We have identified a cDNA (named C114) that encodes novel transcripts induced by IL-11 in mouse 3T3 L1 cells. Northern analysis of RNAs from multiple mouse tissues detects two C114 transcripts of ~1.0 and ~2.0 kb with the highest expression in liver, testis, brain, and kidney. The C114 cDNA contains an open reading frame of 187 amino acids with a predicted mass of 21 kDa. Three putative nuclear localization signals are predicted at amino acids 83–88, 126–131, and 167–178. Using green fluorescent protein (GFP)-C114 fusion plasmids, amino acids 126–131 are shown to be essential for the nuclear localization of C114. An arginine-rich region (amino acids 98–143) spanning the nuclear localization signals (amino acids 126–131) exhibits a double-stranded RNA (dsRNA) binding activity. Competition experiments with different RNA homopolymers demonstrate that C114 preferentially binds to poly(I:C). Similar to other dsRNA-binding proteins, C114 binds to the dsRNA-activated protein kinase, protein kinase R (PKR), via dsRNA-binding domains of PKR and the N-terminal region of the C114 protein. In vitro kinase assays indicate that C114 inhibits PKR activation via dsRNA-independent mechanism. Overexpression of C114 protein inhibits the induction of eIF-2α phosphorylation following poly(I:C) treatment. This is the first demonstration of a novel PKR modulator induced by a gp130 superfamily cytokine that may play a role in cytokine-mediated biological functions.

**MATERIALS AND METHODS**

**Antibodies and Reagents—**3T3 L1, NIH-3T3, and HEK 293 cells were cultured in Dulbecco's modified Eagle's medium containing 10% fetal bovine serum and penicillin/streptomycin. Anti-FLAG monoclonal M2 antibody was from Sigma, and anti-V5 monoclonal antibody was from Abcam. The abbreviations used are: PKR, protein kinase R; dsRNA, double-stranded RNA; GFP, green fluorescent protein; EGFP, enhanced GFP; DRBD, dsRNA-binding domains; PACT, PKR activating protein; TRBP, HIV-1 transactivating response RNA-binding protein.

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**References—**

1. The abbreviations used are: PKR, protein kinase R; dsRNA, double-stranded RNA; GFP, green fluorescent protein; EGFP, enhanced GFP; DRBD, dsRNA-binding domains; PACT, PKR activating protein; TRBP, HIV-1 transactivating response RNA-binding protein.
Invitrogen. The anti-εIF-2α and phosphospecific anti-εIF-2α antibodies were from BIOSOURCE International (Camarillo, CA). Recombinant human IL-11 was kindly provided by Genetics Institute (Cambridge, MA). Various polynucleotide resins were from Amersham Biosciences.

**Polycrystalline DNA Subtraction**—Total cellular RNA was isolated from starved or IL-11-stimulated (500 ng/ml) mouse 3T3 L1 cells using TRIzol reagent (Invitrogen), and poly(A) RNA was purified using oligo(dT) beads (Invitrogen). cDNA synthesis and subcloning were done using the PCR-Select cDNA subtraction kit (Clontech) following manufacturer’s instructions. mRNA of IL-11-treated 3T3 L1 cells was used as a tester, and mRNA of untreated cells was used as a driver. Subtracted PCR products were cloned into pGEM-T Easy vector (Promega) to obtain a subtraction library. DNA fragments were prepared from individual clones by PCR and used as hybridization probes for Northern blot analysis. Total RNA extracted from IL-11-treated or untreated 3T3 L1 cells was prepared as mentioned above. RNA was electrophoresed in a 1.0% agarose gel containing formaldehyde and transferred onto a nylon membrane (Hybond N+, Amersham Biosciences). After a cDNA fragment was confirmed by Northern blot to show a differential expression pattern, the full-length Amersham Biosciences). After a cDNA fragment was confirmed by Northern blot to show a differential expression pattern, the full-length cDNA was cloned from a mouse liver cDNA library (Stratagene) by rapid amplification of cDNA ends. Poly(A)+ RNA blot of mouse tissues (Mouse MTN blot, Clontech) was also used for Northern analysis.

