Cent. Eur. J. Biol. • 7(2) • 2012 • 185-191
DOI: 10.2478/s11535-012-0019-2

VERSITA

Central European Journal of **Biology**

Protein kinase CK2 from two higher eukaryotes of economical importance, the mussel *Mytilus galloprovincialis* and the medfly *Ceratitis capitata*

Mini-Review

Sophia Kouyanou-Koutsoukou[1], Andrea Baier[2], Regina-Maria Kolaitis[1,3], Ryszard Szyszka[2,*]

[1]*Department of Genetics and Biotechnology, Faculty of Biology, University of Athens, 15771 Athens, Greece*

[2]*Department of Molecular Biology, Institute of Biotechnology, 20-718 Lublin, Poland*

[3]*St Jude Children's Research Hospital, 38105 Memphis, TN, U.S.A.*

Received 13 November 2011; Accepted 26 January 2012

Abstract: Protein kinase CK2 is a highly conserved Ser/Thr protein kinase involved in cell cycle control, transcription, signal transduction and cell proliferation. It is upregulated in several diseases and by oxidative stress. CK2 is generally composed of two catalytic subunits and two regulatory subunits and utilizes either ATP or GTP as a phosphate donor. CK2 was isolated from the sea mussel *Mytilus galloprovincialis*, a biomarker of marine pollution, and the Mediterranean fly *Ceratitis capitata*, an insect capable of wreaking extensive damage to a wide range of fruit crops with great economical importance. The catalytic CK2α and regulatory CK2β subunits of *M. galloprovincialis* and *C. capitata* show similar properties. The mussel and fly catalytic subunits and holoenzymes were capable of phosphorylating the recombinant ribosomal stalk P1 protein, implying functional conservation. They also demonstrate the characteristics of a typical CK2: use of ATP and GTP as phosphate donors, inhibition by known modulators of CK2 activity (like benzotriazole derivatives and heparin), and stimulation by polycations. Both organisms seem to be ideal models for the analysis of CK2 in the control of gene expression in response to cellular stress.

Keywords: *CK2 • Phosphorylation • Mytilus galloprovincialis • Ceratitis capitata*

1. Introduction

CK2 is a conserved, ubiquitous protein kinase with more than 300 identified substrates, many of which are implicated in key cellular functions like cell proliferation, differentiation, apoptosis, and signal transduction [1,2]. High levels of CK2 activity have also been described in different types of cancer [3]. Human CK2 is a tetramer comprised of two catalytic α and/or α′ and two regulatory β subunits, forming $\alpha_2\beta_2$, $\alpha\alpha'\beta_2$, and $\alpha'_2\beta_2$ complexes. There are also three isoforms of the catalytic subunit, CK2α, CK2α′ and CK2α" [4]. In *Saccharomyces cerevisiae* CK2 is composed of two catalytic subunits a and a′ and two regulatory subunits β and β′ [5], which may exist in five forms: the free catalytic subunits CK2α and CK2α′ and three forms of holoenzyme αα′ββ′, $\alpha_2\beta\beta'$and $\alpha'_2\beta\beta'$ [6]. The regulatory β-subunit enhances the stability of the catalytic subunits and modulates their substrate specificity. In the fruit fly *Drosophila melanogaster* one gene for the catalytic CK2α subunit and two for the regulatory subunits were identified [7]. *Ceratitis capitata*, one of the most destructive agricultural pests, responds to heat shock by exhibiting complex patterns of spatial and temporal regulation of gene expression [8]. Mussels, like *Mytilus galloprovincialis* response to stress through coordinated changes in protein synthesis [9]. They may develop neoplasia of the haemolymph, associated with pro-apoptotic tumor-suppressor protein p53 isoforms, which are highly conserved between molluscs and vertebrates [10,11]. Furthermore, CK2 is a crucial protein involved in the formation and clearance of aggresomes [12]. These two species are, therefore,

* *E-mail: szyszkar@kul.pl*

ideal model organisms for the study of stress responses at the molecular level.

