Casein Kinase 2 Interacts with Cyclin-dependent Kinase 11 (CDK11) in Vivo and Phosphorylates Both the RNA Polymerase II Carboxyl-terminal Domain and CDK11 in Vitro*

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The PITSLEIRE protein kinases, hereafter referred to as cyclin-dependent kinase 11 (CDK11) due to their association with cyclin L, are part of large molecular weight protein complexes that contain RNA polymerase II (RNAP II) as well as numerous transcription and RNA processing factors. Data presented here demonstrate that the influence of CDK11p110 on transcription and splicing does not involve phosphorylation of the RNAP II carboxyl-terminal domain by CDK11p110. We have isolated a DRB- and heparin-sensitive protein kinase activity that co-purifies with CDK11p110 after ion exchange and affinity purification chromatography. This protein kinase was identified as casein kinase 2 (CK2) by immunoblot and mass spectrometry analyses. In addition to the RNAP II carboxyl-terminal domain, CK2 phosphorylates the CDK11p110 amino-terminal domain. These data suggest that CDK11p110 isoforms participate in signaling pathways that include CK2 and that its function may help to coordinate the regulation of RNA transcription and processing events. Future experiments will determine how phosphorylation of CDK11p110 by CK2 specifically affects RNA transcription and/or processing events.

The complex biochemical events of transcription and RNA processing, resulting in the production of mature RNA transcripts, are now understood to be highly integrated and co-dependent processes (1). It is hypothesized that regulation of these events occurs through the active exchange of associated factors with the RNAP II complex (2–4). This hypothesis is based upon identification of numerous positive and negative regulatory factors/complexes, influencing both transcription and RNA processing enzymes, in physical association with RNAP II. Many of these complexes exert their effects directly or indirectly through association with the RNAP II CTD. In mammals, the RNAP II CTD is composed of 52 heptapeptide repeats with the consensus sequence Tyr-Ser-Pro-Thr-Pro-Ser (YSPTPS), which are essential for viability (5).

The RNAP II CTD is heavily phosphorylated in vivo, and it is likely that sequential phosphorylation events, as well as phosphorylation of specific residues by specific protein kinases, help regulate transcript production. This model appears to fit much of the data coming from numerous laboratories and was recently proposed as the most likely means of coordinating the various steps of transcription, RNA processing, and mRNA export (6). Many protein kinases modify the RNAP II CTD. Several of the CTD kinases identified thus far are from the cyclin-dependent kinase family (CDKs) and include CDK1, CDK7, CDK9, and CDK10. In addition, another regulator of cell cycle events, casein kinase 2 (CK2), is known to phosphorylate a number of transcriptional proteins, including the RNAP II CTD and the RAP74 subunit of TFIIH (7, 8).

Data from this laboratory and others demonstrate that the CDK11p110 (PITSLEIRE) protein kinases associate with the cyclin L regulatory protein, bind directly to various splicing factors, and play a role in pre-mRNA splicing (9–11). Moreover, we recently published results indicating a potential role for CDK11p110 in the regulation of transcription as well (12). Experiments are described here demonstrating that the CDK11p110 protein kinases are members of RNAP II-containing complexes that include CK2. Furthermore, CDK11p110 immunoprecipitation complexes (IP complexes) contain an RNAP II CTD-directed kinase activity. However, we show that CK2, and not CDK11p110, is the kinase responsible for this RNAP II CTD phosphorylation. In addition, we demonstrate that CDK11p110 association with, and amino-terminal phosphorylation by, CK2 in vivo requires the RD/RE protein interaction domain of CDK11p110. Thus, the data herein suggest the existence of CDK11p110 protein complexes in which signaling to the RNA transcriptional and processing machinery may be influenced by CK2 kinase activity.

Materials and Methods

Cell Culture and Transfection—HeLa Tet Off and 293T cells were maintained in Dulbecco’s modified Eagle’s medium supplemented with 10% fetal calf serum, 2% glutamine, and 0.1% gentamicin. CEM C7 cells were maintained in RPMI supplemented with 10% heat-inactivated fetal calf serum, 2% glutamine, and 0.1% gentamicin. Transfections were carried out using FuGENE 6 (Roche Molecular Biochemicals) according to the manufacturer’s instructions with a reagent/DNA ratio of 3:1.

