masks the nuclear import signal and prevents nuclear import. A CRM1-dependent nuclear export signal has been mapped in HDAC4 (amino acids 1056–1069) and HDAC5 (amino acids 1086–1099) [44,46]. This nuclear signal becomes active upon binding of 14-3-3 proteins to the N-terminus of class II HDACs. These observations suggest that phosphorylation of the N-terminus of class IIA HDACs and/or recruitment of 14-3-3 proteins induces a long-distance conformational change that unmasks a latent nuclear export signal in their C-terminus.

The nucleocytoplasmic shuttling of class II HDACs regulates their activities as transcriptional repressor proteins. Overexpression of constitutively active CaMKs or signal-dependent activation of CaMKs induces the relocalization of class IIA HDACs to the cytoplasm and suppresses their repressive activity [22,47]. By contrast, mutation of the phosphorylation sites of class IIA HDACs abolishes their cytoplasmic export and enhances their repressive effects during muscle differentiation and T-cell apoptosis [40,43]. Cytoplasmic relocalization of class II HDACs removes these enzymes from their substrates – the histone proteins in chromatin – and dissociates them from the SMRT/N-CoR–HDAC3 complex, leading to their enzymatic inactivation, as discussed in the next section [16,48].

Regulation of HDAC catalytic activity

Class IIA HDACs interact directly with SMRT and N-CoR through their C-terminal HDAC domains [17,49,50]. Both SMRT and N-CoR interact with unbound nuclear receptors and with a growing list of other transcription factors (reviewed in Ref. [51]). In addition, both SMRT and N-CoR participate in the formation of a stable multiprotein complex consisting of HDAC3, transducin (β)-like 1 (TBL1) [52,53] and GPS2, a protein involved in intracellular signaling [54]. A recent proteomic analysis of the components of the S. cerevisiae SET3 complex showed the presence of two HDACs, Hos2 and Hst1 [55]. Hst1 is related to the yeast Hdai deacetylase, while Hst1 is a Sir2-like protein with NAD-dependent deacetylase activity. The SET3 complex also contains a WD40 protein with homology to TBL1, suggesting that this complex is a yeast ortholog of the SMRT/NCoR complex. It is not clear at this point why multiple HDACs from different classes are assembled in a single multiprotein complex. Distinct enzymes might confer unique substrate specificities to the complex. The dependency of class III enzymes on NAD+ could also link the activity of the complex to the metabolic status of the cell. A similar combination of class II and class III enzymes in a multiprotein complex was recently observed for HDAC6 and SIRT2, a human class III HDAC [56].

SMRT and N-CoR interact both with class IIA HDACs and with HDAC3 through distinct domains [52,53,57,58], an observation that explains why class IIA HDACs communoprecipitate with HDAC3 [5,16,48]. Class IIA HDACs are enzymatically inactive alone as purified recombinant proteins. However, they are associated with enzymatic activity when bound to the SMRT/N-CoR–HDAC3 complex [16,48]. HDAC3 is also catalytically inactive alone as purified protein but becomes enzymatically active when bound to SMRT/N-CoR, even in the absence of a class IIA HDAC [48,58]. By contrast, class IIA HDACs alone are still enzymatically inactive after binding to the SMRT/N-CoR proteins in vitro.

This evidence is compatible with two models. First, class IIA HDACs might not be functional HDACs in the context of the SMRT/N-CoR complex but might serve to recruit pre-existing, enzymatically active SMRT/N-CoR complexes that contain HDAC3. In this model, the SMRT/N-CoR co-repressors provide a structural link between active HDAC3 and inactive class IIA HDACs. In
a second model, class II HDACs might become activated only in the presence of HDAC3. There is extensive evidence for HDAC–HDAC interactions: the solved structure of Rpd3 shows a dimer, HDAC1 and -2 are found in the same multiprotein complex, and HDAC6 contains two tandemly arranged HDAC domains. These interactions might indicate that HDAC–HDAC interactions are important for the regulation of HDAC activity.

Interestingly, we have noted that several mutations in amino acids that form the catalytic pocket of class IIA HDACs also result in a loss of interaction with SMRT/N-CoR. These observations suggest the existence of interactions between amino acids in the catalytic center of class IIA HDACs and the surface of these proteins. Such interactions could regulate the enzymatic activity of the enzyme as a function of its interactions with other proteins and could ensure that the HDACs only become enzymatically active after incorporation in the appropriate multiprotein complex.