2. CK2 is conserved in mussels and insects

CK2 has been extensively studied in many eukaryotes, from yeast to mammals. Extreme sequence conservation of protein kinase CK2 has been noticed among different species. Sequence conservation is translated into conservation of function as well, as shown between human, nematode and yeast, in which the human or the nematode *Caenorhabditis elegans* CK2α catalytic subunit was shown to substitute for the yeast catalytic subunits [13]. We have recently studied CK2 in the Mediterranean mussel *M. galloprovincialis* and the medfly *C. capitata* [14,15]. Cloning and sequence analysis of the cDNAs and the predicted polypeptides showed that both, CK2α and CK2β subunits from *M. galloprovincialis* and *C. capitata* are similar in their theoretical molecular weight and pI compared to their homologues (Table 1).

Alignments of the predicted amino acid sequence of the CK2α and CK2β subunits in the two species showed considerable similarity with all the characteristic subdomains and features conserved (Figure 1). The molecular weight of the catalytic CK2α subunit varies between 39 and 45 kDa. The architecture of this protein can be divided into a smaller N-terminal lobe including the β-strands and the helix αC, and a large C-terminal lobe dominated by α-helix structures. Between these two lobes the ATP binding site is localized represented by the motif G^{44}RGKYS^{49} (motif a*2*). The N-terminal end of the catalytic subunit contains the region between Ser^{5} and Glu^{34} in both mussel and medfly CK2α (motif a*1*), which seems to mediate CK2 constitutive activity [16]. The helix αC is characterized by a basic Lys-rich sequence represented by K^{72}KKKIKR^{78} (motif *a3*). This region is involved in the inhibition of CK2 activity by heparin and in the recognition of the protein substrate at the *n*+3 position [1,2,17,18]. The catalytic loop bears the conserved amino acid tandem $R^{153}D^{154}$ and H^{158} (a*4* and a*5*), and the residues R^{189}, R^{193}, K^{196} (a*7*) of the C-terminal loop, often found in vertebrate homologues.

	Length of gene (bp)	Protein length (aa)	Molecular weight (kDa)	Isoelectric point	Identity/similarity to human subunit
CK2a					
Homo sapiens	1176	391	45143.58	7.62	-
Ratus norvegicus	1176	391	45073.47	7.62	98/99
Ceratitis capitata	1117	338	39946.76	7.22	88/94
Drosophila melanogaster	1111	336	39959.74	6.99	89/94
Caenorhabditis elegans	1183	360	42257.02	6.68	79/88
Mytilus galloprovincialis	1071	356	41987.19	8.33	86/91
*Arabidopsis thaliana**	1002	333	39258.15	8.31	73/88
Zea mays	1002	333	39309.20	8.31	78/89
Saccharomyces cerevisiae	1119	372	44667.58	8.83	59/71
CK2β					
Homo sapiens	648	215	24942.42	5.29	-
Ratus norvegicus	648	215	24942.42	5.29	100/100
Ceratitis capitata	648	215	24829.25	5.30	88/96
Drosophila melanogaster	708	235	27087.69	5.06	88/96
Caenorhabditis elegans	705	234	26435.59	4.88	82/92
Mytilus galloprovincialis	663	221	25579.93	5.30	93/97
Arabidopsis thaliana	872	287	32354.97	5.01	58/73
*Zea mays***	831	276	30940.68	5.02	57/89
Saccharomyces cerevisiae	837	278	32264.78	4.35	42/59

Table 1. Features of CK2α and CK2β from different species.

