Regulation of cAMP-responsive Element-binding Protein-mediated Transcription by the SNF2/SWI-related Protein, SRCAP*

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M. Alexandra Monroy‡, Donald D. Ruhl‡, Xiequn Xu‡, Daryl K. Granner§, Peter Yaciuk§, and John C. Chrivia‡

From the ‡Department of Pharmacological and Physiological Sciences and the §Department of Molecular Microbiology and Immunology, Saint Louis University School of Medicine, Saint Louis, Missouri 63104 and the ¶Department of Molecular Physiology and Biophysics, Vanderbilt University School of Medicine, Nashville, Tennessee 37232

SRCAP (SNF2-related CBP activator protein) belongs to the SNF2 family of proteins whose members participate in various aspects of transcriptional regulation, including chromatin remodeling. It was identified by its ability to bind to cAMP-responsive-binding protein (CREB)-binding protein (CBP), and it increases the transactivation function of CBP. The phosphoenolpyruvate carboxykinase (PEPCK) promoter was used as a model system to explore the role of SRCAP in the regulation of transcription mediated by factors that utilize CBP as a coactivator. We show that transcription of a PEPCK chloramphenicol acetyltransferase (CAT) reporter gene activated by protein kinase A (PKA) is enhanced 7-fold by SRCAP. In the absence of PKA this SRCAP-mediated enhancement does not occur, suggesting that SRCAP functions as a coactivator for PKA-activated factors such as CBP. Replacing the PEPCK promoter binding site for CREB with a binding site for Gal4 (ΔCRE (cAMP-responsive element) Gal4 PEPCK-CAT reporter gene) blocks the ability of SRCAP to activate transcription despite the presence of PKA. Expression of a Gal-CREB chimera restores the ability of PKA to regulate transcription of the ΔCRE Gal4 PEPCK gene and restored the ability of SRCAP to stimulate PKA-activated transcription. In addition, SRCAP in the presence of PKA enhances the ability of the Gal-CREB chimera to activate transcription of a Gal-CAT reporter gene that contains only binding sites for Gal4. SRCAP binds to CBP amino acids 280–460, a region that is important for CBP to function as a coactivator for CREB. Overexpression of a SRCAP peptide corresponding to this CBP binding domain acts as a dominant negative inhibitor of CREB-mediated transcription. Structure-function studies were done to explore the mechanism(s) by which SRCAP regulates transcription. These studies indicate that the N-terminal region of SRCAP, which contains five of the seven regions that comprise the ATPase domain, is not needed for activation of CREB-mediated transcription. SRCAP apparently has several domains that participate in the activation of transcription.

The transcription factor cAMP-responsive element-binding protein (CREB) regulates the transcription of a number of genes (for review, see Refs. 1 and 2). It stimulates a low level of basal transcription, which has been proposed to be mediated through action of CREB domains that bind directly to TAF 110, TAF 130, TFIIB and TBP (3–7). CREB also stimulates a much higher level of transcription when it is activated in response to diverse biological stimuli such as neural and hormonal signals. These signals stimulate phosphorylation of CREB within the kinase-inducible domain. Phosphorylation of serine 133 within the kinase-inducible domain by several kinases, including calmodulin kinase II and IV, protein kinase A, ribosomal S6 kinase 1–3, mitogen- and stress-activated protein kinase 1, and mitogen-activated protein kinase-activated protein kinase 2/3, leads to the activation of transcription (for review, see Ref. 8). Although phosphorylation of serine 133 has been implicated as the trigger for transcriptional activation, other studies have demonstrated that additional phosphorylation sites in the kinase-inducible domain are important for the regulation of the transcriptional activity of CREB. For example, phosphorylation of serine 133 creates a consensus site for phosphorylation of CREB at serine 129 by glycogen synthase kinase 3, and phosphorylation of this latter site is required for full activation of CREB (9, 10). Repression of CREB-mediated transcription has also been reported to result from the phosphorylation of serine 142 by calmodulin kinase II (11).

The phosphorylation of CREB on serine 133 results in the activation of transcription because this modification promotes the association of CREB with CREB-binding protein (CBP) (12, 13). The importance of the interaction of CREB with CBP for activation of transcription is supported by several studies. A CREB mutant in which serine 133 is changed to an alanine can neither activate transcription nor bind CBP (12, 14). Shaywitz et al. (15) demonstrated that the magnitude of transcription activated by CREB is dependent on the strength of the interaction of CREB with CBP. In addition, studies by Cardinaux et al. (16) demonstrated that CREB modified to bind CBP constitutively also activates transcription constitutively.

