From Androgen Receptor to the General Transcription Factor TFIIH

IDENTIFICATION OF cdk ACTIVATING KINASE (CAK) AS AN ANDROGEN RECEPTOR NH$_2$-TERMINAL ASSOCIATED COACTIVATOR*

(Received for publication, July 26, 1999, and in revised form, January 12, 2000)

Dong Kun Lee‡, Hai Ou Duan‡, and Chawnshang Chang§

From the George Whipple Laboratory for Cancer Research, Departments of Pathology, Urology, and Radiation Oncology, and the Cancer Center, University of Rochester Medical Center, Rochester, New York 14642

The androgen receptor (AR), like other steroid receptors, modulates the activity of the general transcription machinery on the core promoter to exert its function as a regulator. Co-immunoprecipitation of prostate cancer LNCaP cell extract using protein A-Sepharose coupled with anti-AR antibody indicates that the AR interacts with the general transcription factor TFIIH in a physiological condition. Co-transfection of cdk activating kinase (CAK), the kinase moiety of TFIIH, enhanced AR-mediated transcription in a ligand-dependent manner in human prostate cancer PC-3 and LNCaP cells, and in a ligand-independent manner in human prostate cancer DU145 cells. Detailed interaction studies further revealed that the AR NH$_2$-terminal domain interacting with CAK was essential for the CAK-induced AR transactivation. Together, our data suggest that the AR may interact with TFIIH for efficient communication with the general transcription factors/RNA polymerase II on the core promoter.

Androgen action is mediated through the androgen receptor (AR) to regulate androgen-responsive genes (1). The AR is a member of the steroid receptor superfamily that is composed of a variable amino-terminal domain, a highly conserved DNA-binding domain (DBD), and a ligand-binding domain (2, 3).

Ligand-dependent transcriptional activation of steroid receptors is mediated by the carboxyl-terminal domain that includes a ligand-binding domain and activation function-2 (3). Crystallographic studies show that ligand-bound steroid receptors undergo a conformational change in the activation function-2 core motif (4, 5). The ligand-induced conformational change presumably recruits coregulators as well as the basal transcriptional machinery for the target gene expression. The coregulators of nuclear receptors (ARA24, ARA54, ARA55, ARA70, ARA160, CBP/p300, p/CIP/ACTR/AIB1, Rb, RIP140, SRC-1/NCoA-1, TIF-2/GRIP1, and TRAPs/DRIPs) have recently been cloned and characterized (6–18). It has been proposed that coregulators function as a bridge between activators and the basal transcription machinery (19). They may potentiate transactivation of nuclear receptors in transient transfection or in vitro transcription assays through the modification of nucleosomal structure or the efficient recruitment of basal transcription machinery. A growing number of coregulators (such as SRC-1, ACTR, and PCAF) of steroid receptors have been reported to possess and/or recruit histone acetyltransferase activity to induce modification of nucleosomal structures leading to activation of transcription (20–22). In contrast to coactivators, corepressors (such as NCoR-1 and SMRT) bind to the nuclear receptors in the absence of ligands, recruit histone deacetyltransferase, and lead to condensation of nucleosomal structures for repression of transcription (23, 24).

The amino-terminal domain of steroid receptors contains a ligand-independent activation function-1 (AF-1), which is under the control of activation function-2. The amino-terminal domain of steroid receptors has been reported to interact with general transcription factors, as exemplified by AR interaction with transcription factor IIF (TFIIF) (25), thyroid receptor interaction with transcription factor IIB (TFIIB) (26), and vitamin D receptor interaction with TFIIB (27). However, the molecular mechanism by which AF-1 synergistically activates transcription remains unclear.

Steroid receptors are phosphoproteins and their activities can be modulated by phosphorylation (28). Recent studies have shown that cross-talk between the receptor signaling pathways and the phosphorylation signal transduction pathways may lead to the hormone refractory tumor growth. The estrogen receptor (ER) and progesterone receptor mediate gene transcription in response to insulin growth factor-1, epidermal growth factor, protein kinase A, and dopamine in the absence of ligand (29, 30). The activity of ER AF-1 has been shown to be dependent on phosphorylation of a highly conserved serine residue, Ser-118 (31). The AR can also be activated by insulin growth factor-1, epidermal growth factor, protein kinase A, and mitogen-activated protein kinase in the absence of androgen (32, 33). In addition to these signaling pathways, mitogen-activated protein kinase phosphorylates Ser-Pro motifs of the AR (34), suggesting that steroid receptors can be phosphorylated through different pathways. Recent studies showed that the CAK induces phosphorylation of the amino-terminal domain of ER, glucocorticoid receptor, and retinoic acid receptor and enhances their activity (35–37).