**Cellular Localization of C114 Protein**—The entire coding region and various mutant forms of C114 cDNA were amplified by PCR using primers containing a EcoRI or BglII and cloned into pcDNA3 (Clontech). These were first washed and resuspended in wash buffer 1 (20 mM Tris, pH 7.5, 100 mM NaCl) and then incubated in pull-down buffer (50 mM Tris, pH 7.5, 100 mM NaCl, 1 mM EDTA, 10% glycerol, 1% Triton X-100) at 4 °C overnight. Protein A-agarose was added for an additional hour followed by washing four times with 500 μl of wash buffer 2 (20 mM Tris, pH 7.5, 50 mM KCl, 0.5 mM EDTA, 0.5% Nonidet P-40) or 1 unit/ml heparin was added as a PKR activator. In some samples, kinase activities were assayed in the presence of the affinity-purified wild-type or mutant form IV of C114 protein. Labeled proteins were analyzed by SDS-PAGE and visualized by autoradiography and Western blotting.

**Partial Purification of FLAG-C114 Proteins**—HEK 293 cells were transfected with plasmids expressing FLAG-tagged wild-type or the mutant form IV of C114 protein (see Fig. 2B). Cells expressing FLAG-tagged fusion proteins were harvested and lysed as described above. The cytoplasmic fraction containing FLAG-tagged C114 was incubated with 1 μg/ml of polyclonal anti-V5 (IC) or 1 unit/ml heparin was added as a PKR activator. In some samples, kinase activities were assayed in the presence of the affinity-purified wild-type or mutant form IV of C114 protein. Labeled proteins were analyzed by SDS-PAGE and visualized by autoradiography and Western blotting.

**Construction of Eukaryotic Expression Vector Encoding C114 with a Flag Epitope**—To generate a FLAG epitope-tagged version of C114 for expression in mammalian cells, the cloning region of C114 was amplified by PCR from C114/pGEM-T using 5’-AGGAAATTCTATGGCCGATCTTTGCTGCCC-3’ and 5’-AAGCATCTGCCCATTAGGACACG-3’ as the forward and reverse primer with a BamHI and EcoRI restriction site, respectively. The 600-bp PCR product was ligated in-frame with a FLAG epitope from pcDNA3-CMV-2 vector.

**Co-immunoprecipitation**—HEK 293 cells were transfected with FLAG epitope-tagged C114 in pCMV-2, FLAG-tagged PACT, and/or V5-tagged PKR in Vet vector (described in Refs. 15 and 17). Transfected cells were washed twice with phosphate-buffered saline, lysed in 20 mM Tris, pH 7.6, 20% glycerol, 2 mM MgCl2, 1 mM dithiothreitol, 100 mM NaCl, 10% glycerol, 1% Triton X-100. Cell debris was removed by centrifugation at 14,000 rpm for 10 min. Lysates were incubated with either M2 anti-FLAG (Sigma) or anti-V5 (Invitrogen) and Protein A-agarose (Roche Molecular Biochemicals) overnight at 4 °C. The immunocomplexes were washed with lysis buffer and separated by SDS-PAGE.

Proteins were transferred to polyvinylidene difluoride membranes and probed with monoclonal anti-V5 or anti-FLAG (1:5,000) followed by appropriate horseradish peroxidase-conjugated secondary antibody and ECL detection (Amersham Biosciences).

**Pull-down Assays**—35S-labeled wild-type or mutated forms of PKR were in vitro translated using TsT-coupled reticulocyte system from Promega (18). FLAG epitope-tagged C114 protein was immunoprecipitated from, heparin-HEK 293 cell lysates with the M2 anti-FLAG (Sigma) and Protein A-agarose (Roche Molecular Biochemicals) as described above. Twenty μl of the in vitro translated 35S-labeled proteins was incubated with FLAG-tagged C114 protein in immunocomplexes containing Protein A-agarose and anti-FLAG antibody in 500 μl of pull-down buffer (20 mM Hepes-ROH, pH 7.5, 100 mM KCl, 1 mM dithiothreitol, and 0.5% Nonidet P-40) at 4 °C for 2 h. The resin was washed four times with 500 μl of pull-down buffer. Proteins were eluted with 40 μl of Laemmli sample buffer, boiled for 5 min, and resolved by SDS-PAGE. The proteins were transblotted to a polyvinylidene difluoride membrane followed by autoradiography and processed for Western blotting with M2 anti-FLAG antibody. Five μl of the in vitro translated 35S-labeled proteins was also resolved by SDS-PAGE to visualize the input proteins.