** - CK2α-1; ** - CK2 regulatory subunit B1.*

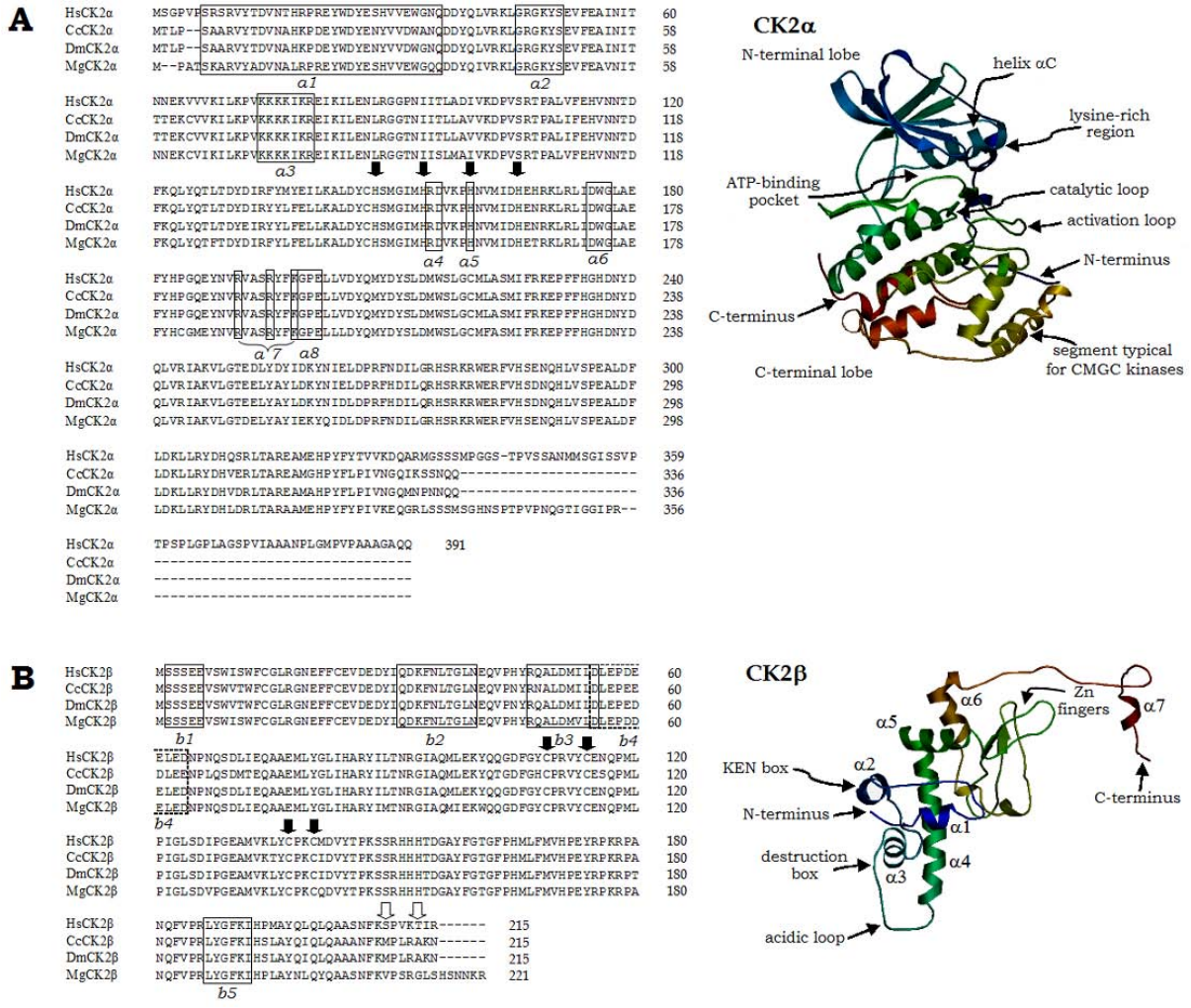

Figure 1. Alignment of the predicted amino acid sequences of CK2α (A) from *M. galloprovincialis* (Mg-FN677519), *C. capitata* (Cc-HQ690086) *D. melanogaster* (Dm-NM080179) and *H. sapiens* (Hs-BT019792) and CK2β regulatory subunits (B) from *M. galloprovincialis* (Mg-FN677520), *C. capitata* (Cc-HQ690087), *D. melanogaster* (Dm-NP996415) and *H. sapiens* (Hs-NM001320). The characteristic domains referred to in the text are marked as *a1-a8* in CK2α and *b1-b6* in CK2β. Model structures of CK2α and CK2β subunits from *M. galloprovincialis* are presented on the right. Structural features of CK2α and CK2β subunits were made using SWISS-MODEL Workspace for protein structure homology modeling [45,46]. 1ds5D [47] and 3EED [48] were used as templates for the α- and β-subunits, respectively.

This triplet of amino acids (*a7*) is responsible for the recognition of the substrate at the n+1 position [18]. The RD tandem is surrounded by four equidistanced histidine residues (marked by black arrows) unique for protein kinase CK2 [19]. The activation loop typical for protein kinases is located between conserved triplets of amino acids DFG ($D^{173}WG^{175}$ in CK2) and APE ($G^{197}PE^{199}$ in CK2) – segments *a6* and *a8*, respectively. Unlike other protein kinases, the activation loop of CK2 is always in the active state. One of the possible reasons is the role played by the N-terminal domain. This part of CK2α blocks the activation loop in its open (active) conformation [16].

