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Heat Shock Mediated Modulation of Protein Kinase CK2 in the Nuclear Matrix

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Abstract Nuclear matrix, a key structure in the nuclear framework, appears to be a particularly responsive target during heat shock treatment of cells. We have previously shown that nuclear matrix is a preferential target for protein kinase CK2 signaling in the nucleus. The levels of CK2 in the nuclear matrix undergo dynamic changes in response to altered growth status in the cell. Here, we have demonstrated that CK2 targeting to the nuclear matrix is profoundly influenced by treatment of the cells to temperatures higher than 37°C. Rapid increase in the nuclear matrix association of CK2 is observed when cells are placed at temperatures of 41 and 45°C. This effect at 45°C was higher than at 41°C, and was time-dependent. Also, different cell lines behaved in a qualitatively similar manner though the quantitative responses differed. The modulations in the nuclear matrix associated CK2 in response to heat shock appear to be due to trafficking of the enzyme between cytosolic and nuclear compartments. In addition, it was noted that isolated nuclei subjected to heat shock also responded by a shuttling of the intrinsic CK2 to the nuclear matrix compartment. These results suggest that modulations in CK2 in the nuclear compartment in response to the heat stress occur not only by a translocation of the enzyme from the cytoplasmic compartment to the nuclear compartment, but also that there is a redistribution of the kinase within the nuclear compartment resulting in a preferential association with the nuclear matrix. The results support the notion that CK2 association with the nuclear matrix in response to heat shock may serve a protective role in the cell response to stress. J. Cell. Biochem. 85: 583–591, 2002. Published 2002 Wiley-Liss, Inc.†

Key words: protein kinase CK2; nuclear matrix; heat shock; cancer cells; signaling

Heat shock induces many changes in cell functions at both the translational and transcriptional levels [for reviews see, Anghileri and Roberts, 1986; Roti Roti and Laszlo, 1988]. The translational effects of heat shock are reflected in the well-documented inhibition of protein synthesis [Duncan, 1996]. A major role is played by modification of the activity of eukaryotic initiation factors [Schamhart et al., 1984; Duncan, 1996; Pain, 1996]. Recent studies have shown that a primary mechanism of control of translation initiation after heat shock is mediated by regulation of eIF2B activity [Scheper et al., 1997]. The transcriptional events in response to heat shock appear to be regulated by the heat shock factor, a pre-existing protein which is transiently activated (via phosphorylation) in response to hyperthermia [Høj and Jakobsen, 1994; Huang et al., 1997].

Considerable evidence also points to heat shock-mediated enhanced translocation of proteins into the nuclear compartment and their association with subnuclear structures, such as chromatin and nuclear matrix. This has been suggested to play a role in cell survival, DNA synthesis and repair, and transcription [Kampinga et al., 1985; Roti Roti and Laszlo, 1988; Fisher, 1990]. Recent studies have clearly documented that changes in the nuclear proteins in response to heat shock are significantly reflected in the nuclear matrix, and further, the modifications in the association of specific proteins

Abbreviations used: CK2 or protein kinase CK2, casein kinase 2; 5α-DHT, 5α-dihydrotestosterone; PMSF, phenylmethylsulfonyl fluoride; DTT, dithiothreitol.

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with the nuclear matrix is of a differential nature [VanderWaal et al., 1996, Roti Roti et al., 1998]. These observations are in accordance with the electron microscopic analysis of nuclear matrix fine structure and composition following heat shock [Wachsberger and Coss, 1993, 1994].

The aforementioned observations on the nuclear matrix association of proteins in response to heat shock are of considerable interest since the nuclear matrix, a filamentous structure that provides the internal scaffold for the nuclear architecture, has been implicated in critical nuclear activities, such as DNA replication, repair and transcription, RNA processing and transport. As such, nuclear matrix serves as a binding site for a wide range of signaling molecules involved in regulation of cell function [Berezney, 1991; Getzenberg et al., 1991; Nickerson and Penman, 1992; Stein et al., 2000]; one such signaling molecule is the protein kinase CK2 (formerly known as casein kinase 2 or II) [Tawfic et al., 1996; Ahmed, 1999].