**Kinase Assays**—HEK 293 cells were transfected with V5-tagged PKR constructs. In some samples, PKR-expressing plasmids was co-transfected with various forms of FLAG-tagged C114 plasmids (see Fig. 2B). Twenty-four hours after transfection, cells were washed with phosphate-buffered saline buffer (50 mM Tris, pH 7.4, 50 mM KCl, 0.5 mM EDTA, 0.5% Nonidet P-40) and lysed in an equal volume of lysis buffer. After centrifugation at 14,000 rpm for 10 min, the supernatants were collected. PKR was immunoprecipitated from aliquots containing 100 μg of total protein using an anti-V5 monoclonal antibody in radio-immune precipitation buffer (50 mM Tris, pH 7.4, 50 mM KCl, 400 mM NaCl, 1 mM EDTA, 10% glycerol, 0.2 mg/ml aprotinin, 0.2 mg/ml leupeptin, 0.2 mg/ml phenylmethylsulfonyl fluoride, 20% glycerol, 1% Triton X-100) at 4 °C overnight. Protein A-agarose was added for an additional hour followed by washing four times with 500 μl of wash buffer 2 (20 mM Tris, 100 mM NaCl, 1 mM EDTA, 0.5% Nonidet P-40, 0.1 M phenylmethylsulfonyl fluoride, 100 μM vanadate, 1 mM NaF, pH 8.0) and twice with activity buffer (20 mM Tris, pH 7.5, 50 mM KCl, 2 mM MgCl2, 2 mM MnCl2, 200 mM glycerol, 100 μM dithiothreitol, 1% Triton X-100) at 4 °C. The immune complex containing PKR was incubated with activity buffer containing 1 μCi of [γ-32P]ATP at room temperature for 30 min. One μg/ml polyclonal anti-V5 or 1 unit/ml heparin was added as a PKR activator. In some samples, kinase activities were assayed in the presence of the affinity-purified wild-type or mutant form IV of C114 protein. Labeled proteins were analyzed by SDS-PAGE and visualized by autoradiography and Western blotting.

**RESULTS**

**Cloning of Mouse C114**—C114 was cloned using PCR-based cDNA subtraction strategy from 3T3 L1 cells treated with human IL-11 (500 ng/ml) for 30 min. Northern blot analysis confirmed induction of C114 expression in IL-11-treated 3T3 L1 cells as early as 30 min and persisting for 24 h (Fig. 1A). Sequencing of C114 revealed that it is identical to several expressed sequence tags deposited in GenBank(TM). To obtain the full-length cDNA sequence for C114, PCRamplification of cDNA ends was performed using a mouse liver cDNA library based on the overlapping sequences of several mouse expressed sequence tags. The full-length cDNA contains an open reading frame of 561 bp, which encodes a 187-amino acid polypeptide with a predicted molecular mass of 21 kDa. The deduced protein sequence contains three putative nuclear localization signals, a basic amino acid-rich region, as well as a highly acidic amino acid tail at its C terminus (Fig. 1B).
identical full-length sequence has since been submitted by others (GenBankTM accession number AK010961). C114 also shares a very high sequence homology with a recently submitted human hypothetical protein FLJ13902 (GenBankTM accession number AK023964). The striking similarity (91% identity at the amino acid level) suggests that FLJ13902 is likely a human counterpart of mouse C114. Sequence alignment with the human genome database revealed that the human FLJ13902 gene consists of four exons and is localized at human chromosome 7q22.1. C114 protein also has significant homology with two other proteins with unknown functions from Caenorhabditis elegans and yeast (GenBankTM accession numbers AE003808 and P41880).

**Fig. 1. Molecular cloning of C114.** A, time course of C114 mRNA expression in 3T3 L1 cells after IL-11 treatment. Total RNAs were prepared from 3T3 L1 cells at various times after treatment with IL-11, and 10 μg of total RNA was loaded. The same filter was stripped and then hybridized with β-actin as a loading control. B, nucleotide and deduced amino acid sequences of C114 cDNA. The nucleotide sequence is presented in 5′ to 3′ orientation, and the amino acid sequence is displayed using the single-letter codes. Putative nuclear localization signals are bold, and the C-terminal acidic region is underlined. The sequence has been deposited to GenBank™ by the RIKEN Genome Exploration Group (accession number AK010359). C, Northern blot analysis of C114 mRNA expression in mouse tissues. A mouse multiple tissue poly(A)⁺ RNA blot was probed with 32P-labeled random primed C114 cDNA. Arrows indicate the two molecular weight markers on the blot.