**Biological roles of class IIA HDACs**

The many interactions between class IIA HDACs and transcriptional regulators suggest a wide variety of potential biological roles. However, most of these interactions have not been examined in a biological context. By contrast, the importance of interactions between MEF2 and class IIA HDACs has been demonstrated in several tissue culture and animal models. MEF2 plays a significant transcriptional regulatory role in myogenesis, in negative selection of developing thymocytes, and in the transcriptional regulation of Epstein–Barr virus (EBV) (for a complete review see Ref. [59]). The striking similarity of MEF2 regulation in neurons and its role in neuronal resistance to excitotoxicity suggests that class IIA HDACs also play a significant role in neurons [60–62].

Class IIA HDACs inhibit myogenesis by binding to MEF2 at several promoters critical for the muscle differentiation program (for recent reviews see Refs [63,64]). HDAC4, -5, -7 and -9 interact with MEF2 proteins through a highly conserved 17 amino acid motif located in their N-termini [7,23,38,65,66]. Expression of an HDAC–VP16 fusion protein, in which the VP16 activation domain replaces the catalytic domain of HDAC4 or -5, enhances myogenic conversion [47]. Activation of the CaMK signaling pathway also overcomes the HDAC-mediated repression of muscle-specific gene expression and induces the myogenic conversion program [22,64]. Further evidence for the role of class IIA HDACs in cardiac and skeletal myogenesis comes from the phenotype of HDAC9-deficient animals. A phosphorylation mutant of HDAC9 in the CaMK IV sites inhibits the myogenic program [45]. In cardiomyocytes, phosphorylation mutants of HDAC5 or MTRR block the induction of hypertrophy-associated genes in response to phenylephrine [45]. These observations suggest that class IIA HDACs are master regulators of myocyte development. Bound to MEF2 proteins in the promoters of multiple genes, they play a critical role in repressing these genes until the appropriate myogenic differentiation signal is delivered.

In the thymus, developing CD4/CD8 double-positive T cells that receive a strong signal from major histocompatibility complex (MHC)–self-peptide through their antigen receptors are deleted by an apoptotic process termed negative selection. The apoptotic process is activated by the expression of Nur77, an orphan steroid receptor [67–69]. Constitutive expression of Nur77 in thymocytes results in a dramatic involution of the thymus, whereas expression of a dominant-negative Nur77 interferes with negative selection [70,71]. The expression of Nur77 in response to antigen receptor signals is tightly controlled through two MEF2-binding sites in the Nur77 promoter (Fig. 3) [72]. As in other systems, MEF2-dependent transcription in T cells is activated by Ca$^{2+}$ signals and by ectopic expression of activated CaMK IV, calcineurin, or ERK5/BMK1 [73–75].

A MEF2-family protein, MEF2-D, is expressed in thymocytes and associates with both HDAC4 and Cabin-1 under basal conditions in T-cell lines (Fig. 3) [25,74,76,77]. Activation of T-cell receptors disrupts the interaction of MEF2-D with HDAC4 and Cabin-1, most probably through a Ca$^{2+}$ signal and CaM activation. HDAC7 is highly expressed in CD4/CD8 double-positive thymocytes, which undergo positive or negative selection (Fig. 3) (F. Dequiedt et al., unpublished). HDAC7 also associates with MEF2-D in CD4/CD8 double-positive T cells, becomes dissociated from MEF2-D during T-cell activation and shuttles out of the nucleus. The nuclear export of HDAC7 in thymocytes is dependent on three serine residues in the N-terminus of the protein, as described above for other class IIA HDACs. HDAC7 overexpression suppresses Nur77 induction and thymocyte apoptosis in response to activation of T-cell receptors. Conversely, expression of an HDAC7–VP16 fusion activates Nur77 expression in the absence of such activation, and knockdown of HDAC7 through RNA interference leads to increased apoptosis in response to T-cell receptor activation. These findings, combined with the recent finding that deletion of the MEF2-interacting domain of Cabin-1 results in no detectable phenotype with respect to thymic negative selection [78], suggest that HDAC7 plays a critical role in the repression of Nur77 during thymic maturation of T cells. Studies are currently under way to validate these observations in transgenic and knockout mice.