The regulatory CK2β subunit is ubiquitous in all eukaryotes and its molecular weight ranges from 25 kDa to 33 kDa (Table 1). These proteins are acidic with isoelectric points (pI) ranging between 4.35 in yeast and 5.30 in *C. capitata* and *M. galloprovincialis*. The genome of mammals encodes a single protein, while baker's yeast expresses two CK2β proteins, and four functional homologues have been discovered in *Arabidopsis thaliana* [20]. The primary sequence of the β subunit has an interesting distribution of acidic and basic residues located at the N- and C-terminal regions of the protein, respectively (Figure 1). The N-terminal domain of the regulatory β-subunit (residues 5-104) has a globular structure, organized as four *α*-helices (*α1-α4*). This part of the protein contains 20 of the 28 acidic residues present in the primary structure. This region presents docking sites for protein substrates

involved in different processes, e.g. localization in the cell, translation and protein degradation [21]. The N-terminal end of the protein appears to represent a pseudo-substrate segment containing two autophosphorylation sites (Ser^2 and Ser^3) in the conservative sequence S^2SSEE^6 (motif *b1*) [22]. The precise function of this phosphorylation remains unknown due to the fact that every β subunit does not contain this segment (e.g. *Z. mays, A. thaliana*). However, studies conducted by Zhang and colleagues suggest that modification of these serine residues enhances CK2β stability [23]. In close proximity to the autophosphorylation segment are two motifs that have previously been characterized as motifs regulating degradation of cyclins (motif *b2* and *b3*). The first is characterized by the sequence KEN which is often surrounded by either an N or D residue (N/DKENX_{0-4}N/D). All compared CK2β subunits contain a similar sequence, namely $D^{32}KFNLTGN^{40}$. The second motif regulating cyclin degradation is a nine amino acid sequence called the destruction box. This motif, which was recognized in CK2β by Allende and Allende, has three highly conserved residues in the consensus sequence RXXLXXXXN/D [24,25]. In *C. capitata* and *M. galloprovincialis* these amino acid sequences are $R^{47}NALDMILD^{55}$ and $R^{47}QALDMVLD^{55}$, respectively. The destruction box is close to the autophosphorylated N-terminal serine residues, and it was shown that replacing these two serines significantly decreased degradation of CK2β. This indicates that autophosphorylation influences the stability of this subunit [23].

The N-terminus of the β polypeptide contains an acidic region (residues 55-64, *b4*) involved in negative regulation of CK2 [22]. Similar clusters of acidic amino acids are typical for substrates of CK2 and for this reason it has been speculated that they represent autoinhibitory sequences, reminiscent of those present in other protein kinases [26]. This region contains a binding motif for polybasic peptides that regulate CK2 activity towards calmodulin [27].

The central part of the regulatory subunit forms the core of the zinc finger mediating CK2β dimer formation. Each Zn^{2+} is coordinated by conserved cysteine residues: Cys^{109}, Cys^{114}, Cys^{137} and Cys^{140} [28].

The C-terminal segment of the CK2β polypeptide (residues 178-205) is involved in formation of regulatory subunit dimers, and it also has functions connected with holoenzyme formation. Results obtained from the crystal structure of the $\alpha_2\beta_2$ holoenzyme show that residues $L^{187}YGFKI^{192}$ (motif *b5*) in this region are responsible for the direct interaction of the CK2β subunit with the catalytic CK2α and CK2α' subunits [29]. The C-terminal region of the regulatory β-subunit is able to bind to the N-terminal lobe of other Ser/Thr protein kinases, including c-Mos, A-Raf, Chk1 and Chk2, to act as either a positive or negative regulator of activity [21,30-34] (Figure 1B).