CBP and its homolog p300 interact with a large number of transcription factors and thus have been implicated in regulating the transcription of a number of genes (for review, see Refs. 1, 2, and 17). The mechanism(s) underlying the ability of CBP/p300 to activate transcription has not been elucidated com-

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† To whom correspondence should be addressed: Dept. of Pharmacological and Physiological Sciences, Saint Louis University School of Medicine, 1402 South Grand, Saint Louis, MO 63104. Tel.: 314-268-5291; Fax: 314-577-8233; E-mail: Chrivia@SLU.edu.

1 The abbreviations used are: CREB, cAMP-responsive element-binding protein; CBP, CREB-binding protein; CRE, cAMP-responsive element; SRCAP, SNF2-related CBP activator protein; PEPCK, phosphoenolpyruvate carboxykinase; CAT, chloramphenicol acetyltransferase; bp, base pairs; PCR, polymerase chain reaction; PKA, protein kinase A; CMV, cytomegalovirus; TAF, TATA box-binding protein; TFIIB, transcription factor B; TBP, TATA box-binding protein.
Activation of CREB-mediated Transcription by SRCAP

completely but is thought to occur, in part, by the interaction of CBP/p300 with general transcription factors such as TFIIH, TBP, and RNA helicase A (13, 18, 19). Efforts to understand how CBP activates transcription have led to the realization that CBP is a histone acetyltransferase capable of acetylating not only histones (20) but several transcription factors such as c-Myb, MyoD, GATA-1, and p53 (21–25). In addition, CBP binds to several proteins that also function as histone acetyltransferases such as P/CAF, p/CIP, and the p160 coactivators such as SRC-1 (26, 27). Precisely how CBP interacts with these coactivators and other cellular factors to activate transcription at a specific promoter is not known. However, the notion that CBP interacts with a specific subset of factors at different promoters has been suggested by the work of Korzus et al. (28). These authors showed that CBP, in conjunction with P/CIP, SRC-1, and P/CAF, is required for activation of transcription of a retinoic acid response element reporter gene by the retinoic acid receptor, whereas only CBP, P/CAF, and p/CIP are needed for activation of a cAMP-responsive element (CRE) reporter gene by CREB.

SNF2-related-CBP activator protein (SRCAP) was identified by our laboratory (29) using a yeast two-hybrid assay. It binds to amino acids 227–460 of CBP, a region important for activation of CREB-mediated transcription (19). This region of CBP lies adjacent to, but does not overlap, the CRE binding domain, which is located between amino acids 586 and 666 (30). SRCAP belongs to the SNF2 family of proteins whose functions include remodeling of chromatin, DNA repair, and regulation of transcription (for review, see Refs. 31–33). A hallmark of the SNF2 family is the presence of seven highly conserved regions that collectively comprise an ATPase domain. Previous studies indicate that SRCAP is an ATPase and that it enhances CBP-activated transcription (29).

In the present report, we have used the well characterized phosphoenolpyruvate carboxykinase (PEPCK) promoter as a model to study the role of SRCAP in CREB-mediated transcription. PEPCK catalyzes a rate-controlling step in hepatic gluconeogenesis. Expression of the protein is regulated primarily at the transcriptional level by the action of several hormones including glucagon, glucocorticoids, thyroid hormone, and insulin (34, 35). Although it has been shown that this promoter contains multiple cis-acting elements that are required to mediate the full transcriptional response to the various hormones, the CRE is absolutely required for CAI induction (36). CREB as well as C/EBP proteins bind to the CRE of this promoter (36). Our cotransfection experiments using a PEPCK-CAT reporter gene and plasmids for expression of CREB, P/CA and SRCAP demonstrate that SRCAP enhances transcription in a CREB-dependent manner.

Studies with a Gal-CREB chimeric protein indicate that SRCAP has several features consistent with a role as a coactivator of CREB-mediated transcription. Increasing intracellular levels of SRCAP result in an increase in CREB-mediated transcription, whereas disruption of the interaction of SRCAP with CBP (using a dominant negative form of SRCAP) results in inhibition of CREB-mediated transcription. These studies also indicate that, although SRCAP functions as an ATPase, mutant SRCAP that lacks a large portion of this domain retains its ability to function as a CREB coactivator.