Protein kinase CK2 is a ubiquitous serine/threonine kinase, which plays multiple roles in the cell, including in protein synthesis and regulation of cell growth and proliferation [Pinna, 1990; Tuazon and Traugh, 1991; Litchfield and Lüscher, 1993; Ahmed, 1994; Allende and Allende, 1995; Guerra and Issinger, 1999; Ahmed et al., 2000; Tawfic et al., 2001]. Our studies have documented that protein kinase CK2 undergoes dynamic association with the nuclear matrix in response to growth signals and that this association is physiologically relevant [Tawfic and Ahmed, 1994a,b; Tawfic et al., 1996; Guo et al., 1999]. Concordance of the loss of CK2 from the nuclear matrix and induction of apoptosis in response to removal of survival factors, and the recent demonstration that CK2 can block chemical-mediated apoptosis in cells has provided evidence that besides the commonly recognized function of CK2 in cell growth, it also plays a role in cell survival [Ahmed, 1999; Ahmed et al., 2000; Guo et al., 2001].

Considering the involvement of the nuclear matrix in binding of nuclear proteins in response to heat shock and its role as an anchor for CK2 signaling, we decided to examine the effect of heat induced stress on the CK2 association with the nuclear matrix in a number of cell lines. We have observed that heat shock induces a transient enhancement of CK2 association with the nuclear matrix. This association declines over time. These changes may be related to effects of CK2 on nuclear integrity and reflect on a protective role of CK2 in response to stress. While these studies were in progress, Gerber et al. [2000] reported that heat induces relocalization of CK2 especially to the nuclear compartment. Thus, our results are in accordance with the report by Gerber et al. [2000], but further extend those observations by characterizing the involvement of the nuclear matrix as a locus of CK2 association in response to heat shock in a number of diverse cell lines.

MATERIALS AND METHODS

Cell Lines

The cell lines used were obtained from the following sources: ALVA-41 from Dr. Richard C. Ostenson, U.S. Department of Veterans Affairs, American Lake VA Medical Center, Tacoma, WA; BPH-1 from Dr. Simon W. Hayward, Department of Anatomy, School of Medicine, University of California at San Francisco, San Francisco, CA; Shionogi 115 from Dr. John Isaacs, Prostate Cancer Laboratories, Oncology Center, Johns Hopkins University, Baltimore, MD; LNCaP from American Type Culture Collection, Rockville, MD.

Chemicals

Defined fetal bovine serum (FBS) and charcoal/dextran stripped fetal bovine serum (CS-FBS) were purchased from HyClone Laboratories, Logan, UT. RPMI-1640 culture medium was obtained from Life Technologies, Inc., (GIBCO/BRL), Grand Island, NY. The specific peptide substrate for CK2 was synthesized by Peptide Technologies Corp., Gaithersburg, MD. Anti-CK2α-subunit antibody was purchased from Calbiochem-Novabiochem International, San Diego, CA. The [γ-^{32}P]ATP was purchased from ICN Biomedicals, Costa Mesa, CA. All reagents were of the highest purity available.

Methods

Cell culture and heat shock treatment. Cells were grown at 37°C in 75 cm^2 culture flasks until they reached 90% confluency. The culture medium used for each of the specific cell types was as follows: ALVA-41, RPMI-1640 with 6% FBS; BPH-1, RPMI-1640 with 8% FBS; LNCaP, RPMI-1640 with 10% FBS supplemented with 10^{-10} M 5α-DHT; and Shionogi 115, RPMI-1640 with 10% CS-FBS supplemented with 10^{-8} M 5α-DHT.

The heat shock treatments were carried out by rapidly transferring flasks from 37 to 45°C incubator for the indicated times of incubation. This experimental approach, rather than treating detached cells, was adopted to provide for minimal stress to cells prior to heat shock. We estimated that the change in the flask temperature from 37 to 45°C occurred within less than 2 min. At the conclusion of the heat treatment, cells were rapidly removed from the flasks by scraping, collected by centrifugation at 600*g* for 5 min, and then were placed on ice. The pelleted cells were washed twice with cold 0.9% saline containing 1 mM phenylmethylsulfonyl fluoride (PMSF) and 2 μg/ml leupeptin. Parallel flasks kept at 37°C were prepared simultaneously. Two flasks were employed for each condition tested.

Preparation of nuclear matrix. The nuclear matrix and cytosol were prepared immediately from the washed cells using a previously described procedure referred to as Method C [Tawfic et al., 1997]. The recovery of protein in the nuclear matrix and cytosol fractions was determined by a modified Coomassie staining procedure [Ahmed et al., 1996].