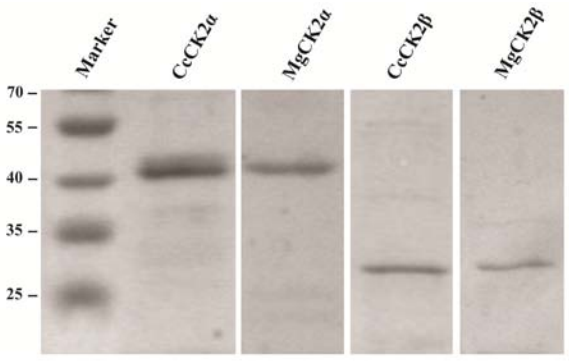

Figure 2. Analysis of purified CK2α and CK2β proteins of *C. capitata* and *M. galloprovincialis* by 12.5% SDS/PAGE after coomassie staining. Positions of molecular weight markers are indicated.

Finally, the carboxy terminal region of the human CK2β contains two residues, Ser^{209} and Thr^{213} (marked by white arrows in Figure 1B). Ser^{209} is phosphorylated in a cell cycle dependent manner by $p34^{cdc2}$ *in vitro* and in mammalian cells [35], while Thr^{213} is phosphorylated by checkpoint kinase Chk1 [36]. Both residues are missing in *M. galloprovincialis* and *C. capitata* CK2β proteins, as is the case in other invertebrates like *D. melanogaster*, *Spotoptera*, and *Ciona intestinalis* [37]. Unusually, mussel CK2β possesses six additional amino acids at the carboxyl end not found in CK2β of human, medfly or other higher eucaryotes, which usually possess 215 amino acids.

3. Recombinant CK2α and CK2β subunits of *M. galloprovincialis* and *C. capitata* have similar properties

The cDNAs of CK2α and CK2β subunits of *M. galloprovincialis* (Mg) and *C. capitata* (Cc) were isolated and the recombinant proteins were purified after expression in *E. coli* [14,15] (Figure 2).

The free catalytic subunits and the reconstituted $\alpha_2\beta_2$ holoenzymes from both species possess properties typical of protein kinase CK2 [14,15]. The phosphorylating acivities were measured and compared with the ones from other species like human, maize or yeast. The addition of the CK2β subunit resulted in enhancement of P1 phosphorylation. Due to the protective function of the regulatory β subunit the holoenzyme is less sensitive towards the presence of NaCl than CK2α. Both

catalytic subunits are sensitive to salt but sensitivity of the enzyme from *M. galloprovincialis* was higher than that of *C. capitata*. NaCl at a concentration of 50 mM reduced MgCK2α activity ~50% while the CcCK2α still had ~95% of control activity. CcCK2α was inhibited 50% when the salt concentration was increased to 125 mM. Increase of salt concentration to 200 mM, in the case of both holoenzymes, inhibited activity over 80%. In some cases, like human, maize or mussel, the holoenzyme is stimulated at lower salt concentrations [38]. The holoenzymes of the medfly, yeast and *T. brucei* do not show such effects [39-41].

CK2 is one of the few protein kinases that are able to utilize ATP as well as GTP as phosphate donors, a characteristic often used to demonstrate the presence of CK2. To measure this characteristic in both new CK2s, GTP was added to the reaction mixture along with ATP. The competitive effect was estimated by measuring the incorporation of radiolabelled phosphate from [γ-^{32}P] ATP. Both holoenzymes were able to use GTP as a phosphate donor better than the free catalytic subunit. A GTP concentration four times higher than ATP was necessary for inhibition of 50% activity, suggesting ATP as the preferred phosphate donor over GTP. In the presence of known chemical modulators of CK2, like heparin, spermine or ATP-competitive inhibitors like 4,5,6,7-tetrabromo-*1H*-benzotriazole (TBB) and 4,5,6,7-tetrabromo-*1H*-benzimidazole (TBI), CK2 activities of both *M. galloprovincialis* and *C. capitata* were influenced similarly to other known CK2 free catalytic subunits and holoenzymes. As with other known CK2s, both catalytic α-subunits, as well as $\alpha_2\beta_2$ holoenzymes, were inhibited by heparin at concentrations below 10 nM and stimulated by 0.5-1 mM spermine. CK2 specific inhibitors TBB and TBI both inhibit kinase activity at concentrations between 0.1 and 0.6 μM.