**EXPERIMENTAL PROCEDURES**

**Plasmids**—The pSRCAP plasmid encoding amino acids 1–2971 of SRCAP was generated by subcloning the 9,121-bp SRCAP cDNA into the pcDNA 3.1 Myc/His plasmid (Invitrogen) digested with the restriction enzymes NheI and BamHI. The plasmids pSRCAP1274–2971, pSRCAP1274–2971, and pSRCAP1360–1670 were constructed by PCR and sequenced to confirm that no changes in DNA sequence occurred. Oligonucleotides used in the PCRs introduced an initiator methionine encoded in a consensus Kozak sequence at the 5′-end of the SRCAP cDNA (37). The pGal-SRCAP1–1196, pGal-SRCAP1274–2971, and pGal-SRCAP1360–1670 plasmids were made by subcloning the corresponding SRCAP cDNA fragments into the pgal-SRCAP plasmid as described previously by Johnston et al. (29). The pPKA promoter containing the cDNA coding for PKA catalytic subunit was a gift from Dr. Uiler (University of Michigan, Ann Arbor). The pGal-CREB chimera was a gift from Rehfuss (McGill University, Montreal). The plasmid encoding CREB (pReRoSV-CREB) (38) and the PEPCK-CAT (pPL32) and pCRE-Gal4 PEPC-KCAT reporter genes have been described previously (39, 40). The CAT-3 vector containing a minimal promoter and two CAT reporters was a gift from Promega.

**Transfections**—HeLa cells were maintained in Dulbecco’s modified Eagle medium, and HepG2 cells were maintained in minimum essential medium with Earle’s salts. Each was supplemented with 10% fetal bovine serum, 50 units/ml penicillin, and 50 μg/ml streptomycin. Cells were seeded either at 1 × 105 cells/35-mm dish or at 5 × 105 cells/10-cm dish, 18 h prior to transfection. Each transfection utilized 100 ng of the pGal-CAT reporter plasmid (pGal4/E1b TATA) or 200 ng of the PEPPC-KAT reporter plasmid and the indicated amounts of each additional plasmid. Each transfection was adjusted to contain equal molar amounts of the CMV promoter using the pcDNA 3.1 Myc/His plasmid and was adjusted to contain the same amount of total DNA using salmon sperm DNA. The LipofectAMINE (Life Technologies, Inc.) transfection method was used for HeLa cells, whereas Lipofectin (Life Technologies, Inc.) was used for HeLa cells. The transcription factor activator protein (Promega Biochemicals) was used for HepG2 cells. Each was used according to the manufacturer’s directions. Cells were harvested 24 or 48 h after transfection and assayed for CAT activity as described (19) or Gal-CREB levels using Western blots. CAT activity reported was normalized for variation of transfection efficiency between samples (the variation in the amount of plasmid taken up by cells in each sample) using a statistical approach where each experimental point was repeated triplicate in at least three separate experiments. We have used this approach because SRCAP regulates (presumably through regulation of the transcription of common reporter genes used as internal controls. For example, we have found that SRCAP activates transcription of a CMV-β-galactosidase reporter gene. In test experiments, using CMV-β-galactosidase as an internal control we found that SRCAP increased CREB-mediated transcription about 6-fold versus 7-fold when corrected by the statistical approach (data not shown).

**Western Blotting**—48 h post-transfection HeLa cell nuclear extracts were prepared by the method of Dignam et al. (41). Equal amounts of each nuclear extract (66 μg) were analyzed for Gal-CREB levels by Western blot analysis using an anti-Gal antibody (19).

**Transcriptional Assays—**Total RNA was prepared using the Trizol reagent (Life Technologies, Inc.). 2 μg of RNA was treated with 2 units of DNase II (New England Biolabs) with 30 cycles of amplification. The amplification of the β-actin cDNA was done using the sense primer 5′-GCTCGTCGTC- GGGTCATCTTCTC-3′ and the antisense primer 5′-CACCATGGACCCTCACCATTTCTC-3′. The SRCAP cDNA was amplified using two distinct sets of primers. Used in reaction 1 (Fig. 3, lane 2) were the sense primer (5′-AAGACCCCCAATCTCCCGCCCA-3′) containing SRCAP nucleotides 7474–7495 and the antisense primer (5′-CACCATGAGCCCTCACCTTT-3′) containing SRCAP nucleotides 8692–8671. Used in reaction 2 (Fig. 3C, lane 4) were the sense primer (5′-GGGATCCGTCGTTGAGCTCTA-3′) containing SRCAP nucleotides 4033–4056 and the antisense primer (5′-GGATCTCTAAGCCTCA-3′) containing SRCAP nucleotides 5162–5137. Note that these last two primers contain an additional eight nucleotides on the 5′-ends coding for restriction sites. The expected size cDNA for β-actin is 353 bp and 1,218 bp for SRCAP in reaction 1 (Fig. 3C, lane 3) and 1,219 bp for SRCAP in reaction 2 (Fig. 3C, lane 4). A sample of each PCR was electrophoresed through a 1.5% agarose gel and visualized with ethidium bromide. Contaminating genomic DNA was not amplified because no PCR products were obtained without first reverse transcribing RNA preparations.