In an effort to analyze AR-mediated transactivation, we performed co-immunoprecipitation of LNCaP nuclear extracts using anti-AR antibody, followed by Western blot with antibodies against various general transcription factors. We found that the AR interacted with TFIIH in a physiological condition and...
that overexpression of CAK, the kinase moiety of TFIIF, enhanced AR-mediated transactivation in prostate cancer cells. We also demonstrated that the AR NH2-terminal domain interacts with CAK and is required for CAK-induced AR transactivation.

MATERIALS AND METHODS

Plasmids—The complementary DNA fragments for cdk7, cyclin H, MAT1, and GAL4-SP1 were generated by polymerase chain reaction and inserted into pSuperFect (Qiagen). The plasmid encoding GAL4-DBD fused with the AR NH2-terminal domain (GAL4-ARN) was constructed by ligation of psG5GAL4-DBD (1-147) and a DNA fragment encoding the AR NH2-terminal domain amino acids from 38 to 561.

Cell Culture and Transfection Assay—DU145 cells, PC-3 cells, and LNCaP cells were maintained in Dulbecco’s modified Eagle’s medium (Life Technologies, Inc.) supplemented with 10% heat inactivated fetal bovine serum, supplemented with 10% fetal bovine serum, respectively. All media contained 50 units/ml penicillin and 50 μg/ml streptomycin. Cells were seeded to be a density of 50–60% confluency for transfection. Cells in 35-mm dishes were refed with fresh medium 2 h before transfection and transfected with 2 μg of DNA according to the “SuperFect Transfection” instruction (Qiagen). After 2–3 h incubation, cells were treated with medium supplemented with charcoal-depleted fetal bovine serum containing either ethanol or ligands. Cells were further incubated at 37 °C for 24 h, washed with phosphate-buffered saline, and harvested. Cell lysates were prepared and used for luciferase assay according to the manufacturer’s instruction (Promega). Relative luciferase activities were plotted using the activity of AR in the absence of ligand and coactivator as 1.

The results were obtained from at least three sets of transfection and presented as mean ± S.D.

Immunoprecipitation—LNCaP cells were grown in RPMI 1640 supplemented with 10% fetal bovine serum. LNCaP nuclear extracts were prepared as described previously (38) and aliquots stored at −70 °C.

For immunoprecipitation, protein A-Sepharose (Amersham Pharmacia Biotech) resins were incubated with bovine serum albumin (1 mg/ml) overnight, washed with phosphate-buffered saline, and coupled to anti-human AR polyclonal antibody (NH27) as follows. Swollen protein A-Sepharose (100 μl) was incubated with 500 μl of crude immune serum raised against AR. IgG was incubated overnight at 4 °C followed by two washes with 0.2 M sodium borate. Diaminodipropylamine from ICN was raised against AR. IgG was incubated overnight at 4 °C followed by two washes with 0.2 M sodium borate.

Ar-P40 (0.5%) (data not shown), suggesting tight interaction between the AR and TFIIF. Although AR interacts with both free CAK and CAK associated with TFIIF, it appears that AR may interact preferentially with free CAK based on quantitation of immunoprecipitated cdk7 and p62 (compare lanes 4 and 6 in Fig. 1). In addition, the reciprocal co-immunoprecipitation of LNCaP nuclear extract with anti-p62 antibody could not detect AR in the immunoprecipitated samples, suggesting that only a fraction of TFIIF is associated with AR.

Rap74, the large subunit of another general transcription factor TFIIB, was also detected in the immunoprecipitated complex of LNCaP nuclear extracts with anti-human AR antibody (data not shown), although interaction between the AR and Rap74 was less resistant to high ionic strength or high concentration of nonionic detergent. In contrast, TBP or TFIIB was not detected in the immunoprecipitated complex of LNCaP nuclear extracts (data not shown) even in a low stringent condition (0.1 M KCl in the absence of Nonidet P-40). Taken together, our immunoprecipitation data suggest that AR can communicate with the general transcription machinery on the core promoter through the interaction with TFIIF and/or TFIIF.
also performed. Although transfection of the individual subunits could moderately enhance AR transactivation, co-expression of the three subunits was most efficient in PC-3 (Fig. 3A) and DU145 cells (Fig. 3B). These data suggest that transfection of one subunit may be able to stimulate other endogenous subunits to form an active CAK complex to enhance AR-mediated transactivation, although simultaneous transfection of three subunits renders higher induction of AR transactivation.