Assay of CK2 activity. The CK2 enzyme activity was measured using a specific peptide substrate, R-R-R-A-D-D-S-D-D-D-D-D [Marin et al., 1994]. Matrix protein (2.5 μg) was incubated for 20 min at 37°C with 30 mM Tris-HCl pH 7.45, 150 mM NaCl, 40 mM β-glycerophosphate, 5 mM $MgCl_2$, 1 mM dithiothreitol (DTT), 0.5 mM PMSF, 10 μg/ml leupeptin, 50 μM ATP (γ-^{32}P-ATP specific activity of 3×10^6 cpm/nmol ATP) with or without 200 μM peptide substrate in a 100 μl final volume. [Guo et al., 2001]. The same procedure was employed for assaying the CK2 activity in the cytosolic fraction.

Western blot analysis for CK2. For immunodetection of CK2, a 50-μg sample of the nuclear matrix protein was separated on a 10% acrylamide gel containing 4 M urea and 0.1 % SDS for Western blotting, as described previously [Guo et al., 1999; Yu et al., 1999]. The primary antibody, anti-CK2α, was used at 2 μg/ml and was incubated with the blot for 2 h at room temperature. The second antibody, alkaline phosphatase conjugated anti-mouse IgG, was used at 0.5 μg/ml and was incubated with the blots for 2 h at room temperature. Immobilized alkaline phosphatase was visualized using 5-bromo-4-chloro-indolyl phosphate and Nitro Blue Tetrazolium as described previously [Guo et al., 1999; Yu et al., 1999].

RESULTS

Effect of Heat Shock on CK2 Dynamics in the Nuclear Matrix of ALVA-41 Cells

We have previously documented that cells treated with apoptosis-inducing chemical agents, such as etoposide or diethylstilbestrol, demonstrate a rapid influx of CK2 to the nuclear matrix compartment, and that this appears to be a protective response of the cell [Guo et al., 2001]. It has been recently reported that heat shock causes a relocalization of CK2 in the cell, especially to the nuclear compartment [Gerber et al., 2000]. We therefore examined the effect of heat shock on ALVA-41 cells to investigate the dynamics of CK2 in the nuclear matrix fraction isolated from these cells. The results in Figure 1A show that under our experimental conditions when cells were transferred from 37 to 45°C, there was a transient initial drop observed at 15 min followed by a time-dependent increase in the CK2 activity in the nuclear matrix fractions isolated from these cells. The change in the nuclear matrix associated activity reached a maximal level exceeding a 2-fold increase at about 45 min of exposure to 45°C compared with the controls at 37°C. However, subsequent to this period, there was a decline in the CK2 activity in the nuclear matrix as observed at 60 min of heat shock at 45°C. The latter decline may have some bearing on the eventual response of the cells to heat shock, i.e., it may have reached a point where these cells may eventually undergo apoptosis. It has been previously documented that about 45% of the PC-3 cells subjected to heat shock of 44°C underwent apoptosis measured at 24 h subsequently [Li and Franklin, 1998]. The ALVA-41 cells were found to behave in an analogous manner, whereas cells treated to lower temperatures, such as 41°C, did not undergo apoptosis subsequent to the heat shock (result not shown).

The above-described changes in the enzyme activity (Fig. 1A) appear to accord with the immunoreactive amount of the enzyme in the nuclear matrix under these conditions (Fig. 1B). To test that the changes in the CK2 activity in the nuclear matrix may be due to trafficking of the kinase from the cytosolic compartment, analysis of the CK2 activity and protein (by immunoblot assay) was undertaken in the