**Fig. 2. Cellular localization of the C114 protein.** As shown in A, pEGFP vector (panel a), mitochondrial protein-fused GFP construct (panel b), and C114-fused GFP construct (panel c) were transfected into NIH 3T3. Living cells were observed by fluorescence microscopy at 48 h after transfection. In B, structures of wild-type and various deletion mutants of C114 are shown with the cellular localization observed. Figures in the bottom panel demonstrate C114 localization in NIH 3T3 cells transfected with pEGFP vector and various GFP-C114 constructs. NLS, nuclear localization signal. N, nuclear localization with high accumulation in nucleolus. C, cytoplasmic localization.

**Cellular Localization of the C114 Protein**—To elucidate possible functions of C114, we examined the cellular localization of the C114 protein. The C114 cDNA was fused in-frame into the N or C terminus of EGFP in the pEGFP vector, which expresses a green fluorescent protein to facilitate protein localization in living cells by confocal microscopy. Addition of C114 to pEGFP resulted in a nuclear localization of the C114 fusion protein with enrichment in the nucleolus (Fig. 2A, panel c). In contrast, the green fluorescent signal distributed throughout the cytoplasm and nucleus of cells transfected with pEGFP plasmid (Fig. 2A, panel b), whereas the signal was detected in mitochondria when transfected with pEGFP-mitochondrial protein plasmid (Fig. 2A, panel b).

There are three clusters of Arg/Lys-rich sequences present in
the basic region of C114 (RSKHLRRR, KRRKKR, and KKKKLKEKK). To determine the sequences responsible for nuclear localization of C114, wild-type C114 and a series of deletion mutants were expressed as GFP fusion proteins, and confocal microscopy was performed 24 h after transfection of NIH 3T3 cells. The pattern of various EGFP-ΔC114 proteins indicated that the last two clusters of the Arg/Lys-rich sequences (KKKLKEKK) are the major nuclear localization signals for the C114 protein (Fig. 2B).

**Nucleotide Binding Analysis of the C114 Protein**—Since C114 protein accumulates in nucleolus, and many nucleolar proteins are dsRNA-binding proteins (12, 13), 35S-labeled in vitro translated C114 was used for its ability to bind various polynucleotide resins. As shown in Fig. 3, A and B, unlike in vitro translated luciferase protein, wild-type C114 bound poly(I-C) but not poly(A) or poly(U) RNA. Competitive binding studies were next performed to compare the binding of wild-type C114 to dsRNA versus dsDNA. For these experiments, in vitro translated C114 was incubated with poly(I-C)-agarose in the presence of either free poly(I-C) or poly(dI-dC) competitors and assayed for the ability to bind to the poly(I-C) resin (Fig. 3C). In the presence of increasing amounts of poly(I-C) RNA, the binding of wild-type C114 to poly(I-C)-agarose decreased 79.5% in the presence of the highest concentration of competitors. In contrast, poly(dI-dC) failed to compete for wild-type C114 binding to the poly(I-C) resin with the highest concentration of competitors. These results suggest that wild-type C114 preferentially binds dsRNA.

Although C114 clearly binds dsRNA, no known dsRNA-binding motifs were identified in the highly basic amino acid-rich region of C114 by domain search analysis. To determine the regions of C114 that are important for dsRNA-binding, a series of deletion constructs of C114 were assayed for their ability to bind dsRNA (Fig. 3D). The N-terminal 56 amino acids (amino acids 1–56, mutant fragment III) and the C-terminal peptide (amino acids 143–187, mutant C114 fragment VI) showed only 15 and 25% poly(I-C) binding capacity as compared with wild-type C114 protein, respectively. On the other hand, the middle region (amino acids 51–143) containing highly basic amino acid residues contains 88% poly(I-C) binding capacity (Fig. 3D). These results suggest that the binding of C114 to dsRNA is mediated by its middle region.