**Fig. 2.** Enhancement of AR-mediated transcription in prostate cancer cells by CAK overexpression. A, AR-positive LNCaP cells were transiently transfected using SuperFect transfection reagent (Qiagen) with 600 ng of murine mammary tumor virus-luciferase reporter plasmid, 50 ng of pRL-CMV plasmid as an internal control of transfection efficiency, and with or without 400 ng of plasmid-encoding CAK subunits as indicated. The total amounts of plasmid were adjusted to 2 μg with vector plasmid pSG5. The results obtained in the presence and absence of DHT are shown in open and closed bars, respectively. B, AR-deficient PC-3 cells were transiently transfected with 600 ng of murine mammary tumor virus-luciferase reporter plasmid, 50 ng of pRL-CMV plasmid, with or without 400 ng of plasmid-encoding CAK subunits. Lanes 5–8 also contain 50 ng of AR expression plasmid (pSG5-AR). The experiments were performed as described above. C, AR-negative DU145 cells were transfected as described in B.

**Fig. 3.** Effect of individual subunit of CAK on AR transactivation. PC-3 cells (A) and DU145 cells (B) were transiently transfected as described in the legend to Fig. 2. Results in lanes 3–8 were obtained with transfection of three plasmids encoding CAK subunits (400 ng each). Results in lanes 9–14 were obtained with transfection of 400 ng of plasmid-encoding single subunit of CAK.
As AR ligand-binding domain associated coregulators (ARAs) have been identified by yeast two-hybrid screening assay (6–9), we were interested in comparing the coregulator activity of CAK with other ARAs in DU145 cells. As shown in Fig. 4, ARA70N and ARA55 induced AR transactivation only in the presence of 1 nM DHT. In contrast, CAK induced AR transactivation in the presence or absence of 1 nM DHT in DU145 cells, suggesting that different coregulators may utilize different mechanisms to enhance AR transactivation.

A recent study suggests that the agonist activity of anti-androgens could be enhanced by selective coregulators, such as ARA70N and ARA55 (9, 40). We were therefore interested in determining the potential effects of anti-androgens on CAK-enhanced AR transactivation. As shown in Fig. 5, hydroxyflutamide, casodex, and RU58841, at the pharmacological concentration of $10^{-6}$ M, efficiently inhibited the CAK-induced AR transactivation, suggesting that only selective AR coregulators may be able to modulate the agonist activity of anti-androgens.

CAK Activates the AR NH2-terminal Domain Fused with the GAL4-DNA-binding Domain (GAL4-ARN)—As AF-1 has been suggested to play an important role in the ligand-independent receptor activation and our data showed CAK could induce ligand-independent AR transactivation in DU145 cells (Fig. 2C), we therefore analyzed whether CAK can activate the AR transactivation through the AF-1 domain. An expression vector for GAL4-ARN and the reporter plasmid E1b-luciferase containing 5 GAL4-binding sites were used to replace the full-length AR and the reporter plasmid murine mammary tumor virus-luciferase used in the previous transient transfection assay. As shown in Fig. 6, addition of GAL4-ARN resulted in approximately 4-fold induction of transcription of the reporter gene (lanes 1 versus 3). While co-transfection of CAK did not enhance GAL4-DBD-mediated transcription (lanes 1 versus 2), co-transfection of CAK further enhanced GAL4-ARN mediated transcription approximately 2-fold (lanes 3 versus 4). When another GAL4-fused activator, GAL4-SP1, was used in place of GAL4-ARN, CAK co-transfection showed only a marginal effect on transcription of the reporter gene (lanes 5 and 6), suggesting that not every GAL4-fused activator could be enhanced by CAK and that CAK-induced GAL4-ARN transactivation was specific. Similar results were obtained when we replaced PC-3 cells with DU145 cells (data not shown). Together, these results clearly indicate that CAK-induced AR transactivation is mediated through the AR AF-1 domain.