4. Conclusions and future perspectives

Our studies have shown that purified free catalytic subunit and holoezyme of the mussel *M. galloprovincialis* and the medfly *C. capitata* possess kinase activity and are conserved during evolution, since they are able to phosphorylate the ribosomal stalk P1 protein. The ribosomal stalk is involved in the control of protein synthesis by affecting the expression of specific mRNAs and the phosphorylation of P-proteins by CK2 kinase seems to control the ribosomal activity [42]. *M. galloprovincialis* is used as an indicator of marine pollution and the ribosomal MgP0 protein is overexpressed in response to environmental stress [43]. As mentioned above, *C. capitata* and *M. galloprovincialis* seem to be ideal models for the study of cellular stress and gene expression but also for the analysis of human diseases [44], since neoplasia is also detected in mussels as a response to marine pollution. Both organisms need simple conditions for cultivation. As shown in Table 1, *M. galloprovincialis* and *C. capitata* show highest similarity towards human CK2 compared with other models used previously, like *S. cerevisiae* and *A. thaliana*.

References

[1] Meggio F., Pinna L.A., One-thousand-and-one substrates of protein kinase CK2?, FASEB J., 2003, 17, 349-368

[2] Litchfield D.W., Protein kinase CK2: Structure, regulation and role in cellular decisions of life and death, Biochem. J., 2003, 369, 1–15

[3] Ahmad K.A., Wang G., Slaton J., Unger G., Ahmed K., Targeting CK2 for cancer therapy, Anticancer Drugs, 2005, 16, 1037-1043

[4] Pinna L.A., Protein kinase CK2, Int. J. Biochem. Cell Biol., 1997, 29, 551–554

[5] Glover C.V.C, On the physiological role of casein kinase II in Saccharomyces cerevisiae, Prog. Nucleic Acid Res. Mol. Biol., 1998, 59, 95–133

[6] Abramczyk O., Zień P., Zieliński R., Pilecki M., Helman U., Szyszka R., The protein kinase 60S is a free catalytic CK2α' subunit and form an inactive complex with superoxide dismutase SOD1, Biochem. Biophys. Res. Commun., 2003, 307, 31–40

[7] Saxena A., Padmanabha R., Glover C.V.C, Isolation and sequencing of cDNA clones encoding alpha and beta subunits of Drosophila melanogaster casein kinase II, Mol Cell Biol., 1987, 7, 3409–3417

[8] Theodoraki M.A., Mintzas A.C., cDNA cloning, heat shock regulation and developmental expression of the hsp83 gene in the Mediterranean fruit fly Ceratitis capitata, Insect Mol. Biol., 2006, 15, 839-852

[9] Kalpaxis D.L., Theos C., Xaplanteri M.A., Dinos G.P., Catsiki A.V., Leotsinidis M., Biomonitoring of Gulf of Patras, N. Peloponnesus, Greece. Application of a biomarker suite including evaluation of translation efficiency in Mytilus galloprovincialis cells, Environ. Res., 2004, 94, 211–220

[10] Muttray A.F., O'Toole T.F., Morrill W., Van Beneden R.J., Baldwin S.A., An invertebrate mdm homolog

interacts with p53 and is differentially expressed together with p53 and ras in neoplastic Mytilus trossulus haemocytes, Comp. Biochem. Physiol., 2010, 156, 298-308

[11] Pantzartzi C., Drosopoulou E., Yiangou M., Drozdov I., Tsoka S., Ouzounis C.A., et al., Promoter complexity and tissue-specific expression of stress response components in Mytilus galloprovincialis, a sessile marine invertebrate species, PLoS Comput. Biol., 2010, 6, e1000847

[12] Watabe M., Nakaki T., Protein kinase CK2 regulates the formation and clearance of aggresomes in response to stress, J. Cell Sci., 2011, 124, 1519-1532

[13] Dotan I., Ziv E., Dafni N., Beckman J.S., McCann R.O., Glover C.V.C., et al., Functional conservation between the human, nematode and yeast CK2 cell cycle genes, Biochem. Biophys. Res. Commun., 2001, 288, 603–609

[14] Kolaiti R.M., Baier A., Szyszka R., Kouyanou-Koutsoukou S., Isolation of a CK2α Subunit and the holoenzyme from the mussel Mytilus galloprovincialis and construction of the CK2α and CK2β cDNAs, Mar. Biotechnol., 2011, 13, 505-516