EBV is a human herpesvirus capable of latently infecting B cells. The latent virus can be reactivated by cross-linking of the B-cell antigen receptor [79,80]. Reactivation of latent EBV proceeds through three MEF2-binding sites in the promoter for the immediate-early gene BZLF1, which encodes the transcriptional activator ZEBRA. MEF2-dependent transcription of BZLF1 is activated by Ca$^{2+}$ flux; a similar mechanism governs transcription of the Nur77 promoter in T cells [81]. In a B-cell line carrying latent EBV, transfection of HDAC4– or HDAC5–VP16 fusions reactivates viral expression [82]. These results indicate that EBV latency, like myogenesis and Nur77 expression, is regulated by a Ca$^{2+}$-dependent MEF2 switch in which class IIA HDACs mediate basal repression.
The class IIb HDACs: HDAC6 and HDAC10

Class IIb HDACs are characterized by duplicated HDAC domains, although this duplication is partial in the case of HDAC10 (Fig. 1b). Class IIb HDACs also show some degree of tissue-specific gene expression: HDAC6 is predominantly expressed in testis [13,83], and HDAC10 is expressed in liver, spleen and kidney [8,10,12]. Different splice variants are observed for HDAC10, as shown for HDAC6 in the thymus [13,83], and HDAC10 is dominantly expressed in testis [13,83], and HDAC10 is primarily cytoplasmic but shows significant nuclear staining in several cell lines [8–10,12]. The subcellular localization of HDAC6 is dependent on a strong nuclear export signal (NES1) in the N-terminus of the protein [85]. Several putative export sequences were identified in HDAC10 [8,12], but it is not known whether they function as true export signals.

HDAC6 is part of a multiprotein complex that includes two mammalian orthologs of yeast proteins involved in the control of protein ubiquitination: p97/VCP, a mammalian homolog of yeast Cdc48p, and phospholipase A2 activating protein, a homolog of yeast UFD3 (ubiquitin fusion degradation protein 3) (Fig. 4) [83]. HDAC6 contains a C-terminal zinc finger that shows significant homology to a zinc finger located in several ubiquitin-specific proteases (ZnF-UBP) [83] (Fig. 4). The ZnF-UBP motif (also identified as a polyubiquitin-associated zinc finger or PAZ domain) [86] mediates the binding of ubiquitin to HDAC6 [83,86]. The specific interaction of proteins involved in protein ubiquitination and the fact that both acetylation and ubiquitination target lysine residues suggest that HDAC6 could participate in the deacetylation of proteins before their ubiquitination.

Cytoplasmic HDAC6 shows striking co-localization with the microtubule network [87,88]. Acetylation of α-tubulin, at lysine 40, has been used as a marker of microtubule stability [89]. HDAC6 functions as a specific tubulin deacetylase in vivo, and purified HDAC6 deacetylates α-tubulin in assembled microtubules in vitro [87,88]. HDAC6 overexpression promotes chemotactic cell movement, a cellular function dependent on microtubules. We have independently observed that SIRT2, a NAD⁺-dependent class III HDAC, deacetylates lysine 40 of α-tubulin.
α-tubulin both in vitro and in vivo [56]. Both HDAC6 and SIRT2 interact and co-localize in the cytoplasm with the microtubule network (Fig. 4) [56]. Suppression of either HDAC6 or SIRT2 mediated by siRNA leads to a relative hyperacetylation of α-tubulin acetylation in vitro [56,87,88]. The identification of specific enzymes mediating tubulin deacetylation should allow further work to proceed on the role of this modification in microtubule dynamics and functions.

Future questions

The purification, cloning and characterization of class II HDACs have provided important insights into how chromatin controls transcription and have revealed unexpected biological functions for acetylation. The past two years have seen the elucidation of discrete biological pathways in which class II HDACs play crucial regulatory roles. Whereas class IIa HDACs are frequently considered functionally redundant, it is likely that further study will reveal discrete biological functions specific for each family member and its splice variants. Future studies should focus on determining the relative contribution of each HDAC in distinct cell types. By virtue of their ability to interact with distinct transcription factors that each bind at multiple sites in the genome, HDACs are likely to be master regulators that control differentiation pathways. Emphasis should therefore be placed on identifying the subsets of genes controlled by individual HDACs in various cell types. Genome-wide mapping of the histone deacetylation targets of the yeast HDAC proteins (RPD3, HDA1, Sir2, HocI and Hoc2) has shown a clear division of labor between these HDACs [90]. For example, of 815 genomic regions targeted by RPD3 and of 647 regions targeted by HDA1, only 139 (~10%) are targeted by both HDACs. Whereas most published work has focused on nuclear HDACs acting on histone proteins, nonhistone proteins are probable targets for these enzymes, as recently illustrated for HDAC6 and tubulin.