Cdk7 and Cyclin H Interact with the NH2-terminal Domain of AR—To further confirm that CAK may enhance AR transactivation through the AF-1 domain, interaction studies between the AR NH2-terminal domain and CAK subunits were performed. 35S-Labeled cdk7, cyclin H, and MAT1 were incubated with bacterial lysates containing histidine-tagged AR NH2-terminal domain (Fig. 7 lanes 2, 5, and 8). For the control, bacterial lysate without histidine-tagged AR NH2-terminal domain was used in parallel (lanes 3, 6, and 9). The proteins were
bound to Ni resins, and the resins were extensively washed. The proteins eluted from the resins were analyzed on SDS-polyacrylamide gels. About 5% of TNT expressed samples were loaded on lanes 1, 4, and 7.

FIG. 7. The AR NH2-terminal domain interacts with cdk7 and cyclin H. Bacterial lysate containing histidine-tagged AR NH2-terminal domain was incubated with Ni resins. For the control, bacterial lysate without histidine-tagged AR NH2-terminal domain was used in parallel. The resins were incubated with TNT-expressed 35S-labeled cdk7, cyclin H, and MAT1. The resins were extensively washed with 20 mM HEPES (pH 7.8), 20% glycerol, 0.1% Nonidet P-40, 0.5 mM dithiothreitol, and 200 mM KCl. Proteins were eluted and analyzed on SDS-polyacrylamide gels. About 5% of TNT expressed samples were loaded on lanes 1, 4, and 7.

FIG. 6. The AR NH2-terminal domain is required for CAK-induced AR activation. PC-3 cells were transiently transfected with 400 ng of p5GEluciferase reporter plasmid containing 5 GAL4-binding sites, 50 ng of pRL-CMV, and with or without plasmids encoding CAK as indicated. Lanes 1 and 2 are results obtained with 200 ng of plasmids encoding GAL4-DBD, lanes 3 and 4 with GAL4-ARN, and lanes 5 and 6 with GAL4-Sp1.

In this paper, we show that AR interacts with the general transcription factor TFIIH in a physiological condition (Fig. 1). A study of the physical interaction between the AR and TFIIH indicates that cdk7 and cyclin H, two subunits of CAK, specifically interact with the AR NH2-terminal domain (Fig. 7). Early studies showed that CAK could also interact with a few activators, such as POU domain and retinoic acid receptor α, and modulate their transcriptional activity (36, 42). Although it is unknown whether these interactions result in transcriptional activation through the same mechanism, it is generally accepted that they may modulate activity of the general transcription machinery on the promoter. The AR interaction with TFIIH may provide efficient communication between the AR and the general transcription factors/RNA polymerase II on the promoter.

To analyze the significance of AR interaction with cdk7 and cyclin H in a physiological context, prostate cancer cell lines were used in a transient transfection assay. Co-transfection of CAK enhanced AR transactivation in LNCaP and PC-3 cells predominantly in a ligand-dependent manner and in prostate cancer DU145 cells in a ligand-independent manner (Fig. 2). The difference of the CAK effect on the ligand dependence of AR-mediated transactivation might be due to differences in cell environments of cell lines and needs to be further studied. The mechanism of CAK-induced AR transactivation was further analyzed using chimeric activators fused with the GAL4-DNA-binding domain (Fig. 6). The GAL4-ARN in conjunction with CAK could enhance transcription of the reporter gene containing 5 GAL4-binding sites much more efficiently than GAL4-Sp1 in conjunction with CAK. This result demonstrates that the AR AF-1 motif is required for the CAK-induced AR transactivation. Taken together, CAK interacts with the AR NH2-terminal domain and enhances AR transactivation through AR AF-1.