Antibodies—The PITSLEIRE/CDK11 antibodies P2N100, P1C, and GN1 have been described previously (9, 12, 13). Commercial antibodies used include anti-CK2a (C-18), anti-ERK3 (D23), anti-TFIIH p62 (P-19), anti-CDK7 (C-19), and anti-FLAG (Oct-A D8) antibodies from

D. Hu, A. Mayeda, J. H. Trembley, J. M. Lahti, and V. J. Kidd, manuscript in preparation.

J. H. Trembley, P. Loyer, D. Hu, and V. J. Kidd, unpublished data.
Production of Recombinant Protein—The GST-CTD\\textsuperscript{52-52} construct was made using a PCR product from an EST clone. The GST-CTD\\textsuperscript{WT14} construct was a gift from Dr. J. Corden (14). GST fusion proteins were induced with 0.1 mM isopropyl-1-thio-galactoside at room temperature for 3 h. The cells were then pelleted by centrifugation, resuspended in cold PBS, and then sonicated on ice. Triton X-100 was added to 1%, and the lysate was spun at 10,000 \( \times \) g for 20 min at 4°C. The supernatant was incubated with glutathione-Sepharose 4B beads overnight, rotating at 4°C. The beads were washed three times in 100 bed volumes of cold PBS, and the remaining bound proteins were eluted in 4 bed volumes of 50 mM Tris (pH 8) containing 20 mM glutathione. The eluted proteins were dialyzed into 40 mM Hepes (pH 7.9), 100 mM KCl, 50 \( \mu \)M ZnSO\(_4\), and 10% glycerol.

Mapping of the CK2 Binding Region to CDK11\(^{p110}\) and the Region of Phosphorylation—The RD/RE and poly(E) deletion constructs were made using the QuikChange\\textsuperscript{TM} site-directed mutagenesis kit (Stratagene) with modifications as described by Wang and Malcolm (15). CDK11\(^{p110}\) amino-terminal deletion constructs (M91, N290, N375, and N424) are either described in Ref. 16 or were made using PCR as previously described in Ref. 16. All constructs were verified before use by DNA sequence analysis.

Immunoprecipitations and Immunoblots—Transfected cells were lysed in 50 mM Hepes (pH 7.9), 150 mM NaCl, 0.1 mM EDTA, 0.5% Tween 20, 10% glycerol, and complete protease inhibitors (Roche Molecular Biochemicals). Incubations with antibodies for the purpose of immunoprecipitation of protein complexes were performed in lysis buffer for 2 h at 4°C. Washes were performed three times using 1 ml of lysis buffer. Immunoblot analysis was performed as previously described (9).

Protein Kinase Assays—For the CTD kinase assays, immunoprecipitations performed as described above were resuspended in 10 ml of kinase buffer (without ATP). Substrate (1 \( \mu \)g) was added in a total volume of 10 \( \mu \)l of water, followed by 10 \( \mu \)l of 2 \( \times \) kinase buffer containing cold and \([\gamma^{32P}]ATP\), making the final volume 30 \( \mu \)l. The kinase reactions were incubated for 10 min at 30°C. The final protein kinase reaction buffer contained 40 mM Hepes (pH 7.4), 10 mM MgCl\(_2\), 5 mM EGTA, 1 mM dithiothreitol, 0.5 mg/ml acetylated BSA, 10 \( \mu \)M ATP, 3–5 \( \mu \)Ci of \([\gamma^{32P}]ATP\), 2 mM benzamidine, 60 mM \( \beta \)-glycerophosphate, 0.1 mM Na\(_2\)VO\(_4\), and 0.1 mM NaF. For the heparin- and DRB-containing protein kinase reaction, the drugs were incubated with the beads for 5 min at room temperature prior to the addition of substrate and ATP-containing kinase buffer. Heparin was obtained from Sigma (H-4784; stock solution made in water at 50 mg/ml) and American Pharmaceutical Partners, Inc. (100 US units/ml). The effective concentration range (with no effect on TFIIH) for the Sigma heparin was 2–10 \( \mu \)g/ml, and the range for the American Pharmaceutical Partners, Inc. heparin was 0.33–2.5 units/ml (0.01–0.075 units/ml0.3\( \mu \)l reaction volume). The protein kinase reaction supernatants were boiled in sample buffer and subjected to 10% SDS-PAGE analysis. The gels were washed extensively in 40% methanol, 10% acetic acid; dried; and exposed to x-ray film.

Protein Chromatography—Using a Bio-Rad BioLogic HR chromatography system, a cellulose phosphate P11 (Whatman) cation exchange film. The RD/RE and poly(E) deletion constructs were subjected to 10% SDS-PAGE analysis. The gels were washed extensively in 40% methanol, 10% acetic acid; dried; and exposed to x-ray film.

RESULTS

An RNAP II CTD-directed Kinase Activity Co-immunoprecipitates with CDK11\(^{p110}\) Protein Kinase—We recently published data demonstrating that CDK11\(^{p110}\) affinity-purified complexes contain RNAP II (12). Furthermore, we observed that interference with CDK11\(^{p110}\) activity negatively affected transcript production in vitro. Given that CDK11\(^{p110}\) is found in RNAP II complexes, it was reasonable to determine whether the RNAP II CTD was a substrate for this kinase. Protein kinase assays, from immunoprecipitations using several affinity-purified CDK11\(^{p110}\) antibodies in parallel with known CTD kinases such as CDK7 and CDK1, suggested that the RNAP II CTD was a good substrate for CDK11\(^{p110}\) (data not shown). Characterization of this kinase activity revealed that the imperfect consensus repeats (repeats 32–52) were a much better substrate for this kinase activity than the perfect repeats (Fig. 1A). To verify that this CTD kinase activity was due to CDK11\(^{p110}\) and not to a co-immunoprecipitating kinase, three different kinase-inactive, FLAG-tagged CDK11\(^{p110}\) mutants were transiently transfected into HeLa cells in parallel with a FLAG-tagged version of the wild-type CDK11\(^{p110}\) kinase. The point mutations for the kinase inactive forms of CDK11\(^{p110}\) included K439N, D534N, and D552N. These mutations were selected based upon previous studies of serine/threonine kinase structure and function, which demonstrated the requirement of specific conserved amino acids for enzymatic activity (19–22). Once the mutant forms of CDK11\(^{p110}\) were transfected into HeLa cells and given time to express their corresponding proteins, the FLAG epitope was used to immunoprecipitate the exogenous protein and kinase assays performed using the GST-CDT\textsuperscript{52-52} substrate. The surprising result was that there was no change in the CTD-directed kinase activity between the

![Fig. 1](http://www.jbc.org)
wild-type and kinase-inactive forms of FLAG-CDK11p110 (Fig. 1B). Two-hybrid and co-immunoprecipitation analyses indicated that the CDK11p110 isoforms do not form dimers or other oligomers (data not shown). Also, a reduction in CTD-directed kinase activity between wild-type and kinase-inactive forms would be expected if the activity seen with the kinase-dead form of FLAG-CDK11p110 were due to additional, active endogenous CDK11 p110 kinase in these IP complexes. All of these results suggested that another kinase was present in the CDK11p110 IP complexes. This CTD-directed kinase activity was determined to be DRB-sensitive, with a 50% decrease in activity between 10 and 100 μM concentration of DRB (data not shown). Immunoblot analyses performed to detect cyclin K, CDK1, CDK7, CDK8, CDK9, ERK1, ERK2, and ERK3 in CDK11p110 immunoprecipitates were all negative (data not shown), indicating that none of these proteins were responsible for this associated kinase activity.

**CDK11p110 Amino-terminal Domain-directed Kinase Activity Is Also Present in CDK11 IP Complexes**—A phosphorylated 110-kDa protein band also appeared in kinase assays using FLAG-immunoprecipitated kinase-inactive forms of CDK11p110 indicated that it was not due to autophosphorylation. IP kinase assays were carried out with several different CDK11p110 FLAG-tagged deletion constructs corresponding to various portions of the CDK11p110 protein to determine whether the CTD-directed kinase activity would co-immunoprecipitate with and phosphorylate these various fusion proteins (see Fig. 2C for construct diagrams). Protein kinase assays were carried out both in the presence and absence of substrate. The results shown in Fig. 2, A and B, demonstrate that the CTD kinase activity co-immunoprecipitates with the amino-terminal domain of CDK11p110 and phosphorylates a region of CDK11p110 between amino acid residues 92 and 375.

**CDK11 Complexes Contain CK2**—The results suggested that an unknown DRB-sensitive protein kinase co-immunoprecipitates with CDK11p110 and that it is this associated protein kinase activity that is responsible for the observed CTD- and CDK11p110-directed phosphorylations. To examine this more carefully, cation exchange chromatography was performed as a first step toward the purification and identification of the unknown DRB-sensitive kinase(s). HeLa nuclear extract was loaded onto
a P11 phosphocellulose column, and the proteins were eluted using a linear gradient of 0.1 to 1.0 M KCl. Aliquots from the collected fractions (labeled above the lanes) were analyzed by immunoblot using the CDK11p110 P2N100 antibody. The concentration of KCl in which the protein was eluted from the column is indicated below the immunoblot panel. B, immunoblot analysis and kinase assays following P2N100 immunoprecipitation. Selected P11 fractions (200 µl) were dialyzed overnight into 0.1 M P11 buffer and then subjected to immunoprecipitation using 5 µg of P2N100 antibody and 30 µl of Gammabind Plus-Sepharose. The resulting bead complexes were divided for parallel immunoblot analysis and kinase reactions. The upper panel represents the immunoblot incubated with P2N100 antibody. The far left lane contains 10 µg of HeLa total cell lysate, and the second from left lane represents a positive control P2N100 immunoprecipitation from HeLa total cell lysate. The remaining lanes represent immunoprecipitation from the dialyzed P11 samples, with the identity of the sample shown above the lanes. The lower panel represents the corresponding kinase reactions from the immunoprecipitated P11 samples using 1 µg of GST-CTD32–52 as substrate. C, the immunoblot described for B was incubated with a polyclonal antibody to CK2α. HeLa cell lysate was used as a positive control for CK2, and Gammabind beads plus rabbit IgG were incubated with HeLa cell lysate as a negative control. The IgG heavy chain identified by the CK2 polyclonal antibody is indicated to the left of the panel. D, outline of the chromatography purification scheme used to purify CDK11p110 protein complexes that contain CK2. E, HeLa cell lysates were immunoprecipitated with the CDK11p110 P2N100 and TFIIH p62 subunit antibodies. The immunoprecipitate beads were divided evenly for immunoblot analysis and kinase reactions. 1 µg of GST-CTD32–52 was used in each kinase reaction. Heparin was added to the paired kinase reactions as described under "Materials and Methods." The components contained in each reaction are indicated above each lane. The immunoblot analyses indicated that the IPs for CDK11p110 and TFIIH (CDK7) were successful (data not shown). F, 293T cells were transfected with FLAG-CK2α wild type (WT) or kinase-dead (KD) and AU.1-CK2β expression constructs (as indicated above the lanes). CDK11 IPs from the transfected cell lysates and control cells were divided evenly and subjected to either immunoblot analyses (left panel) or kinase assays using 1 µg of GST-CTD32–52 as substrate (right panel). The CK2β immunoblot signal from the CDK11 IP is not shown because it is the same size as the IgG light chain signal.

CDK11p110 kinase complexes were then immunoprecipitated from the dialyzed samples using the affinity-purified P2N100 antibody and divided for parallel immunoblot analyses and protein kinase assays. The results are shown in Fig. 3B. CDK11p110 was recovered from fraction 42, 50, and 58. The CTD-directed kinase activity was present only in fractions 50 and 58.

Previously published data led us to believe that the CDK11p110-associated protein kinase might be CK2. First, there are three consensus CK2 phosphorylation sites in the imperfect CTD repeat domain that was phosphorylated but not in the perfect CTD repeat domain that was not phosphorylated. Second, CK2 had previously been reported to phosphorylate the RNAP II CTD (8). To determine whether CK2α was associated...
with the CDK11<sup>p110</sup> in vivo, the eluted fractions from the P11 column shown in Fig. 3B were immunoblotted with a human CK2α antibody (Fig. 3C). As anticipated, CK2α was associated with the CDK11<sup>p110</sup> immunoprecipitated from the HeLa lysate, as well as the P11 column fractions that eluted between 0.8 and 1.0 M KCl. Conversely, CK2α was not associated with the CDK11<sup>p110</sup> protein in the P11 column fractions that eluted at salt concentrations less than 0.8 M KCl. CK2α co-immunoprecipitated with CDK11<sup>p110</sup> only in those samples that also demonstrated the CTD directed protein kinase activity. Finally, both the CK2β and CK2α protein kinase subunits co-immunoprecipitate with the CDK11<sup>p110</sup> protein kinase isolated from nontransformed human foreskin fibroblast cells (data not shown).

**CK2 Specifically Co-purifies with CDK11 following Ion Exchange and Affinity Chromatography—**Biochemical purification of CDK11<sup>p110</sup>-containing complexes was undertaken to further characterize proteins associated with CDK11<sup>p110</sup>. Soluble HeLa cell nuclear extract was subjected to chromatography using a series of columns as outlined in Fig. 3D. The eluants from these various columns were analyzed to identify the proteins contained in each fraction. CK2α was identified by combined liquid chromatography/tandem mass spectrometry analysis as a CDK11<sup>p110</sup>-co-purifying protein by assignment of MS<sup>2</sup> spectra from nine peptides to the known sequence of CK2α. It may also be of interest to note that CK2α specifically copurifies with a subpopulation of the CDK11<sup>p110</sup>-RNAP II complexes that, in a batch elution protocol, elute from the P11 column at 0.8 M KCl and from the DEAE column at 0.5 M KCl.

**The Kinase Activity Phosphorylating the RNAP II CTD Is Inhibited by Heparin—**If CK2 is responsible for the phosphorylation of both the RNAP II CTD and the CDK11<sup>p110</sup> amino-terminal domain in CDK11<sup>p110</sup> IP complexes, then this kinase activity should be inhibited by heparin. Heparin is known to be a rather potent and somewhat specific inhibitor of CK2 activity (23), whereas the ability of DRB to inhibit CK2 has been reported to be variable (24). Kinase assays were carried out following immunoprecipitation of endogenous CDK11<sup>p110</sup> and TFIIH. GST-CTD<sup>12–52</sup> was added to these kinase reactions along with increasing amounts of heparin. Two formulations of heparin were tested (see "Materials and Methods"), and both were found to be effective at inhibiting CK2 kinase activity. The results shown in Fig. 3E demonstrate that the kinase activity associated with CDK11<sup>p110</sup> and directed against the CTD was inhibited by heparin. In contrast, TFIIH kinase activity directed against the CTD was not inhibited. Heparin also inhibited phosphorylation of endogenous CDK11<sup>p110</sup> and the CDK11<sup>p110</sup> amino-terminal domain N375-FLAG, which was transiently expressed in HeLa cells and subjected to an IP kinase assay (data not shown).

**Expression of Kinase-dead CK2α Along with CK2β Significantly Reduces CDK11-associated CTD Kinase Activity—**We tested whether ectopic expression of kinase dead CK2α would compete with endogenous CK2α for association with CDK11<sup>p110</sup> and thereby reduce the amount of CTD kinase activity in a CDK11<sup>p110</sup> IP. The human cell line 293T was transfected with combinations of wild type or D156A kinase-dead (25) CK2α and CK2β. Following expression of the CK2 proteins, the transfected and control cells, which had not been transfected, were subjected to CDK11<sup>p110</sup> IP kinase assays using GST-CTD<sup>12–52</sup> substrate. The results shown in Fig. 3F demonstrate that the transfections and IPs were successful and that expression of kinase-dead CK2α significantly reduced the amount of CTD phosphorylation associated with CDK11<sup>p110</sup> as compared with wild type. The results also suggest that expression of CK2β is necessary for increased association of ectopically expressed CK2α with CDK11<sup>p110</sup>. The results further indicate that ectopic CK2β expression alone is sufficient to increase the amount of CTD kinase activity associated with endogenous CDK11<sup>p110</sup>. Thus, these results reconfirms that CK2 association with CDK11<sup>p110</sup> is responsible for a significant amount of the CTD kinase activity in CDK11<sup>p110</sup> IP complexes.

**Mapping the Region of the CDK11 and CK2 Association—**To further map the association between CDK11<sup>p110</sup> and CK2, specific CDK11<sup>p110</sup> amino-terminal deletion constructs were expressed in cells and examined for the ability to co-immunoprecipitate CK2. Based upon previous studies by Stamm and colleagues (26), which indicated that the shuttling of the alternative splicing factor YT521B is regulated by both RD/RE repeats in its amino terminus and a poly(E) repeat at its carboxyl terminus, these regions were deleted from CDK11<sup>p110</sup>. Deletion of the RD/RE (i.e. ∆RE), but not the poly(E) (i.e. ∆E), repeat region resulted in the loss of CDK11<sup>p110</sup> and CK2 association as determined by co-immunoprecipitation.immunoblot analysis (Fig. 4, left panel). In addition, when the CK2 protein kinase did not physically associate with CDK11-N424 in vitro, phosphorylation of the amino-terminal region of CDK11<sup>p110</sup> was not observed (Fig. 4, right panel). We consistently observed equal or greater phosphorylation of the CDK11-N424 ∆E protein as compared with the wild-type CDK11<sup>p110</sup>. It is possible that the deletion of the highly charged glutamic acid repeats improved the ability of CK2 to interact with CDK11<sup>p110</sup>. Thus, the RE domain of CDK11<sup>p110</sup> is at least required for association with CK2. This RE domain is also required for CDK11<sup>p110</sup> interaction with RNPS1 and for nuclear speckle localization of CDK11<sup>p110</sup>.CDK11<sup>p110</sup> and CK2 do not co-immunoprecipitate using CDK11<sup>p110</sup> and CK2 do not co-immunoprecipitate using in vitro transcription and translation products. It is possible that other proteins, factors, or modifications are required for the stable association of these proteins. However, the

![Fig. 4. CK2 cannot associate with a CDK11<sup>p110</sup> deletion mutant lacking the RD/RE repeat region.](http://www.jbc.org)
phosphorylation of CDK11<sup>p110</sup> by CK2 suggests that these proteins do interact, at least in an indirect manner.