**RESULTS**

We demonstrated previously that SRCAP binds CBP and enhances its ability to activate transcription (29). This suggested that SRCAP might regulate the activity of transcription factors such as CREB which utilize CBP as a transcriptional coactivator. To test this hypothesis we asked whether SRCAP could enhance the transcriptional activity of the PEPPCK gene promoter, which is known to be regulated by CREB (34). For
CAT reporter gene induced by PKA in the CAT enzymatic activity was determined by dividing the CAT enzymatic activity of each sample by the transcriptional activity of the PEPCK-CAT reporter gene (pSRCAP) where indicated. The relative CAT enzymatic activity was determined by dividing the CAT enzymatic activity of each sample by the transcriptional activity of the PEPCK-CAT reporter gene induced by PKA in the left panel and the transcriptional activity of the ΔCRE-Gal4 PEPCK reporter gene induced by PKA and Gal-CREB in the right panel (which was assigned a relative value of 1). Values represent the means ± S.E. from three separate experiments in which each sample was assayed in triplicate.

This purpose we transfected the PEPCK-CAT reporter gene (39) into the HepG2 human hepatoma cell line. The transcriptional activity of this reporter gene, as shown in Fig. 1, is minimally activated by transfection with a plasmid encoding CREB in the absence of activated PKA. A 10-fold activation of transcription of the PEPCK promoter was observed following transfection of a plasmid encoding the catalytic subunit of PKA in HepG2 cells (43). A similar activation was achieved when plasmids encoding both CREB and PKA were cotransfected. Cotransfection of the plasmid encoding SRCAP (pSRCAP) with the plasmid encoding PKA or with both the plasmids encoding CREB and PKA resulted in an additional 7-fold increase in the activation of transcription. Cotransfection of pSRCAP with only the plasmid encoding CREB (in the absence of PKA) did not activate transcription.

The observation that SRCAP strongly activates transcription only in the presence of PKA suggested that SRCAP is a coactivator for CREB or C/EBPα, either of which mediates PKA-activated transcription of the PEPCK promoter (43). To test this hypothesis, we made use of a PEPCk gene promoter in which the binding site for CREB (the CRE) was replaced by a Gal4 binding site (40). Transfection of either a plasmid encoding a Gal-CREB chimera or a plasmid encoding the catalytic subunit of PKA resulted in a weak activation of the modified reporter gene, ΔCRE-Gal4 PEPCk. In contrast, if plasmids expressing both Gal-CREB and PKA were cotransfected, SRCAP transcription was increased by more than 11-fold. In contrast to the effects on the PEPCk promoter, we found that SRCAP had a much smaller effect on the transcriptional activity (2.5-fold) of a control reporter gene pCAT-3 whose expression is driven by the basal SV40 promoter (data not shown).

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To test more directly the hypothesis that SRCAP acts as a coactivator for CREB-mediated transcription, we asked whether SRCAP could regulate Gal-CREB-mediated transcription from a simple reporter gene containing only binding sites for Gal4 (pGAL-CAT). As shown in Fig. 2, cotransfection of plasmids encoding pSRCAP, Gal-CREB, and the catalytic subunit of PKA activates transcription by about 9-fold in HeLa cells. SRCAP also enhances transcription mediated by the Gal-CREB chimera by 25-fold in HepG2 cells (data not shown). As shown in Fig. 2, the cotransfection of pSRCAP had only a small effect on transcriptional activation by a Gal-Vp16 chimeric protein. This chimera was chosen as a control because the VP16 protein has not been reported to use CBP as a coactivator, but rather appears to regulate transcription by direct contact with TBP (44).