CAK is a proline-directed protein kinase. The earlier studies showed that a fraction of CAK is associated with TFIIH (39). Human TFIIH consists of 6 core subunits (p89, p80, p62, p52, p44, and p34) and 3 subunits (MAT1, cyclin H, and cdk7) for the protein kinase moiety (39). TFIIH-associated CAK can phosphorylate the COOH-terminal domain of the largest subunit of RNA polymerase II (39). The phosphorylation of the COOH-terminal domain has been shown to be a key step needed to enter an elongation mode from the preinitiation complex formation on the promoter. The interaction between AR and TFIIH could enhance AR-mediated transcription through two different pathways. First, the AR bound TFIIH-associated CAK can enhance phosphorylation of the RNA polymerase COOH-terminal domain, which subsequently facilitates a transition from an initiation mode to an elongation mode. Second, the TFIIH-associated CAK could increase phosphorylation of AR. Phosphorylation of the receptor can play a pivotal role in regulation of the receptor, such as nuclear translocation, DNA binding, and interaction with regulatory proteins (28). A recent study suggests that the TFIIH-associated CAK can phosphorylate the NH2-terminal domain of retinoic acid receptor α and enhance its transcriptional activity in a ligand-dependent manner (36). Other studies indicate that the CAK can also induce phosphorylation of glucocorticoid receptor or ER and lead to the ligand-independent activation of the receptors (35, 37). Thus, the first pathway activates transcription through the enhanced efficiency of transcription elongation, while the second pathway activates transcription through the increasing number of preinitiation complexes formed on the core promoter. Since results of a co-immunoprecipitation assay demonstrate that the AR associates with both core TFIIH and CAK, it is highly possible that the TFIIH-associated CAK interacts with the AR NH2-terminal domain and enhances AR-mediated transcription through the AR AF-1. Further studies may tell us how stimulation of the AR AF-1 by CAK results in the activation of AR-mediated transcription in prostate cancer cells.

DISCUSSION

In this study, we show that AR interacts with the general transcription factor TFIIH in a physiological condition (Fig. 1). A study of the physical interaction between the AR and TFIIH indicates that cdk7 and cyclin H, two subunits of CAK, specifically interact with the AR NH2-terminal domain (Fig. 7). Early studies showed that CAK could also interact with a few activators, such as POU domain and retinoic acid receptor α, and modulate their transcriptional activity (36, 42). Although it is unknown whether these interactions result in transcriptional activation through the same mechanism, it is generally accepted that they may modulate activity of the general transcription machinery on the promoter. The AR interaction with TFIIH may provide efficient communication between the AR and the general transcription factors/RNA polymerase II on the promoter.

To analyze the significance of AR interaction with cdk7 and cyclin H in a physiological context, prostate cancer cell lines were used in a transient transfection assay. Co-transfection of CAK enhanced AR transactivation in LNCaP and PC-3 cells predominantly in a ligand-dependent manner and in prostate cancer DU145 cells in a ligand-independent manner (Fig. 2). The difference of the CAK effect on the ligand dependence of AR-mediated transactivation might be due to differences in cell environments of cell lines and needs to be further studied. The mechanism of CAK-induced AR transactivation was further analyzed using chimeric activators fused with the GAL4-DNA-binding domain (Fig. 6). The GAL4-ARN in conjunction with CAK could enhance transcription of the reporter gene containing 5 GAL4-binding sites much more efficiently than GAL4-Sp1 in conjunction with CAK. This result demonstrates that the AR AF-1 motif is required for the CAK-induced AR transactivation. Taken together, CAK interacts with the AR NH2-terminal domain and enhances AR transactivation through AR AF-1.

CAK is a proline-directed protein kinase. The earlier studies showed that a fraction of CAK is associated with TFIIH (39). Human TFIIH consists of 6 core subunits (p89, p80, p62, p52, p44, and p34) and 3 subunits (MAT1, cyclin H, and cdk7) for the protein kinase moiety (39). TFIIH-associated CAK can phosphorylate the COOH-terminal domain of the largest subunit of RNA polymerase II (39). The phosphorylation of the COOH-terminal domain has been shown to be a key step needed to enter an elongation mode from the preinitiation complex formation on the promoter. The interaction between AR and TFIIH could enhance AR-mediated transcription through two different pathways. First, the AR bound TFIIH-associated CAK can enhance phosphorylation of the RNA polymerase COOH-terminal domain, which subsequently facilitates a transition from an initiation mode to an elongation mode. Second, the TFIIH-associated CAK could increase phosphorylation of AR. Phosphorylation of the receptor can play a pivotal role in regulation of the receptor, such as nuclear translocation, DNA binding, and interaction with regulatory proteins (28). A recent study suggests that the TFIIH-associated CAK can phosphorylate the NH2-terminal domain of retinoic acid receptor α and enhance its transcriptional activity in a ligand-dependent manner (36). Other studies indicate that the CAK can also induce phosphorylation of glucocorticoid receptor or ER and lead to the ligand-independent activation of the receptors (35, 37). Thus, the first pathway activates transcription through the enhanced efficiency of transcription elongation, while the second pathway activates transcription through the increasing number of preinitiation complexes formed on the core promoter. Since results of a co-immunoprecipitation assay demonstrate that the AR associates with both core TFIIH and CAK, it is highly possible that the TFIIH-associated CAK interacts with the AR NH2-terminal domain and enhances AR-mediated transcription through the AR AF-1. Further studies may tell us how stimulation of the AR AF-1 by CAK results in the activation of AR-mediated transcription in prostate cancer cells.
Acknowledgments—We thank Yi-Fen Lee, Pei-Wen Hsiao, and Shuyuan Yeh for discussion; Karen Wolf for critical comments on the manuscript; J. D. Morgan for plasmids; and R. G. Roeder for plasmids and antisera.