**C114 Interacts with the dsRNA-dependent Protein Kinase PKR**—Different dsRNA-binding proteins, including the viral proteins HIV-1 transactivator of transcription (Tat), TRBP, and vaccinia virus E3 protein, and cellular proteins such as PACT and NF90, interact with PKR (13, 18). We therefore tested whether C114 can interact with PKR. Co-immunoprecipitations were performed with overexpressed FLAG-tagged C114 and V5-tagged PKR constructs in HEK 293 cells. When FLAG-tagged C114 was immunoprecipitated with an antibody against FLAG, V5-tagged PKR could be detected when the immunoprecipitates were immumoblotted with anti-V5 antibody (Fig. 4A). In addition, a comparable amount of FLAG-C114 (14%) was found to associate with PKR as compared with FLAG-PACT (17%), a well characterized PKR-interacting activator (Fig. 4B). The co-immunoprecipitation results also demonstrate that the N-terminal 50 amino acids of C114 are responsible for its association with PKR in cells (Fig. 4A, lane 4, and B, lane 6).

We also mapped the regions of PKR that interact with FLAG-tagged C114 protein. Wild-type PKR or its deletion mutants were individually expressed as [35S]methionine-labeled proteins and incubated with purified FLAG-tagged C114 protein. As shown in Fig. 4C, panel b (lanes 1–3), wild-type PKR and two deletion mutants containing two DRBDs can interact with the C114 protein. Purified FLAG-C114 associated with Protein A-agarose did not pull down the PKR deletion mutant containing only the kinase domain or in vitro translated luciferase (lanes 4 and 5). These results suggest that C114 can interact with DRBDs in the N terminus of PKR.

**C114 Inhibits PKR Kinase Activity**—Since several RNA-binding proteins including cellular proteins such as PACT and
NF90 (14–16) and viral proteins such as TRBP and E3L (19, 20) are known to affect PKR activity, we tested whether C114 can modulate the activity of PKR. Expression constructs of FLAG-tagged C114 or its mutant form IV and V5-tagged PKR were co-transfected into HEK 293 cells. The V5-PKR protein was immunoprecipitated with monoclonal antibody against V5 and co-immunoprecipitated with transfected C114 proteins. When kinase assays were performed, PKR immunoprecipitated...
from C114-expressing cells was less activated in the presence of poly(I:C) or heparin (Fig. 5A, lanes 3 and 6). However, similar levels of PKR autophosphorylation were observed with immunoprecipitated V5-PKR from V5-PKR expression alone or the mutant form IV of C114 co-expressing cells (Fig. 5A, lanes 2, 4, 5, and 7). Comparable results were observed when kinase assays were performed using V5-PKR mixed with partially immunoprecipitated FLAG-C114 or FLAG-tagged mutant form IV of C114 protein in vitro (as described under “Materials and Methods,” data not shown). Although the IV mutant form of C114 retained 98% of the poly(I:C) binding ability as compared with wild-type C114 (Fig. 3D), it lost its binding ability to PKR (Fig. 4A, lane 4) and the effect on PKR activation. When PKR mixed with the IV deletion mutant of C114, similar levels
of PKR phosphorylation could be achieved by the PKR activators in the same assay (Fig. 5A, lanes 4 and 7). These results suggest that the inhibition of PKR activity is mediated through direct interaction of C114 and PKR and is independent of dsRNA binding. This scenario is supported by the fact that wild-type C114 can also inhibit PKR activation in the presence of heparin (Fig. 5A, lane 6). To further test the negative regulatory role of C114 on PKR function in cells, we examined the levels of phosphorylation of endogenous eIF-2a in cells following poly(I:C) treatment of cells for 2 h. Overexpression of C114 in HEK 293 or HT 1080 cells resulted in lower levels of poly(I:C)-stimulated eIF-2a phosphorylation (Fig. 5B). In contrast, overexpressed C114 IV mutant did not complex with PKR (Fig. 4, A and B) and had no effect on eIF-2a phosphorylation (Fig. 5C, lane 6). Taken together, these results suggest that C114 inhibits cellular PKR function through the interaction between C114 and PKR protein.