**DISCUSSION**

Further characterization of CDK11<sup>p110</sup> signaling and protein complexes and the role they play in transcription and RNA processing identified CK2 as a member of the CDK11<sup>p110</sup> complexes. CDK2, a known mediator of cell cycle and transcriptional events (7, 27, 28), phosphorylates the CTD. In a recent publication, Gottesfeld and co-workers (11) demonstrated that a cyclin L-associated kinase activity, attributed to the PITSLRE/CDK11p110 protein kinase, phosphorylated the CTD. Although human CDK11<sup>p110</sup> does interact with human cyclin L in vitro,<sup>2,3</sup> we have shown here that CDK11<sup>p110</sup> is, in fact, not a CTD kinase. This was demonstrated through the use of several different CDK11<sup>p110</sup> kinase-inactive tagged mutants from mammalian cells in the in vitro CTD kinase assays, by examining the sensitivity of the CTD kinase to heparin, and by ectopic expression of kinase-dead CK2α. Gottesfeld and co-workers (11) did not use kinase-inactive CDK11 p110 controls, resulting in the discrepant conclusion that CDK11<sup>p110</sup> kinase activity was responsible for CTD phosphorylation. Rather, as we have shown here, it is the associated activity of CK2 with CDK11<sup>p110</sup> in vitro that is most likely responsible for CTD-directed kinase activity. It is still possible that another cyclin L-associated CDK may play a role in CTD phosphorylation as well.

The data presented in this report also demonstrate that CK2 phosphorylates the amino-terminal domain of CDK11<sup>p110</sup> in vitro. We have identified the RD/RE repeat region of the CDK11<sup>p110</sup> amino-terminal domain as an essential component for its association with CK2. In addition, the ΔRE mutation disrupts the ability of the CDK11<sup>p110</sup> kinase to properly localize within nuclear structures.<sup>5</sup> CK2 interacts with multiple signaling pathways, and this protein kinase is proposed to be an important mediator of cell survival. Increased CK2 activity is associated with increased cellular proliferation and response to stress, and conversely, loss of CK2 activity is associated with cell death (see Ref. 29 and references therein). In one case, CK2 is reported to regulate p53 in response to DNA damage. Following UV irradiation, CK2 purifies in a complex with the FACT transcriptional elongation factor and phosphorolyses serine 392 of p53, thus enhancing p53 activity (30). Interestingly, both subunits of FACT co-purified with CDK11<sup>p110</sup> and CK2, as identified by both mass spectrometry and immunoblot analysis (data not shown). The data reported here further suggest a role for CK2 in regulating the function of various components of large molecular weight RNA transcription and processing complexes, including CDK11<sup>p110</sup>, FACT, and RAPN II. The association(s) between CK2 and these proteins as well as their phosphorylation by CK2 may provide further insight into the mechanism(s) involved in CK2 regulation of RNA transcript production.

**Acknowledgments**—We thank J. Grenet and S. Bothner for excellent technical assistance. We also thank Dr. S. Elledge for providing the cyclin K antibodies and Dr. J. Corden for providing GST-CTD constructs. We thank Dr. Jason Weber for assistance with chromatography, Ashutosh Mishra for assistance with protein chemistry, and Dr. Sandra Pierre for the GST-CDT<sup>2270</sup>-<sup>255</sup> protein. The assistance of Dr. C. Naev and the Hartwell Center for Bioinformatics and Biotechnology at St. Jude Children’s Research Hospital in the production of oligonucleotides and DNA sequencing analysis is also acknowledged.

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Casein Kinase 2 Interacts with Cyclin-dependent Kinase 11 (CDK11) in Vivo and Phosphorylates Both the RNA Polymerase II Carboxyl-terminal Domain and CDK11 in Vitro

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J. Biol. Chem. 2003, 278:2265-2270.
doi: 10.1074/jbc.M207518200 originally published online November 11, 2002

Access the most updated version of this article at doi: 10.1074/jbc.M207518200

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