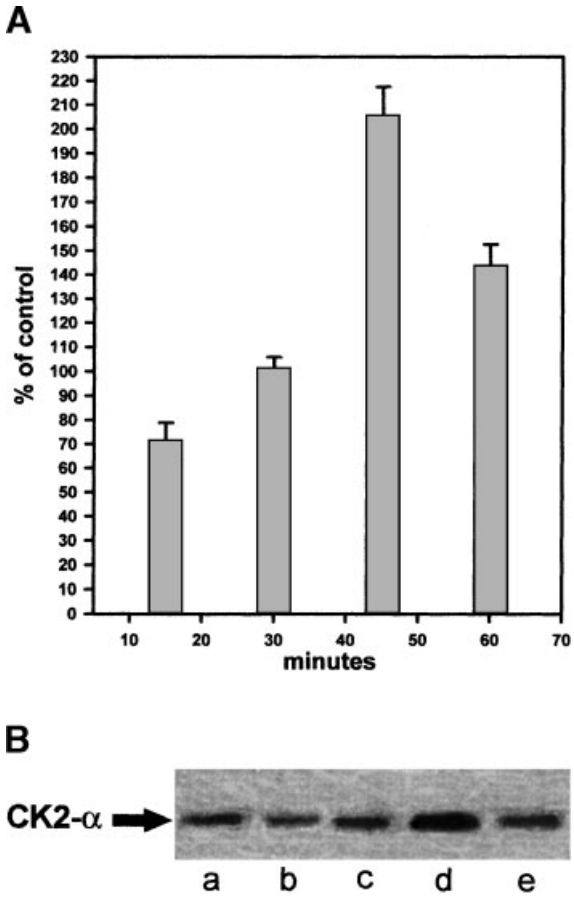

Fig. 1. Effect of heat shock on CK2 association with the nuclear matrix of ALVA-41 cells. **Panel A**: cells were subjected to 45°C, and at the indicated times were harvested for isolation of the nuclear matrix as described under Methods. CK2 activity was determined in these fractions. Data are presented as percent of the corresponding controls at 37°C. **Panel B**: immunoblot analysis of the nuclear matrix-associated CK2 was carried out as described under Methods. **Lane a**, 37°C control; **lane b–e**, 45°C for 15 min (lane b), 30 min (lane c), 45 min (lane d), and 60 min (lane e), respectively. The relative densitometric values corresponding to the immunoblot are 1.0, 0.7, 1.1, 1.9, and 1.2, for lanes a–e, respectively.

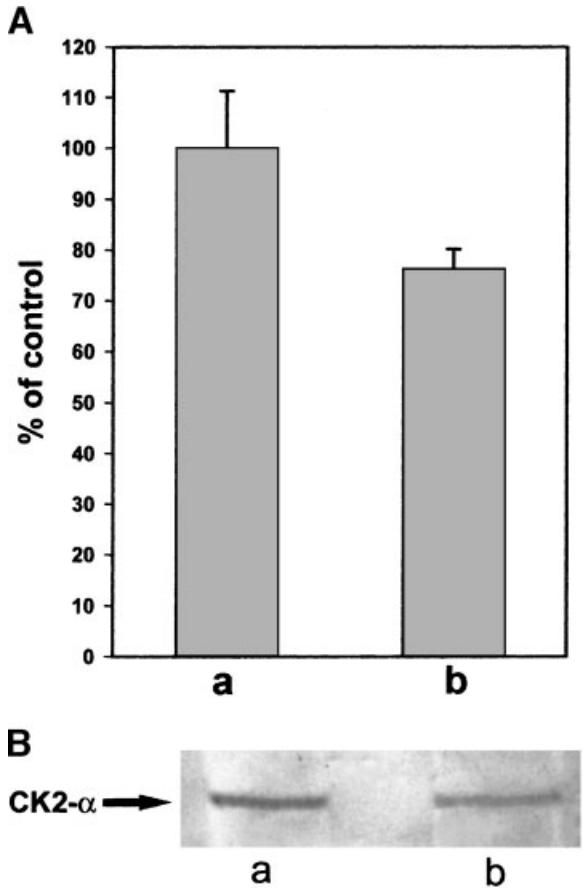

Fig. 2. Effect of heat shock on cytosolic CK2 in ALVA-41 cells. **Panel A**: cells were subjected to 37 and 45°C for 45 min. Cytosolic fraction was isolated and CK2 activity was determined as described under Methods. **Lane a**, 37°C treatment; **lane b**, 45°C treatment. **Panel B**: immunoblot of CK2-α in the cytosolic fraction corresponding to the activity measurement shown in panel A. Lane a, 37°C control; lane b, 45°C treatment for 45 min. The densitometric values corresponding to the immunostain were 1.0 and 0.75, for lane a and b, respectively.

cytosolic fraction. The results show that there was a decrease in the CK2 activity (Fig. 2A) and immunoreactive CK2-α (Fig. 2B) in the cytosolic fraction isolated from ALVA-41 cells treated at 45°C compared with 37°C. The results support the notion that heat shock mediated reduction in CK2 in the cytoplasmic fraction may reflect the translocation of CK2 protein to the nucleus under these conditions.