[15] Kouyanou-Koutsoukou S., Baier A., Kolaitis R.M., Maniatopoulou E., Thanopoulou K., Szyszka R., Cloning and purification of protein kinase CK2 recombinant alpha and beta subunits from the Mediterranean fly Ceratitis capitata, Mol. Cell. Biochem., 2011, 356, 261-267

[16] Sarno S. Ghisellini P., Pinna L.A., Unique activation mechanism of protein kinase CK2. The N-terminal segment is essential for constitutive activity of the catalytic subunit but not of the holoenzyme, J. Biol. Chem., 2002, 277, 22509-22514

[17] Cozza G., Bortolato A., Moro S., How druggable is protein kinase CK2?, Med. Res. Rev., 2009, 30, 1-44

[18] Sarno S., Vaglio P., Meggio F., Issinger O.-G., Pinna L.A., Protein kinase CK2 mutants defective in substrate recognition. Purification and kinetic analysis., J. Biol. Chem., 1996, 271, 10595-10601

[19] Sarno S., Vaglio P., Marin O., Meggio F., Issinger O.-G., Pinna L.A., Basic residues in the 74-83 and 191-198 segments of protein kinase CK2 catalytic subunit are implicated in the negative but not in the positive regulation by the beta-subunit, Eur. J. Biochem., 1997, 248, 290-295

[20] Salinas P., Fuentes D., Vidal E., Jordana X., Echeverria M., Holuigue L., An extensive survey of CK2 α and β subunits in Arabidopsis: Multiple isoforms exhibit differential subcellular localization, Plant Cell. Physiol., 2006, 47, 1295-1308

[21] Bibby A.C., Litchfield D.W., The multiple personalities of the regulatory subunit of protein kinase CK2: CK2 dependent and CK2 independent roles reveal a secret identity for CK2β, Int. J. Biol. Sci., 2005, 1, 67-79

[22] Boldyreff B., Meggio F., Pinna L.A, Issinger O.-G., Reconstitution of normal and hyperactivated forms of casein kinase-2 by variably mutated beta-subunits, Biochemistry, 1993, 32, 12672-12677

[23] Zhang C., Vilk G., Canton D.A., Litchfield D.W., Phosphorylation regulates the stability of the regulatory CK2beta subunit, Oncogene, 2002, 21, 3754-3764

[24] Allende J.E., Allende, C.C., Protein kinases. 4. Protein kinase CK2: an enzyme with multiple substrates and a puzzling regulation, FASEB J., 1995, 9, 313-323

[25] Bolanos-Garcia V.M., Fernandez-Recio J., Allende J.E., Blundell, T.L., Identifying interaction motifs in CK2β – a ubiquitous kinase regulatory subunit, TRENDS Biochem. Sci., 2006, 31, 654-660

[26] Soderling T.R., Protein kinases and phosphatases: regulation by autoinhibitory domains, Biotechnol. Appl. Biochem., 1993, 18, 185-200

[27] Meggio F., Boldyreff B., Issinger O.-G. Pinna L.A., Casein kinase 2 down-regulation and activation by polybasic peptides aremediated by acidic residues in the 55-64 region of the beta-subunit. A study by the calmodulin as phosphorylatable substrate, Biochemistry, 1994, 33, 6998-7004

[28] Chantalat L., Leroy D., Filhol O., Nueda A., Benitez M.J., Chambaz E.M., et al., Crystal structure of the human protein kinase CK2 regulatory subunit reveals its zinc finger-mediated dimerization, EMBO J., 1999, 18, 2930-2940

[29] Niefind K., Guerra B., Ermakowa I., Issinger O.-G., Crystal structure of human protein kinase CK2: insights into basic properties of the CK2 holoenzyme, EMBO J., 2001, 20, 5320-5331

[30] Hagemann C., Kalmes A., Wixler V., Wixler L., Schuster T., Rapp U.R., The regulatory subunit of protein kinase CK2 is a specific A-Raf activator, FEBS Lett., 1997, 403, 200-202

[31] Chen M., Li D., Krebs E.G., Cooper J.A., The casein kinase II beta subunit binds to Mos and inhibits Mos activity, Mol. Cell. Biol., 1997, 17, 1904-1912