REFERENCES

1. Chang, C., Salezman, A., Yeh, S., Young, W., Keller, E., Lee, H. J., Wang, C., and Mizokami, A. (1995) Crit. Rev. Eukaryotic Gene Exp. 5, 97–125
2. Chang, C., Kokontis, J., and Liao, S. T. (1988) Science 240, 334–336
3. Evans, R. M. (1988) Science 240, 889–895
4. Brzozowski, A. M., Pike, A. C. W., Dauter, Z., Hubbard, R. E., Bonn, T., Engstrom, O., Ohman, L., Greene, G. L., Gustafsson, J.-A., and Carlquist, M. (1997) Nature 389, 753–757
5. Williams, S. P., and Sigler, P. B. (1998) Nature 393, 392–396
6. Yeh, S., and Chang, C. (1996) Proc. Natl. Acad. Sci. U. S. A. 93, 5517–5521
7. Kang, H. Y., Yeh, S., Fugimoto, N., and Chang, C. (1999) J. Biol. Chem. 274, 8570–8576
8. Yeh, S., Miyamoto, H., Nishimura, N., Kang, H., Ludlow, J., Hsiao, P., Wang, C., and Chang, C. (1998) Biochim. Biophys. Res. Commun. 248, 361–361
9. Fugimoto, N., Yeh, S., Kang, H. Y., Inui, S., Chang, H.-C., Mizokami, A., and Chang, C. (1999) J. Biol. Chem. 274, 8316–8321
10. Hsiao, P.-W., and Chang, C. (1999) J. Biol. Chem. 274, 22375–22379
11. Hsiao, P.-W., Lin, D.-L., Nakao, R., and Chang, C. (1999) J. Biol. Chem. 274, 20229–20234
12. Glass, C. K., Rose, D. W., and Rosenfeld, M. G. (1997) Curr. Opin. Cell Biol. 9, 222–233
13. Chen, H. W., Lin, R. J., Schiltz, R. L., Chakravati, D., Nash, L., Privalsky, M. L., Nakatani, Y., and Evans, R. M. (1997) Cell 90, 589–589
14. Hong, H., Kohli, K., Garabedian, M. J., and Stallcup, M. R. (1997) Mol. Cell. Biol. 17, 397–403
15. Li, H., Gomes, P. J., and Chen, D. J. (1997) Proc. Natl. Acad. Sci. U. S. A. 94, 8479–8484
16. Fendell, J. J., Ge, H., and Roeder, R. G. (1996) Proc. Natl. Acad. Sci. U. S. A. 93, 8329–8333
17. Rachez, C., Suldan, Z., Ward, J., Chang, C.-P. B., Burakov, D., Erdjument-Bromage, H., Tempst, P., and Freedman, L. (1998) Genes Dev. 12, 1787–1800
18. Vogel, J. J., Heine, M. J., Zechel, C., Champon, P., and Gronemeyer, H. (1996) EMBO J. 15, 3461–3468
19. Beato, M., and Sanchez-Pacheco, A. (1996) Endocr. Rev. 17, 587–609
20. Bannister, A. J., and Kouzarides, T. (1996) Nature 384, 641–644
21. Dryzko, V. V., Schlitz, R. L. Russanov, V., Howard, B. H., and Nakatani, Y. (1996) Cell 89, 953–959
22. Spencer, T. E., Jenster, G., Burcin, M. M., Allis, C. D., Zhou, J. X., Mizzen, C. A., McKenna, N. J., Onate, S. A., Tsai, S. Y., Tsai, M. J., and O'Malley, B. W. (1997) Nature 389, 3594–3597
23. Heinzel, T., Lavinsky, R. M., Mullen, T. M., Soderstrom, M., Laherty, C. D., Torchia, J., Yang, W. M., Brad, G., Ngo, S. D., Davie, J. R., Seto, E., Eisenman, R. N., Rose, D. W., Glass, C. K., and Rosenfeld, M. G. (1997) Nature 387, 45–48