The severity of the heat shock is known to influence the adaptive response of the cells and recovery from the heat shock [Scheper et al., 1997; Li and Franklin, 1998]. For example, the recovery of cells from heat shock of 42°C has been found to be complete, whereas at temperatures higher than 42°C, there was a progressive induction of apoptosis over time [Li and Franklin, 1998]. Since the response of ALVA-41 cells to heat shock was along similar lines, we compared the dynamics of nuclear matrix associated CK2 in cells treated to 41 or 45°C. The results in Figure 3 show that the response of cells to 41°C with respect to changes in the nuclear matrix-associated CK2 activity is smaller than that observed in the nuclear matrix fractions from cells treated at 45°C. At 41°C compared with 37°C, there was minimal change in nuclear matrix-associated CK2 during the first 30 min; however, a significant increase in CK2

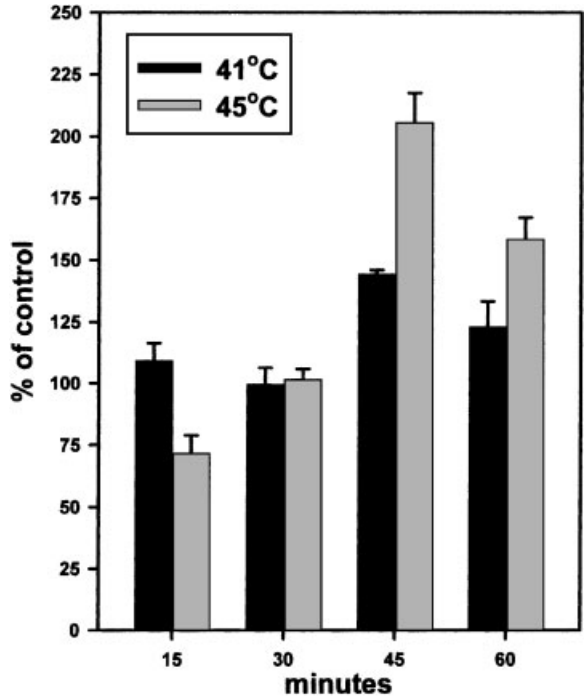

Fig. 3. Effect of different temperatures on association of CK2 with the nuclear matrix of ALVA-41 cells. Cells were treated to a temperature of 41 or 45°C for the indicated periods of time. Nuclear matrix preparations were isolated and the intrinsic CK2 activity in these fractions was determined. CK2 activity data are indicated as percent of the corresponding control values for nuclear matrix isolated from cells kept at 37°C.

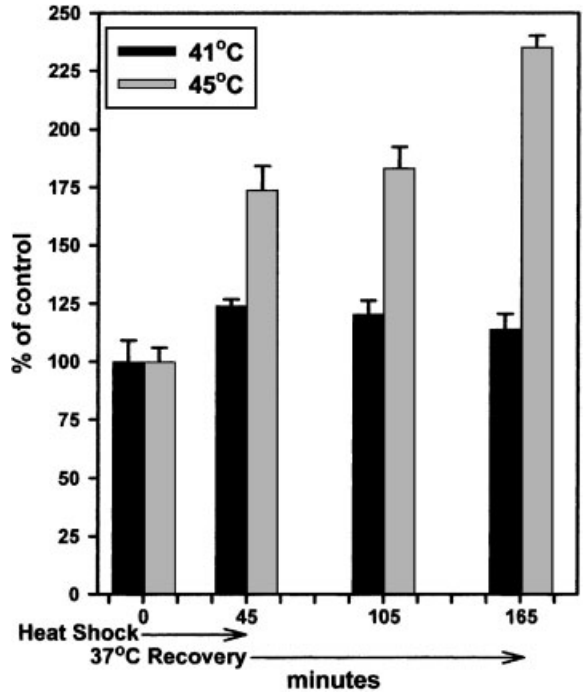

Fig. 4. Effects on nuclear matrix-associated CK2 during recovery of ALVA-41 cells from heat shock. Cells were treated for 45 min at 41 or 45°C, and then transferred to 37°C for additional periods of time up to 120 min. CK2 activity in the nuclear matrix isolated from these cells was determined. The CK2 activity data are expressed as percent of that at 37°C.