**DISCUSSION**

In this study, we have identified C114 as a novel 21-kDa dsRNA-binding protein that interacts with PKR and inhibits PKR activity by a dsRNA-independent mechanism. C114 was isolated through a differential screening for IL-11-inducible genes in a mouse preadipocyte cell line, 3T3 L1. IL-11 is a multifunctional cytokine in the bone marrow microenvironment (1, 21). It shares a common signal transducer, gp130, with other IL-6-type cytokines, such as IL-6, leukemia inhibitory factor, oncostatin M, ciliary neurotrophic factor, and cardiotrophin-1 (CT-1). These cytokines play important roles in the regulation of complex cellular processes such as gene activation, proliferation, and differentiation (22). The main components of their signaling pathways are Janus kinases, Jak1, Jak2, and Tyk2, and the signal transducers and activators of transcription STAT1 and STAT3 (23). However, mechanisms underlying IL-11 in growth and differentiation signaling have not been elucidated. Accumulated evidence suggests the requirement of PKR in response to a variety of biological stimuli, including cytokines (4). Recently, PKR has been shown to interact with STAT3 activated by platelet-derived growth factor to induce c-fos expression (11). However, the direct signaling link between IL-6 family cytokines and PKR function has never been established.

PKR is critical in interferon-mediated antiviral defense, apoptosis, signal transduction, and cell growth but is also implicated in the onset of differentiation (4, 7–8). Analysis of phosphoproteins has demonstrated increased phosphorylation of PKR and eIF-2a during 3T3 F442A adipogenesis. Consistently, inhibition of adipocyte differentiation by cat serum correlated with reduced PKR activation, diminished eIF-2a phosphorylation, and elevated growth rate (7, 8), suggesting a role of PKR in adipogenesis. Furthermore, introduction of a kinase-deficient PKR construct, which is expressed with C114 in the HEK 293 cells (data not shown), also demonstrates that C114 can interact with the DRBDs of PKR protein. Transient transfection experiments showed an increased amount of PKR in the nuclear fraction when coexpressed with C114 in the HEK 293 cells (data not shown), suggesting that C114 might play a role in nuclear import and export of PKR in cells.

In many of the experimental systems, what regulates PKR in the cells has remained an enigma, especially in the cases where synthetic or viral dsRNA is not involved. As a novel cellular inhibitor of PKR, expression of C114 in 3T3 L1 cells can be induced by IL-11 and insulin as well as poly(I:C) treatment but not by interferon-γ, transforming growth factor-β1, IL-4, and IL-9 (data not shown). C114 may modulate intracellular PKR activity under a variety of growth and differentiation conditions and in response to various extracellular stimuli, within and outside the context of virus infection. Further functional studies of this novel PKR modulator should provide important insights into the role of PKR in cell growth and differentiation.

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**REFERENCES**

1. Paul, S. R., Bennett, F., Calvetti, J. A., Kelleher, K., Wood, C. R., O'Hara, R. M., Jr., Cleary, A. C., Sibley, B., Clark, S. C., Williams, D. A., and Yang, Y. (1990) Proc. Natl. Acad. Sci. U. S. A. 87, 7512–7516

2. Kawashima, I., Osumi, J., Mito-Honjo, K., Shimoda-Takano, K., Ishikawa, H., Sakakibara, S. Miyadai, K., and Takiguchi, Y. (1991) FEBS Lett. 283, 199–202

3. Yin, T., Miyazawa, K., and Yang, Y. C. (1992) J. Biol. Chem. 267, 8347–8351

4. Williams, B. R. (2001) Science’s STKE http://stke.sciencemag.org/cgi/content/full/sigtrans/2001/89/er2

5. Deb, A., Haque, S. J., Mogensen, T. H., Silverman, R. H., and Williams, B. R. G. (2001) J. Immunol. 166, 6170–6180

6. Meurs, R. F., Galabur, J., Barber, G. N., Katze, M. G., and Hovanessian, A. G. (1993) Proc. Natl. Acad. Sci. U. S. A. 80, 232–236

7. Judware, R., and Petryshyn, R. (1991) Mol. Cell. Biol. 11, 3259–3267

8. Woldehiwet, G., Nekhum, S., and Petryshyn, R. (1999) Mol. Cell. Biochem. 198, 7–17

9. Osman, F., Jarrous, N., Ben-Asoudi, Y., and Kaempfer, R. (1999) Genes Dev. 13, 3280–3293

10. Demarchi, F., