Human histone deacetylases I (HDAC1) and II (HDAC2) are homologous proteins (84% identity) that catalyze release of acetyl groups from modified N-terminal lysines of core histones. Histone deacetylation is correlated with both transient and persistent states of transcriptional inactivity (i.e. silencing) in many eukaryotes. In this study, we analyzed complexes containing HDAC1 and HDAC2 to identify the proteins most stably associated with these deacetylases. Complex cI (9.5 S) contained transcriptional corepressor CoREST/kiaa0071 and a protein homologous to FAD-dependent oxidoreductases, kiaa0601. Complex cII (15 S) contained ≥15 proteins, including CHD3/4 (MI-2), Mta-L1, RbAp48/46, and MBD3, characteristic of vertebrate nucleosome-remodeling complexes. Under native conditions, cI and cII may contain HDAC1, HDAC2 or both; these can be dissociated to cI and cII core complexes containing only HDAC1 or HDAC2. The CpG-binding protein MBD2 was associated only with the HDAC1 cII core complex. A model is proposed in which HDAC1 core complexes can be targeted to methylated DNA via MBD2 with recruitment of HDAC2 occurring through formation of HDAC1/cII cII dimers. We note that the cI component CoREST/kiaa0071 and the cII component Mta-L1 share a region of homology that includes a SANT domain; this domain may play a role in complex assembly.

Core histones are subject to reversible acetylation at selected lysine residues in their N-terminal domains. Histone acetylation is correlated with transcriptional activity or competence such that hyperacetylation within chromatin domains favors transcriptional competency, whereas hypoacetylation favors transcriptional silencing. Acetylation neutralizes positive charges on lysine ε-amino groups and may alter nucleosome conformation by weakening interactions of the N-terminal domains with DNA or adjacent nucleosomes. In addition, acetylation at specific residues may create or abolish binding sites for non-histone chromosomal proteins (1–3). Acetylation states are maintained by the coordinate activity of histone acetyltransferases and histone deacetylases (HDACs). Histone acetyltransferases are oxidoreductases, transferring an acetyl group from acetyl-CoA, whereas HDACs remove acetyl groups by hydrolysis (4, 5). Most HDACs belong to a superfamily of zinc metalloenzymes with a conserved ~380-residue catalytic domain (6, 7). The class I HDACs (~500 residues in length) are the best characterized with respect to function. These HDACs are involved in maintaining both short-term (induction/repression) and long-term (epigenetic) patterns of gene activity (8–10). HDAC mutants of Rpd3 in S. cerevisiae and Clr6 in Schizosaccharomyces pombe affect telomeric silencing (11, 12); similarly, HDAC mutants in Drosophila, RPD3 (13), and Caenorhabditis elegans, HDA-1 (14), affect silencing of developmentally regulated genes.

Three class I HDACs have been identified in human. HDAC1 (482 residues) (15) and HDAC2 (488 residues) (16) share 84% identity, whereas HDAC3 (428 residues) (17, 18) is more divergent, sharing 51% identity with HDAC1/2. It is unclear whether HDAC1 and HDAC2 have distinct functions, but they appear to play complementary roles in transcriptional repression. For example, in GH3 pituitary cells, thyroid-stimulating hormone-β expression is negatively regulated by the thyroid hormone triiodothyronine. This triiodothyronine-dependent regulation requires HDAC activity, as indicated by its sensitivity to the inhibitor trichostatin A. An HDAC1 multiprotein complex binds constitutively to a negative regulatory element in the thyroid-stimulating hormone-β promoter. However, chromatin remodeling and transcriptional repression at the thyroid-stimulating hormone-β promoter require (in addition) triiodothyronine-dependent recruitment of an HDAC2 complex to the negative regulatory element (19).

Immunopurification of either HDAC1 or HDAC2 from human cell lines typically yields multiprotein complexes containing both HDAC1 and HDAC2. These include HDAC complexes containing transcriptional corepressor mSin3A (20–22) and chromatin-remodeling ATPase Mi-2 (NURD complex) (23–28). To gain further insight into the mechanism by which HDAC1 and HDAC2 complexes may be independently recruited to specific sites in chromatin, we have analyzed core complexes containing either HDAC1 or HDAC2. Two major HDAC1/2 complexes were identified in HeLa cells: cI is a novel complex containing transcriptional corepressor CoREST/kiaa0071 (29) and protein kiaa0601, inferred to be an FAD-dependent enzyme; cII is similar to the Mi-2 remodeling complex. Under native conditions, cI and cII may contain HDAC1, HDAC2, or both, but these can be dissociated by a mild chaotrope to core monoclonal antibody; MES, 4-morpholineethanesulfonic acid; DTT, dithiothreitol; CHAPS, 3-[3-cholamidopropyl]dimethylammonio]-1-propanesulfonic acid; PAGE, polyacrylamide gel electrophoresis.
complexes containing only HDAC1 or HDAC2. This behavior suggests a general model for interaction between HDAC1 and HDAC2 via dimerization of εI- or εII-specific components.

We identified a potential HDAC-targeting factor, 15αCpG-binding protein MBDB2 (30), as an integral component of the HDAC1 εI complex. MBDB2 was not detected in HDAC2 εI complexes, implying that targeting of HDAC2 may occur via dimerization with HDAC1. Finally, we note that a region of sequence similarity exists between εI component CoREST/kiaa0071 and εI component Mta-L1 (31), containing SANT domains (32). SANT domain proteins are also components of HDAC3 core complexes (33) and may play a general role in HDAC complex assembly.

EXPERIMENTAL PROCEDURES

Cell Culture and Transduction—HeLa S3 cells were grown in suspension culture as previously described (34). Cells were transduced with a retroviral construct (pOZ) expressing a bicistronic mRNA encoding FLAG-tagged HDAC1 protein linked to an interleukin-2 receptor subunit surface marker, and the transduced population was purified by repeated cycles of affinity cell sorting (34). A cDNA construct encoding human HDAC1 with a C-terminal FLAG tag, used to construct the retroviral vector, was generously provided by Dr. Stuart L. Schreiber. A cDNA encoding human HDAC2 (accession number NP_001518) was isolated by performing polymerase chain reaction using gene-specific primers located in the 5′- and 3′-untranslated regions with a CLONTECH Marathon cDNA library; this cDNA clone was used to prepare an HDAC3 core complexes (33) and may play a general role in HDAC complex assembly.
Stable Histone Deacetylase Complexes

Abstract

The polypeptide composition of immunopurified complexes containing endogenous or FLAG-tagged HDAC1. Left panel, proteins binding to anti-FLAG M2-agarose from the Q-Sepharose pool prepared from 5 × 10^6 untransduced control cells or from cells expressing FLAG-tagged HDAC1 were eluted with FLAG peptide. Right panel, proteins from the Q-Sepharose pool binding to preimmune (Preimm) or anti-HDAC1 (aHDAC1) IgG-agarose were eluted in pH 2.5 buffer. Proteins were resolved by SDS-PAGE and visualized by Coomassie Blue staining. The bands indicated (●) were excised for amino acid sequence analysis (see “Experimental Procedures”). Dashed lines indicate the same proteins associated with either epitope-tagged or endogenous HDAC1.

Fig. 2. Polypeptide composition of immunopurified complexes containing endogenous or FLAG-tagged HDAC1. Left panel, proteins binding to anti-FLAG M2-agarose from the Q-Sepharose pool prepared from 5 × 10^6 untransduced control cells or from cells expressing FLAG-tagged HDAC1 were eluted with FLAG peptide. Right panel, proteins from the Q-Sepharose pool binding to preimmune (Preimm) or anti-HDAC1 (aHDAC1) IgG-agarose were eluted in pH 2.5 buffer. Proteins were resolved by SDS-PAGE and visualized by Coomassie Blue staining. The bands indicated (●) were excised for amino acid sequence analysis (see “Experimental Procedures”). Dashed lines indicate the same proteins associated with either epitope-tagged or endogenous HDAC1.

The polypeptides common to both endogenous and FLAG-tagged HDAC1 proteins were identified by mass spectrometry (34), revealing components characteristic of deacetylase chromatin-remodeling complexes: Mi-2 (p240, ATPase), Mta-L1 (p78, a SANT domain and zinc finger protein, also termed Mta2), RbAp48/46 (p56/p53, WD40 repeat proteins), and MBD3 (p36/p33, “CpG-binding domain homology”) (23, 25, 27, 28). In addition, we identified MBD2 (p50/p53, a “CpG-binding protein”) (30), kiaa0601 (p115, a protein homologous to FAD-dependent enzymes) (see Fig. 8), and an additional SANT domain protein (kiaa0071) (see Fig. 9), co-considering with HDAC1 (p63) (35). The p63 and p61 bands both contained HDAC1; no HDAC2-specific peptides were identified in either band.

Sedimentation Analysis of HDAC1 and HDAC2 Complexes—The variable staining intensities of the HDAC1-associated polypeptides suggested that they might represent a mixture of different multiprotein complexes. We employed velocity sedimentation in a glycerol density gradient to separate HDAC1-F complexes differing in size and shape. Histone deacetylase enzyme activity sedimented as a 15 S peak with a 9.5 S shoulder (Fig. 3, upper panel). The distribution of HDAC1-F by Western blotting (Fig. 3, lower panel) was similar to the activity profile, indicating similar specific activities for all sedimenting species of HDAC1.

Different polypeptides co-sedimented with HDAC1-F in the 9.5 S and 15 S regions of the gradient (Fig. 3, middle panel), indicating that these fractions represent different core complexes, designated cl (9.5 S) and cII (15 S). The polypeptide components of cl (fractions 6 and 7) and cII (fractions 9 and 10) were analyzed by mass spectrometry (see above). The p63 band in both cl and cII contained HDAC1 and kiaa0071. The p115 band in cl contained kiaa0601. cII contained the remodeling components Mi-2 (p240), Mta-L1 (p78), RbAp48/46 (p55/p53), and MBD3 (p36/p33) and, in addition, MBD2 (p50/p53). Additional bands were identified in cII: p70 is a human homolog of the Xenopus laevis HDAC-associated zinc finger protein p66 (24); p59 and p38 represent truncated forms of Mta-L1. The narrow width of the 15 S peak (same as the sedimentation standards) suggests that cII represents a single multiprotein complex. (This idea is further supported by immunopurification studies described below.) The variation in staining intensity of the bands could be due either to different stoichiometries (i.e. 3–5 mol of p240/p78/p63/p55/p53 per mol of p50/p36/p33) or to differences in the amount of Coomassie Blue dye bound per mol of each protein.

To obtain specific probes for cl and cII, affinity-purified anti-peptide antibodies were prepared against the C-terminal 16 residues of kiaa0601, kiaa0071, Mta-L1, and MBD2. kiaa0601 and kiaa0071 were found predominantly in cl, whereas Mta-L1 and MBD2 were found exclusively in cII (Fig. 3, lower panel). The data from Coomassie Blue staining and Western blotting suggest that cl is a multiprotein complex composed of kiaa0601 (p115), kiaa0071 (p63), HDAC1 (p63), and p37, which is consistent with the predicted molecular mass for a 9.5 S complex, ~200 kDa. The predicted molecular mass for a 15 S complex, ~400 kDa, would appear to be an underestimate for cII. Assuming only 1 mol of each visible band in the multiprotein complex would indicate a molecular mass of at least 1 MDa.

Fig. 1. A, quantitation of endogenous and FLAG-tagged HDAC1 proteins in HeLa subcellular fractions. Aliquots (5 × 10^6 cells) of the cytosol (Cyto), STM wash, Triton wash (TW), low Mg2+ wash (LM), high salt extract (HS), and residual nuclei (Nuc) prepared as described under “Experimental Procedures” were resolved by SDS-PAGE; proteins were visualized by Western blotting using rabbit anti-HDAC1 antibody and mouse anti-FLAG mAb M2. The quantitation standard was a recombinant HDAC1 protein with an N-terminal FLAG tag expressed in Sf9 cells. B, immunopurification of endogenous HDAC1. High salt extract (load) was applied either to affinity-purified rabbit anti-HDAC1 antibody coupled to protein A-agarose or to control agarose containing preimmune IgG (Control). Unbound protein was collected (flow-through), and the agarose was extensively washed and then eluted with 0.1 M glycine (pH 2.5) (eluants E). Alternatively, the extract was chromatographed on Q-Sepharose (Q-S), and a pool of fractions containing HDAC1 was applied to the immunoadsorbents. HDAC1 and HDAC2 in these fractions were detected by Western blotting.
However, sedimentation coefficients are a function of both the molecular mass and frictional ratio, the latter being related to particle asymmetry (43). In view of the wide size range of the proteins in cII, it is likely to have a greater frictional ratio than the sedimentation standards; thus, 400 kDa would represent only a minimum estimate.

FLAG-tagged HDAC2 was isolated using the same procedures employed for HDAC1 (see above). In contrast to HDAC1, HDAC2 deacetylase activity sedimented as a single broad peak centered around 15 S (Fig. 4). This HDAC2 core complex contained the same major components as the HDAC1 cII complex: Mi-2 (p240), Mta-L1 (p78), p70, RbAp48/46 (p55/p53), and MBD3 (p36); but did not contain MBD2, as judged by Western blotting.

Endogenous HDAC1 and HDAC2 Are in Distinct cI and cII Core Complexes—To determine whether endogenous HDAC1 and HDAC2 in normal (untransduced) HeLa cells exist as distinct cI and cII core complexes, we employed antibody adsorbents specific for cI (anti-kiaa0601 and anti-kiaa0071) and cII (anti-Mta-L1 and anti-MBD2) components. Binding was performed using the native high salt extract (no urea treatment) under non-stringent conditions (see “Experimental Procedures”). After extensive washing, the adsorbents were eluted with pH 2.5 buffer, and the eluates were analyzed by SDS-PAGE (Fig. 5A). As expected, all adsorbents (except the control) bound HDAC1. (Protein recovery from the anti-MBD2 adsorbent was relatively low.) Also as predicted, the cI components kiaa0601 and kiaa0071 bound to anti-HDAC1, anti-kiaa0601, and anti-kiaa0071 adsorbents, but not to anti-Mta-L1 and anti-MBD2 adsorbents; conversely, the cII components Mta-L1 and MBD2 bound to both anti-Mta-L1 and anti-MBD2 adsorbents, but not to anti-kiaa0601 and anti-kiaa0071 adsorbents. This demonstrates that cI and cII are distinct HDAC1 complexes in the native high salt extract. Blotting indicated that mSin3A was not associated with either cI or cII.

HDAC2 was also bound by both cI- and cII-specific adsorbents (Fig. 5A), as might be expected, since some HDAC2 is associated with HDAC1 (Fig. 1). To examine whether HDAC2 exists as cI or cII complexes independently of HDAC1, the fraction of endogenous HDAC2 not associated with HDAC1 (Fig. 1) was isolated from the anti-HDAC1 flow-through (i.e. depleted of HDAC1) using an anti-HDAC2 adsorbent. Both cI components kiaa0071 and kiaa0601 and the cII component Mta-L1 co-immunopurified with HDAC2 (Fig. 5A). However, MBD2 was not detected and appears not be associated with endogenous HDAC2 cII, consistent with our analysis of FLAG-tagged HDAC2 (Fig. 4).

Further insight into the composition and potential significance of cI and cII can be gleaned from examination of the polypeptide composition of the eluates (Fig. 5B). The anti-kiaa0071 eluate is similar to the cII region of the glycerol gradient, except for the additional p61 band (which is characteristic of endogenous HDAC1) (Fig. 2), supporting our interpretation that kiaa0601, kiaa0071, HDAC1, and p37 compose a multiprotein complex. The absence of any major polypeptides in the anti-kiaa0071 eluate besides the cII components indicates that cI represents the quantitatively major
form of kiaa0071 in the high salt extract. The anti-kiaa0601 eluate is similar to the anti-kiaa0071 eluate, except for a few additional polypeptides, notably p140 and p160. These polypeptides did not appear to cross-react with the anti-kiaa0601 antibody in Western blotting; we favor the interpretation that they are components of other multiprotein complexes containing kiaa0601, but not kiaa0071 or HDAC1/2.

When the polypeptide composition of the anti-Mta-L1 eluate was examined, it proved to be similar to the cII region of the gradients (Figs. 3 and 4). The absence of any other major polypeptides in the anti-Mta-L1 eluate besides the cII components indicates that cII represents the quantitatively major form of Mta-L1 in the high salt extract. The anti-MBD2 eluate is similar to the anti-Mta-L1 eluate. Despite the large difference in staining intensity between Mta-L1 (p78) and MBD2 (p50), these polypeptides appeared in a fixed ratio in all preparations containing cII, supporting our interpretation that cII represents a single molecular species (see above). Overall, our analysis has demonstrated that the majority of HDAC1 and HDAC2 in HeLa cells exist in two distinct types of multiprotein complexes, cI and cII, which may contain HDAC1, HDAC2, or both. cI and cII can be dissociated to core complexes containing only HDAC1 or HDAC2 in association with other enzyme and targeting factors. We propose a general model for interaction between HDAC1 and HDAC2 via dimerization of cI- or cII-specific components (see “Discussion” and Fig. 7).

Complex cI Contains Riboflavin—The cI component kiaa0601 exhibits sequence similarity to a superfamily of FAD-dependent enzymes (see Fig. 8). To examine whether kiaa0601 may contain FAD, HeLa cells were radiolabeled in vivo with [3H]riboflavin (see “Experimental Procedures”). Riboflavin is converted to FMN and subsequently to FAD. The immunoadsorbents specific for cI (anti-kiaa0071 and anti-kiaa0601) both bound ~5% of the radiolabeled flavin in the high salt extract (Table I), whereas the anti-Mta-L1 and control adsorbents bound negligible amounts (~0.01%). Since kiaa0601 and kiaa0071 are the major proteins bound specifically by the cI adsorbents (Fig. 5B), it is reasonable to infer that kiaa0601 contains the radiolabeled flavin.

Subcellular Localization of cI and cII Components—To gain further insight into the possible role of cI and cII components as targeting factors for HDACs, we examined their subcellular localization in human skin fibroblasts. The cI components kiaa0071 and kiaa0601 were distributed similarly to HDAC1, in the nucleoplasm and excluded from the nucleoli (Fig. 6). The cII component Mta-L1 was localized to the nucleoplasm and was also detected in the juxtanuclear Golgi complex (47). MBD2 exhibited a punctate distribution in nuclei, differing from HDAC1 and Mta-L1. This may be explained by the fact that only a minor fraction of MBD2 (~30%) was extractable with the HDACs in 0.5 M NaCl; possibly the majority of MBD2 is in different complexes, tightly bound to chromatin.

DISCUSSION

Two Distinct HDAC1/2 Core Complexes—HDAC1 and HDAC2 are closely related mammalian histone deacetylases that appear to mediate complementary functions in transcriptional regulation at specific sites in chromatin (see the Introduction). To gain further insight into the mechanisms by which HDAC1 and HDAC2 interact, we have analyzed multiprotein complexes from HeLa cell nuclei containing HDAC1 and HDAC2. Complex cI is composed of kiaa0601 (p116), kiaa0071 (p63), p37 (unidentified), and HDAC, apparently in an equimolar ratio, based on sedimentation behavior (see “Results” and Fig. 3). Complex cII is similar to vertebrate deacetylase nucleosome-remodeling (NURD) complexes (23–28) in that it contains Mi-2 (p240), Mta-L1/Mta2 (p78), RbAp48/46 (p55/p53), and MBD3 (p36/p38) as well as a homolog of the Xenopus-specific component p66 (p70). Under native conditions, cI and cII may contain HDAC1, HDAC2, or both; however, mild dissociation by 1 M urea yields core complexes containing only HDAC1 or HDAC2. This behavior suggests a general model for interaction
between HDAC1 and HDAC2 via dimerization of cI- or cII-specific components (Fig. 7).

Association with specific folding partners appears to be required for HDAC1/2 function in vivo. When overexpressed in Sf9 insect cells, human HDAC1 and HDAC2 are largely insoluble and have little enzymatic activity, suggesting incorrect folding. Coexpression with RbAp48/46 and Mta2 (also termed Mta-L1) is required to assemble soluble, enzymatically active HDAC complexes (23). The polypeptide complement required to assemble active HDAC complexes has been termed the “core complex” (23, 25). The core complex components serve as folding partners for HDACs and, in addition, may mediate substrate binding, association with complementary enzymatic functions, and targeting of HDACs to specific sites in chromatin (e.g. promoters).