in the nuclear matrix was apparent by 45 min at 41°C. The effect of treating the cells at 45°C was qualitatively similar, although the extent of change in nuclear matrix-associated CK2 in cells treated at 45°C were significantly greater than that observed at 41°C. However, in both cases, the increase in CK2 activity was no longer apparent at 60 min of heat shock. Considering that the cells subjected to 41°C do not show any long-term damage, it would seem that the reduction of CK2 at 60 min at 41°C may indicate that the cells had adapted to this temperature. On the other hand, the decline in the CK2 in the nuclear matrix of cells at 45°C might be related more to the impending decline in cell viability.

Nuclear Matrix-Associated CK2 During Recovery From Heat Shock

Experiments were undertaken to determine the response of the nuclear matrix-associated CK2 when cells were treated at 41 or 45°C for 45 min and then allowed to recover at 37°C for an additional period of 120 min. The results in Figure 4 demonstrate that in cells that were initially subjected to 41°C shock, there was the initial increase in the nuclear matrix-associated CK2 analogous to that shown in Figure 3. This level of nuclear matrix-associated CK2 in these cells was sustained for the next 60 min but returned to the normal control levels by 120 min, following the initiation of the recovery period at 37°C. On the other hand, cells that were initially subjected to 45°C of heat shock for 45 min, the enhancement in nuclear matrix-associated CK2 was sustained over time and did not return to lower levels even at 120 min of the recovery period at 37°C. This further suggests that the original stress induced by the 45°C temperature was not reversed on transferring the cells to 37°C. The persistence of the higher level of CK2 under these conditions is reminiscent of that observed when cells were treated with etoposide which resulted in a large increase in nuclear matrix association of CK2 [Guo et al., 2001]. It may be recalled that agents, such as etoposide induce DNA damage; it is likely that heat shock treatment of cells at 45°C also induces DNA damage, since there is extensive induction of

apoptosis in cells subjected to this level of heat shock. As documented previously, the persistently high level of CK2 in the nuclear matrix under these conditions may reflect an adaptive cell survival response [Gerber et al., 2000; Guo et al., 2001].

Evidence for Intranuclear Trafficking of CK2 in Response to Heat Shock

The translocation of proteins from the cytoplasm to the nuclear compartment in response to heat shock has been well documented [Roti Roti and Turkel, 1994; VanderWaal et al., 1996]. The results shown in Figures 1 and 2 suggested that cells subjected to heat shock demonstrated elevated CK2 in the nuclear matrix isolated from these cells, and this response appeared to be due to shuttling of the kinase from the cytoplasm to the nuclear matrix in response to heat shock. Experiments were undertaken to test whether or not there was also an intranuclear redistribution of CK2 in the nuclear matrix in response to heat shock. To that end, we prepared the nuclear fraction from cells and subjected the isolated nuclei to 41°C treatment for 15–60 min, followed by an examination of the intranuclear status of CK2 in the nuclear matrix isolated from these nuclei. The results in Figure 5 show that under these conditions, the nuclear matrix prepared from nuclei treated at 37°C showed no significant alteration in the association of CK2 with this fraction. However, nuclear matrix isolated from nuclei that were subjected to 41°C demonstrated time-dependent fluctuations in the CK2 association in a manner that was qualitatively similar to that observed for treatment of cells at this temperature, as was shown in Figure 3. These results suggest that besides translocation from the cytoplasmic fraction, there may also be significant redistribution of the nuclear associated CK2 resulting in altered association with the nuclear matrix structure in response to the heat shock. Therefore, it appears that the dynamic changes in the trafficking of CK2 to the nuclear matrix occur even under the mild conditions of heat shock which do not produce a permanent injury to the cells.