These results indicate that SRCAP functions as a positive regulator of CREB-mediated transcription and suggest that the cellular level of SRCAP protein might be a limiting factor for activation of CREB-mediated transcription. To test this hypothesis, we asked whether disruption of the CBP-SRCAP interaction in HeLa cells (which express SRCAP; see Fig. 3C) would result in the disruption of CREB-mediated transcription. A peptide that corresponds to the CBP binding domain of SRCAP was expressed in cells by transfection using the plasmid pSRCAP1380 – 1670 to disrupt CBP-SRCAP interaction. SRCAP1380 – 1670 acts as a dominant negative inhibitor and blocks CREB-mediated transcription by 95% but has only a slight effect on the transcriptional activity of the Gal-Vp16 chimera (Fig. 3A).

Western blot analysis was used to examine the level of Gal-CREB protein in transfected cells to ensure that the alterations in CREB-mediated transcription observed were the result of changes in the transcription activity of the Gal-CREB chimera rather than changes in levels of the Gal-CREB protein. The transfection of plasmids encoding either SRCAP or the dominant negative SRCAP peptide did not alter Gal-CREB protein expression (Fig. 3B).
The function of several SNF2 family members is dependent on their ability to hydrolyze ATP. This prompted us to determine whether the SRCAP ATPase domain is required for coactivation with CREB. For these studies, we tested the activity of an N-terminal truncated SRCAP that lacks five of the seven conserved regions that collectively make up the ATPase domain of SRCAP (see Fig. 4A). The transcriptional activation afforded by SRCAP 1275–2971 is not significantly different from that provided by wild-type SRCAP (Fig. 4B). The observation that the ATPase domain of SRCAP is not needed for activation of CREB-mediated transcription suggests that SRCAP must provide some additional function. To identify regions within SRCAP which might contain this function the transcriptional activity of several Gal-SRCAP chimeras was assessed. A Gal-SRCAP chimera encoding a portion of the N-terminal end of SRCAP (Gal-SRCAP 1–1186), or a portion of the
C-terminal end of SRCAP (Gal-SRCAP2316–2971) activated transcription of the Gal-CAT reporter gene 10–20-fold more than Gal1–147 (Fig. 5). These two chimeras also activate transcription to levels similar to those observed with a Gal-SRCAP1275–2971 chimera, which activates transcription to the same extent as a Gal-CBP chimera (29). Neither the Gal-SRCAP1–1186 chimera nor the Gal-SRCAP2316–2971 chimera contains the CBP binding domain of SRCAP, suggesting that they activate transcription through a CBP-independent mechanism.

**DISCUSSION**

Several coactivators are essential for activation of CREB-mediated transcription. These include CBP (and its homolog p300) and a number of factors that bind CBP, such as p/CIP and PCAF. Studies with these coactivators suggest that they are present in limiting amounts for activation of transcription because when they are introduced into cells, they enhance transcription (13, 28, 45). In similar studies, we find that by increasing the cellular levels of SRCAP, we can increase the ability of CREB to activate transcription. One possible explanation for this observation is that activities associated with both CBP and SRCAP are needed for activation of CREB-mediated transcription (see model in Fig. 6). Similar observations have been reported for other coactivator proteins that interact with CBP, such as p/CIP and p/CAF. This has been demonstrated through the use of approaches that either limit the activity of the coactivator, such as microinjection of antibodies (28, 46), or antisense constructs that decrease the level of the coactivator (47, 48).

We show here that SRCAP significantly enhances CREB-dependent transcription from the PEPECK promoter. Although there are multiple cis-acting elements involved in PEPECK gene regulation (33, 34), SRCAP does not activate this promoter in the absence of PKA. This suggests that SRCAP is not involved in basal transcription, but rather it functions as a coactivator of a primed promoter. The activation observed from the ∆CRE-Gal4 PEPECK-CAT reporter by the Gal-CREB chimeric protein indicates that CREB is involved in SRCAP function. This conclusion is also supported by experiments demonstrating that SRCAP enhances CREB-mediated transcription of a simple reporter gene, Gal-CAT, which only contains binding sites for Gal4. Furthermore, SRCAP activates the transcription of other cAMP- and CREB-regulated promoters, such as those contained in somatostatin and enkephalin reporter genes (−18-fold increase; data not shown). Therefore, we conclude that SRCAP may be a general enhancer of CREB-mediated transcription.

We introduced a plasmid encoding the peptide corresponding to the CBP binding domain within SRCAP into cells to test the hypothesis that a SRCAP-CBP interaction is needed for activation of CREB-mediated transcription. This peptide, when expressed in cells, functioned as a dominant inhibitor of CREB-mediated transcription. Because this deleted portion of SRCAP lacks with the SRCAP binding domain also prevents CBP from functioning as a CREB coactivator (19).