A requirement for HDAC-folding partners can also be inferred from the behavior of epitope-tagged HDAC1/2 stably expressed by our retroviral vector in transduced cells. The levels of expression of HDAC1/2 obtained using this system in mammalian cells appear to be strictly limited compared with expression in bacteria or insect cells. At most, we have been able to obtain only a 4–5-fold excess of recombinant over endogenous HDAC1 (in normal mouse skin fibroblasts), and this was accompanied by a decreased level of endogenous HDAC1, amounting to only a 3-fold increase overall. The absence of significant amounts of free (monomeric) HDAC1 and HDAC2 implies that they must associate with specific folding partners for metabolic stability; presumably, excess HDAC1/2 is turned over and does not accumulate. Comparison of the relative abundance of cI- and cII-specific components associated with endogenous versus FLAG-tagged HDAC1 indicates that recombinant HDAC1 has a greater tendency to form cII complexes (Fig. 2). Similarly, FLAG-tagged HDAC2 formed only cII complexes (Fig. 4), although endogenous HDAC2 formed both cI and cII complexes (Fig. 5). This tendency to form cII complexes may be due to a greater availability of the cII components as folding partners or could be due to an effect of the FLAG tag. HDAC1 cII contains additional polypeptides not present in HDAC2 cII (Figs. 4 and 5). One of these polypeptides was

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identified as the \(^{60}\)CpG-binding protein MBD2 (30). MBD2 is a transcriptional corepressor (48) that binds specifically to CpG residues in DNA and exhibits a preference for densely methylated regions. In vitro, MBD2 is localized to heterochromatic regions in mouse cells (30). MBD2 may direct Mi-2 remodeling complexes to methylated regions in chromatin, mediating transcriptional silencing (23, 24). Based on our model (Fig. 7), HDAC1 cII could be recruited directly to methylated regions in mouse cells (30). MBD2 is localized to heterochromatic regions.

**Significance of Complex cI—** Protein kiaa0071, also termed CoREST, binds to the RE1 silencing transcription factor (REST) in vitro and forms a complex with REST in the L6 skeletal muscle cell line (29). CoREST exhibits transcriptional corepressor activity in a Gal4 DNA-binding domain-mediated reporter assay, even in cells lacking REST. It is plausible that CoREST may function as a corepressor by recruiting HDAC1 to promoters, as has been proposed for MBD2 (see above) and other deacetylase-associated transcriptional repressors (48). REST is a transcriptional silencer of neural-specific genes in non-neural cells; it may serve to target cII complexes to promoters for neural-specific genes.

Protein kiaa0061 appears to belong to a superfamily of FAD-dependent enzymes (49, 50) based on sequence similarity (Fig. 8) and binding radiolabeled flavin (Table I). Conservation is strong at residues contacting FAD (Fig. 8) within the three FAD-binding domains of maize polyamine oxidase (51). Particularly significant is the conservation at Gly\(^{57}\) and Lys\(^{100}\). These residues in polyamine oxidase position a water molecule at the site of hydrogen exchange (N-5) in the isoalloxazine ring and may represent the catalytic center. The N-terminal one-third of kiaa0061 resembles that of CoREST/kiaa0071 in having a block of alamines and also has similarity to conserved region 1 of the SWI3-like subunits of the SWI/SNF chromatin-remodeling complex (52). The fact that a large fraction of kiaa0061 exists in a complex with a histone deacetylase and a transcriptional corepressor (Fig. 5) suggests that kiaa0061 may be an enzyme with an activity complementary to that of the deacetylase in transcriptional silencing. The superfamily of FAD enzymes to which kiaa0061 apparently belongs includes a diverse group of oxidases and dehydrogenases involved mostly in biosynthetic/degradative pathways (49). In the context of cI, it seems plausible that kia0061 may be an oxidoreductase involved in covalent modification of chromatin constituents.

**Role of Conserved Domains in HDAC Core Complex Assembly—** The cI component kiaa0071 and the cII component Mta-L1 (Mta2) share sequence similarity in an \(~200\)-residue segment that is tandemly repeated in kiaa0071 (Fig. 9). This region of similarity between kiaa0071 and Mta-L1 contains a SANT domain (32). Interestingly, the transcriptional corepressors SMRT and NCoR, which have recently been identified as components of HDAC3 core complexes (33),\(^{3}\) are likewise SANT domain proteins, suggesting a general role for SANT domain proteins as folding partners for HDACs. The \(~60\)-residue SANT domain (related to the Myb DNA-binding domain) is found in a variety of transcription factors, present in one to three copies, and may mediate protein-protein interactions. We further note that the arrangement of the two SANT domains in kiaa0071, separated by an \(~100\)-residue spacer, is similar to that in SMRT and NCoR (29). This suggests that differing configurations of the conserved SANT domains in kiaa0071 and Mta-L1 may have a role in specific assembly of cI and cII core complexes.

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