Heat Shock Response of Nuclear Matrix-Associated CK2 in Different Cell Lines

In order to determine that CK2 dynamics in the nuclear matrix fraction were evident as a general response to heat shock, we examined

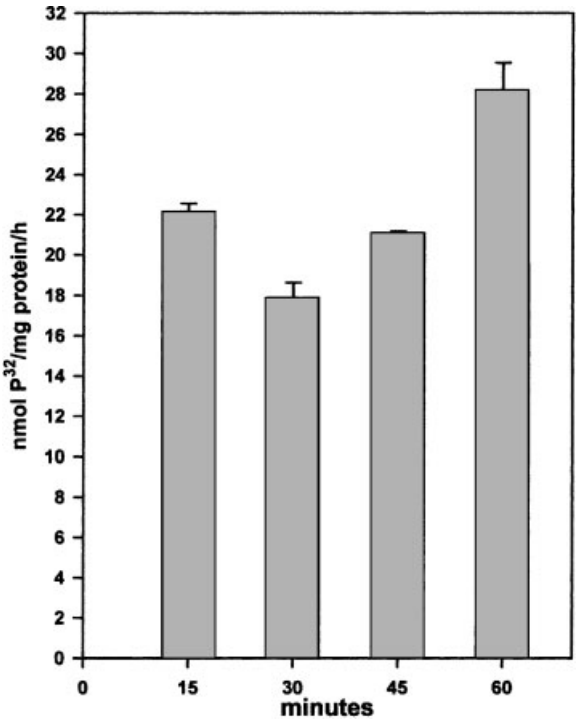

Fig. 5. Redistribution of CK2 in the nuclear matrix of ALVA-41 cells following heat shock treatment of isolated nuclei. Purified nuclei were subjected to a temperature of 41°C for the indicated periods of time. Nuclear matrix fractions were isolated and intrinsic CK2 activity was determined.

the effect of heat shock on diverse cell lines. The results in Figure 6 show the response of LNCaP (a prostate cancer cell line), Shionogi carcinoma (a mouse mammary tumor cell line), and BPH-1 (a prostate epithelial cell line from benign prostatic hyperplasia) to heat shock mediated changes in the nuclear matrix-associated CK2. The results in Figure 6 show that maintenance of these cells at 45°C resulted in a time-dependent increase in nuclear matrix-associated CK2; the response of the various cells varied quantitatively, though it was qualitatively similar. These results suggest that dynamic changes in the nuclear matrix with respect to the CK2 signal are of a general nature and not restricted to a specific cell type.

DISCUSSION

In recent years, nuclear matrix has emerged as an important subnuclear structure that plays a key role in chromatin organization and cell growth. In addition to the proteins that are intrinsic structural components of the nuclear matrix, it appears to also serve as a locus for the

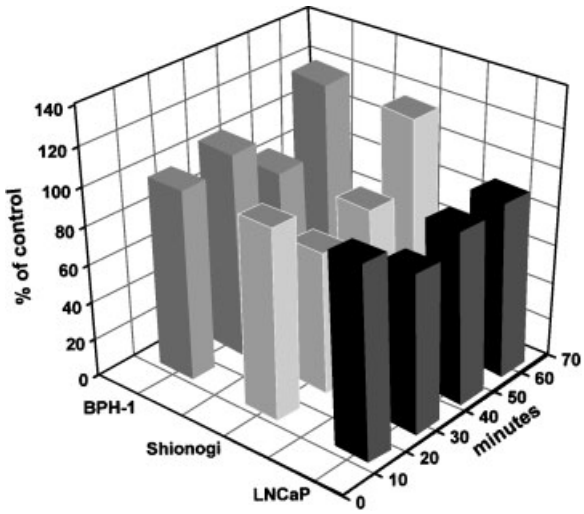

Fig. 6. Effect of heat shock treatment on nuclear matrix association of CK2 in different cell lines. Three cell lines with different characteristics (LNCaP, Shionogi, and BPH-1) were subjected to 45°C temperature for the indicated periods of time. Nuclear matrix associated CK2 was then determined as described under Methods.

targeting of specific regulatory molecules [Berezney, 1991; Getzenberg et al., 1991; Nickerson and Penman, 1992; Stein et al., 2000], and protein kinase CK2 can be considered as one such protein. We have previously documented that CK2, a ubiquitous multifunctional protein serine/threonine kinase, undergoes dynamic modulations in the nuclear matrix in response to diverse stimuli that induce cell growth or cell death [Ahmed, 1999; Ahmed et al., 2000; Tawfic et al., 2001].

Considerable evidence has also emerged to indicate that nuclear matrix is a particularly sensitive nuclear site for the cell response to heat shock such that dynamic changes in its structure and composition have been documented in response to heat shock [VanderWaal et al., 1996; Roti Roti et al., 1998; Neri et al., 1997; Lepock et al., 2001]. This is of particular interest in view of a potential role of heat treatment in cancer therapy [Li and Franklin, 1998], and in this regard it was noteworthy that cells subjected to temperatures lower than 42°C did not sustain an injury while those treated to temperatures higher than 42°C exhibited evidence of significant apoptotic injury. In the present work, we have shown that CK2 undergoes dynamic and reversible translocation to the nuclear matrix in response to heat shock in a time- and temperature-dependent manner. Our results indicate that the shuttling of the CK2 to the nuclear matrix occurs from the cytoplasmic compartment in response to even a mild heat shock, such as 41°C. Interestingly, it is also apparent that some intranuclear trafficking of CK2 also occurs under these conditions as indicated in the experiments where isolated nuclei were subjected to temperatures greater than 37°C which resulted in a dynamic increase in the association of CK2 with the nuclear matrix. This further points to a possible key role played by the nuclear matrix structure in the nuclear function in response to heat shock. The dynamic nature of the CK2 in the nuclear structure is indicated by several of the features of its association with the nuclear matrix in response to heat shock. These include, e.g., the oscillatory behavior of the association of CK2 with the nuclear matrix, its time- and temperature-dependence, and its reversibility. Furthermore, the similarity of the dynamic nature of the CK2 association with the nuclear matrix in response to heat shock in diverse cell types suggests the general nature of this adaptive process.

Our experiments on the study of nuclear matrix dynamics of CK2 in cells subjected to higher level of heat shock, such as 45°C, are analogous to our observations on etoposide treatment of cells described previously [Guo et al., 2001]. In both of these cases, there is a substantial trafficking of CK2 to the nuclear matrix. In the case of etoposide, its ability to induce apoptosis in cells (associated with DNA damage) is well documented [Sun et al., 1999], and it appears that heat shock (such as, 45°C employed by us) of cells also evokes a similar DNA damage and apoptotic response [Gerber et al., 2000]. Our results suggest that both forms of injury in these cells appear to demonstrate similar dynamics of CK2 in the nuclear matrix. Thus, it is likely that CK2 trafficking to the nuclear matrix in response to heat shock may also reflect an adaptive cellular response to this injury analogous to that described previously for agents, such as etoposide and diethylstilbestrol [Guo et al., 2001].

Our results are in accordance with those of Gerber et al. [2000], who found that heat treatment of cells (at 42–45°C) resulted in redistribution of CK2 to the subnuclear structures, such as nucleolus, interchromatin space, and nuclear speckles. However, we have extended these observations by demonstrating that the heat shock mediated nuclear changes are also reflected in the isolated purified nuclear

matrix preparations derived from these cells as well in nuclear matrix prepared from isolated nuclei subjected to heat shock. The general nature of these observations raises the question of the role of CK2 shuttling to the nuclear matrix in response to heat shock. In our previous work, we had shown that modulations of CK2 in the nuclear matrix was related to cell growth and cell death. In various studies, it was demonstrated that trafficking of CK2 to the nuclear matrix was associated with cell growth, whereas loss of CK2 from this structure occurred concordant with or related to induction of apoptosis [Ahmed, 1999; Ahmed et al., 2000; Tawfic et al., 2001; Wang et al., 2002]. Further, we observed that treatment of cells with chemical mediators of apoptosis resulted in trafficking of the CK2 to the nuclear matrix. This was found to be a protective response of the cell to the induction of apoptosis, since prior overexpression of CK2 resulted in suppression of the chemical-mediated apoptosis [Guo et al., 2001]. Thus, the present results would imply that the translocation of CK2 to the nuclear matrix in response to heat shock might also be a protective response of the cell to this form of stress.

In summary, we have demonstrated that protein kinase CK2 undergoes rapid reversible translocation to the nuclear matrix in response to heat shock. This protein kinase has been previously implicated in cell growth and proliferation; however, it now appears to also play a key role in promoting cell survival in response to stress. Our results corroborate the studies on a role of the nuclear matrix in cellular integrity and suggest that trafficking of CK2 to the nuclear matrix serves as a protective mechanism for the cell subjected to heat shock stress.

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