The mechanism by which the interaction of SRCAP with CBP leads to activation of CREB-mediated transcription remains unclear. However, the results of our structure-function studies indicate that deletion of the N-terminal end of SRCAP (amino acids 1–1274) does not prevent SRCAP from enhancing CREB-mediated transcription. Because this deleted portion

**Fig. 5.** SRCAP contains multiple domains capable of activating transcription. The ability of Gal-SRCAP1–1186, Gal-SRCAP2316–2971, and Gal-SRCAP1275–2971 chimeras to activate transcription was compared with that of Gal1–147. HeLa cells were transiently transfected with the pGal-CAT reporter gene and equal molar amounts of plasmids encoding each of the Gal-SRCAP chimeric proteins. The relative CAT enzymatic activity was determined by dividing CAT enzymatic activity of each sample by the transcriptional activity induced by the Gal-SRCAP1275–2971 chimera (the activity of this chimera was assigned a relative value of 1). Values represent the means ± S.E. from two separate experiments in which each sample was assayed in triplicate.

**Fig. 6.** Model for activation of CREB-mediated transcription by SRCAP. Panel A, in cells containing low levels of SRCAP protein, CREB-mediated transcription is limited. Panel B, in the presence of excess SRCAP such as occurs in the presence of exogenously introduced SRCAP, CREB-mediated transcription is activated. Panel C, blocking the interaction of SRCAP with CBP by expression of a peptide corresponding to the CBP binding domain of SRCAP (SRCAp-CBD) inhibits CREB-mediated transcription.
Activation of CREB-mediated Transcription by SRCAP

These findings suggest that activation of transcription by SNF2 occurs through at least two distinct mechanisms, one requiring the ATPase function (e.g. the chromatin remodeling activity) and one that does not. Multiple functions have also been reported for the SNF2 family member Cockayne Syndrome B. Mutation of the ATPase domain of Cockayne Syndrome B also prevents it from remodeling chromatin but does not inhibit its ability to function as a topoisomerase (50). Our data suggest that SRCAP may also have multiple functions. One activity is independent of the ATPase function and allows SRCAP to activate CREB-mediated transcription, and a second function (not yet determined) requires ATPase activity.

Other proteins, most notably CBP and p300, have multiple domains with distinct activities which collectively contribute to their ability to activate transcription. Early studies of the function of CBP using Gal-CBP chimeras showed that several domains of CBP were able to activate transcription independently (19, 51). Subsequent studies with CBP have determined that several domains with distinct activities which collectively contribute to the ability of CBP to activate transcription include transcription factors, coactivators (p/CIP, P/CAF, and SRCAP), and C-terminal domains have the ability to bind proteins that function of CBP. The studies presented in this paper indicate that SRCAP and CBP to activate transcription also utilize SRCAP (an ability that has been reported recently for a number of CBP, contains at least 20 other proteins (54). We have found in immunoprecipitation studies with an anti-SRCAP antibody that SRCAP is part of a large multiprotein complex which, in addition to containing CBP (an ability that has been reported recently for a number of proteins, most notably CBP and p300, have multiple domains with distinct activities which collectively contribute to their ability to activate transcription. Early studies of the function of CBP using Gal-CBP chimeras showed that several domains of CBP were able to activate transcription independently (19, 51). Subsequent studies with CBP have determined that several domains with distinct activities which collectively contribute to the ability of CBP to activate transcription include transcription factors, coactivators (p/CIP, P/CAF, and SRCAP), and C-terminal domains have the ability to bind proteins that function of CBP. The studies presented in this paper indicate that SRCAP and CBP to activate transcription also utilize SRCAP (an ability that has been reported recently for a number of CBP, contains at least 20 other proteins (54). We have found in immunoprecipitation studies with an anti-SRCAP antibody that SRCAP is part of a large multiprotein complex which, in addition to containing CBP (an ability that has been reported recently for a number of proteins, most notably CBP and p300, have multiple domains with distinct activities which collectively contribute to their ability to activate transcription. Early studies of the function of CBP using Gal-CBP chimeras showed that several domains of CBP were able to activate transcription independently (19, 51). Subsequent studies with CBP have determined that several domains with distinct activities which collectively contribute to the ability of CBP to activate transcription include transcription factors, coactivators (p/CIP, P/CAF, and SRCAP), and C-terminal domains have the ability to bind proteins that...
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