A full understanding of the biology of class II HDACs will also require a detailed analysis of how these factors function biochemically as repressors of transcription. Because HDACs have proved difficult to purify as enzymatically active proteins, little is known about their enzymatic specificity. It will be important to determine which histones in the nucleosome and which lysine residues in each histone are deacetylated by individual HDACs. Since most HDACs reside in multiprotein complexes containing several HDACs, the potential contribution of different HDACs to enzymatic specificity will need to be addressed.

Finally, the identification of HDAC6 and SIRT2 as part of a single complex with tubulin deacetylase activity raises many new questions. The involvement of the HDAC6/SIRT2 complex in both tubulin deacetylation and protein ubiquitination suggests the existence of cross-talk between these two processes, a dialogue that is likely to be repeated in many proteins that are regulated by ubiquitination. A focus on in vivo experiments, including the development of a mouse knockout for each HDAC, together with a renewed effort to characterize the enzymatic activities of these proteins, will allow these important questions to be addressed.

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References

6 Miska, E.A. et al. (1999) HDAC4 deacylates associates with and represses the MEF2 transcription factor. EMBO J. 18, 5099–5107
16 Fischle, W. et al. (2001) Human HDAC7 histone deacetylase reveals that class I and class II deacetylases promote SMRT-mediated repression. Genes Dev. 15, 55−66
17 Kao, H.Y. et al. (2000) Isolation of a novel histone deacetylase reveals (HDAC1) modulates its biological activities. J. Biol. Chem. 277, 23658−23663
27 Lu, J. et al. (2000) Regulation of skeletal myogenesis by association of the MEF2 transcription factor with class II histone deacetylases. Mol. Cell 6, 233−244
28 Fischle, W. et al. (2002) Enzymatic activity associated with class II HDACs is dependent on a multiprotein complex containing HDAC3 and SMRT/CoR. Mol. Cell 9, 45−57
29 Huang, E.Y. et al. (2000) Nuclear receptor co-repressors partner with class II histone deacetylases in a Sin3-independent repression pathway. Genes Dev. 14, 45−54
31 Aranda, A. et al. (2001) Nuclear hormone receptors and gene expression. Physiol. Rev. 81, 1289−1304
33 Guenther, M.G. et al. (2001) A core SMRT co-repressor complex containing HDAC3 and TBL1, a WD40-repeat protein linked to deafness. Genes Dev. 14, 1048−1057
35 Pijnappel, W.W. et al. (2001) The S. cerevisiae SET3 complex includes two histone deacetylases, Hos2 and Hat1, and is a meiotic-specific repressor of the sporulation gene program. Genes Dev. 15, 2991−3004
65 Sparrow, D.B. et al. (1999) MEF-2 function is modified by a novel co-repressor, MITR. EMBO J. 18, 5085–5098
69 Ryseck, R.P. et al. (1989) Structure, mapping and expression of a growth factor inducible gene encoding a putative nuclear hormonal binding receptor. EMBO J. 8, 3327–3335
74 Youn, H.D. et al. (2000) Integration of calcineurin and MEF2 signals by the coactivator p300 during T-cell apoptosis. EMBO J. 19, 4323–4331
76 Youn, H.D. et al. (1999) Apoptosis of T cells mediated by Ca(2+) -induced release of the transcription factor MEF2. Science 286, 790–793
78 Esau, C. et al. (2001) Depletion of calcineurin and myocyte enhancer factor 2 (MEF2) binding domain of Cabin1 results in enhanced cytokine gene expression in T cells. J. Exp. Med. 194, 1449–1459
79 Tovey, M.G. et al. (1978) Activation of latent Epstein–Barr virus by antibody to human IgM. Nature 276, 270–272
80 zur Hausen, H. et al. (1978) Persisting oncogenic herpesvirus induced by the tumour promoter TPA. Nature 272, 373–375
82 Gruffat, H. et al. (2002) MEF2-mediated recruitment of class II HDAC at the EBV immediate early gene BZLF1 links latency and chromatin remodeling. EMBO Rep. 3, 141–146
88 Matsuyama, A. et al. (2002) In vivo destabilization of dynamic microtubules by HDAC6-mediated deacetylation. EMBO J. 21, 6820–6821