[32] Guerra B., Issinger O.-G., Wang J.Y., Modulation of human checkpoint kinase Chk1 by the regulatory beta-subunit of protein kinase CK2, Oncogene, 2003, 22, 4933-4942

[33] Bjørling-Poulsen M., Siehler S., Wiesmüller L., Meek D., Niefind K., Issinger O.-G., The 'regulatory' beta-subunit of protein kinase CK2 negatively influences p53-mediated allosteric effects on Chk2 activation, Oncogene, 2005, 24, 6194-6200

[34] Litchfield D.W., Bosc D.G., Slominski E., The protein kinase from mitotic human cells that phosphorylates Ser-209 on the casein kinase II beta-subunit is p34cdc2, Biochim. Biophys. Acta, 1995, 1269, 69-78
[35] Olsen, B.B., Niefind, K., Issinger, O.-G., Inter- and supramolecular interactions of protein kinase CK2 and their relevance for genome integrity. In: D.-H. Lankeman (Ed.) Genome Dynamics and Stability: Genome Integrity, Springer Berlin Heidelberg, 2007
[36] Kristensen L.P., Larsen M.R., Højrup P., Issinger O.G., Guerra B., Phosphorylation of the regulatory beta-subunit of protein kinase CK2 by checkpoint kinase Chk1: identification of the in vitro CK2beta phosphorylation site, FEBS Lett., 2004, 569, 217-223
[37] Russo G.L., Tosto M., Mupo A., Castellano I., Cuomo A., Tosti E., Biochemical and functional characterization of protein kinase CK2 in ascidian Ciona intestinalis oocytes at fertilization, J. Biol. Chem., 2004, 279, 33012–33023
[38] Riera M., Pages M., Issinger O.-G., Guerra B., Purification and characterization of recombinant protein kinase CK2 from Zea mays expressed in Escherichia coli, Protein Expr. Purif., 2003, 29, 24–32
[39] Jensen B.C., Kifer C.T., Brekken D.L., Randall A.C., Wang Q., Drees B.L., et al., Characterization of protein kinase CK2 from Trypanosoma brucei, Mol. Biochem. Parasitol., 2007, 151, 28–40
[40] Meggio F., Grankowski N., Kudlicki W., Szyszka R., Gąsior E., Pinna L.A., Structure and properties of casein kinase-2 from Saccharomyces cerevisiae. A comparison with the liver enzyme, Eur. J. Biochem., 1986, 159, 31–38
[41] Domańska K., Zieliński R., Kubiński K., Sajnaga E., Masłyk M., Bretner M., et al., Protein kinase CK2 from Saccharomyces cerevisiae, Acta Biochim. Polon., 2005, 52, 947–951
[42] Ballesta J.P.G., Remacha M., The large ribosomal subunit stalk as a regulatory element of the eukaryotic translational machinery, Prog. Nucleic Acid Res. Mol. Biol., 1996, 55, 157–193
[43] Kolaiti R.M., Lucas J.M., Kouyanou-Koutsoukou S., Molecular cloning of the ribosomal P-proteins MgP1, MgP2, MgP0, and superoxide dismutase (SOD) in the mussel Mytilus galloprovincialis and analysis of MgP0 at stress conditions, Gene, 2009, 430, 77-85
[44] Guerra B., Issinger O.-G., Protein kinase CK2 in human diseases, Curr. Med. Chem., 2008, 15, 1870-1886
[45] Arnold K., Bordoli L., Kopp J., Schwede T., The SWISS-MODEL workspace: a web-based environment for protein structure homology modelling, Bioinformatics, 2006, 22, 195-201
[46] Kopp J., Schwede T., Automated protein structure homology modeling: a progress report, Pharmacogenomics, 2004, 5, 405-416
[47] Battistutta R., Sarno S., De Moliner E., Marin O., Issinger O.-G., Zanotti G., et al., The crystal structure of the complex of Zea mays alpha subunit with a fragment of human beta subunit provides the clue to the architecture of protein kinase CK2 holoenzyme, Eur. J. Biochem., 2000, 267, 5184-5190
[48] Raaf J., Brunstein E., Issinger O.-G., Niefind K., The interaction of CK2alpha and CK2beta, the subunits of protein kinase CK2, requires CK2beta in a preformed conformation and is enthalpically driven, Protein Sci., 2008, 17, 2180-2186