24. Nagy, L., Kao, H. Y., Chakravati, D., Lin, R. J., Hasseig, C. A., Ayer, D. E., Schreiber, S. L., and Evans, R. M. (1997) Cell 89, 373–380
25. McEwan, I. J., and Gustafsson, J. A. (1997) Proc. Natl. Acad. Sci. U. S. A. 94, 8483–8489
26. Hadzic, E., Desai-Yajnik, V., Helmer, E., Guo, S., Wu, S., Koudinova, N., Casanova, J., Raaka, B. M., and Samuels, H. H. (1995) Mol. Cell. Biol. 15, 4507–4517
27. Blanco, J., Wang, I., Tsai, S., Tsai, M., O'Malley, B., Jurutka, P., Haussler, M., and Ozato, K. (1995) Proc. Natl. Acad. Sci. U. S. A. 92, 1535–1539
28. Weigel, N. L. (1996) Biochem. J. 319, 657–667
29. O'Malley, B. W., Schrader, W. T., Mani, S., Smith, C., Weigel, N. L., Connelly, O. M., and Clark, J. H. (1995) Recent Prog. Hormone Res. 50, 333–347
30. Picard, D., Bunone, G., Liu, J. W., and Donze, O. (1997) Biochem. Soc. Trans. 25, 597–602
31. Le Goff, P., Montano, M. M., Schodin, D. J., and Katzenellenbogen, B. S. (1994) J. Biol. Chem. 269, 4458–4466
32. Culig, Z., Hobiisch, A., Cremauer, M. V., Radmayer, C., Trappman, J., Hittmair, A., Bartsh, G., and Klocker, H. (1994) Cancer Res. 54, 5472–5479
33. Nazareth, L. V., and Weigel, N. L. (1997) J. Biol. Chem. 271, 19900–19907
34. Yeh, S., Lin, H. K., Kang, H. Y., and Chang, C. (1999) Proc. Natl. Acad. Sci. U. S. A. 96, 5458–5463
35. Kretic, M. D., Rogatsky, I., Yamamoto, K. R., and Garabedian, M. J. (1997) Mol. Cell. Biol. 17, 3947–3954
36. Rochette-Egly, C., Adam, S., Rossignol, M., Egly, J.-M., and Champon, P. (1997) Cell 90, 97–107
37. Trowbridge, J. M., Rogatsky, I., and Garabedian, M. J. (1997) Proc. Natl. Acad. Sci. U. S. A. 94, 10132–10137
38. Andrews, N. C., and Faller, D. V. (1991) Nucleic Acids Res. 19, 2499
39. Svejstrup, J. Q., Vivhi, P., and Egly, J.-M. (1996) Trends Biochem. Sci. 21, 346–350
40. Miyamoto, H., Yeh, S., Wilding, G., and Chang, C. (1998) Proc. Natl. Acad. Sci. U. S. A. 95, 7379–7384
41. Langley, E., Kemppainen, J. A., and Wilson, E. M. (1998) J. Biol. Chem. 273, 92–101
42. Inamoto, S., Segil, N., Pan, Z. Q., Kimura, M., and Roeder, R. G. (1997) J. Biol. Chem. 272, 26852–26858
From Androgen Receptor to the General Transcription Factor TFIIH: IDENTIFICATION OF cdk ACTIVATING KINASE (CAK) AS AN ANDROGEN RECEPTOR NH2-TERMINAL ASSOCIATED COACTIVATOR
Dong Kun Lee, Hai Ou Duan and Chawnshang Chang

J. Biol. Chem. 2000, 275:9308-9313.
doi: 10.1074/jbc.275.13.9308

Access the most updated version of this article at http://www.jbc.org/content/275/13/9308

Alerts:
• When this article is cited
• When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 42 references, 23 of which can be accessed free at http://www.jbc.org/content/275/13/9308.full.html#ref-list-1