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CK2 kinase activity but not its binding to *CK2* promoter regions is implicated in the regulation of *CK2α* and *CK2β* gene expressions

Sarah Lupp · Catalina Gumhold · Emmanuel Ampofo · Mathias Montenarh · Karen Rother

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Abstract Protein kinase CK2, a ubiquitous serine/threonine kinase in control of a variety of crucial cellular functions, is composed of catalytic α- and α′-subunits and non-catalytic β-subunits which form holoenzymes such as $CK2(\alpha\beta)_2$, $CK2\alpha\alpha'\beta_2$, or $CK2(\alpha'\beta)_2$. In addition, there is ample evidence for the occurrence of the individual subunits beside the holoenzyme. While the CK2 subunits are well analyzed on the protein level, only little is known about the regulation of their transcription. The existence of multiple forms of CK2 subunits raised the question about a mutual regulation of their expression. Here we defined two 5′-upstream regions of the *CK2α* and the *CK2β* genes, respectively, as sequences with promoter activities. We found that CK2α and CK2α′ stimulated the expression of the reporter constructs whereas, CK2β was inactive. Using chromatin immunoprecipitation assays, we were unable to detect binding of endogenous CK2 subunits to these promoter sequences in vivo. However, it turned out that inhibition of the kinase activity of CK2 attenuated the promoter activity indicating that CK2α and CK2α′ might regulate their gene expression indirectly by phosphorylation reactions. Thus, we have shown here (i) that under normal physiological conditions CK2 does not bind to *CK2* promoter regions and (ii) that the CK2 kinase activity is implicated in the regulation of its own expression.

Keywords Protein kinase CK2 · Gene expression · Transcriptional regulation · DNA binding

Introduction

Protein kinase CK2, formerly known as casein kinase 2, is known for more than 50 years [1]. It is a ubiquitously expressed protein kinase which phosphorylates more than 500 different substrates and this number is steadily increasing. This large number of different substrates indicates that CK2 is implicated in numerous cellular processes including regulation of cell proliferation and survival [2, 3]. An elevated expression level and an increased kinase activity for CK2 were found in tumor cells compared to normal, non-transformed cells [4]. This later observation made CK2 an interesting pharmacological target for the treatment of cancer [5, 6].

Thornburg and Lindell [7] first described CK2 as a multi-subunit protein kinase that is generated by the association of two α- and/or α′-subunits with a dimer of the β-subunit. This structure and composition of CK2 was quickly confirmed by Dahmus and Natzle [8]. Stigare, however reported in 1993, that CK2α was tightly bound to nuclear structures in the absence of its β-subunit [9] indicating that the CK2 subunits exist not only in the holoenzyme but also in a free form or individually associated with other cellular proteins or structures. An unbalanced expression of CK2α and CK2β subunits was later on described for different mammalian tissues [10–12]. CK2α is not only active as a phosphotransferase in the holoenzyme but also in the absence of CK2β. Loss of CK2β is

Mathias Montenarh and Karen Rother have contributed equally to this work.

S. Lupp · C. Gumhold · E. Ampofo · M. Montenarh · K. Rother
Department of Medical Biochemistry and Molecular Biology, Saarland University, 66421 Homburg, Germany

C. Gumhold · K. Rother (✉)
Department of Medical Biochemistry and Molecular Biology, Center of Human and Molecular Biology, Saarland University, Building 44, 66421 Homburg, Germany
e-mail: karen.rother@uks.eu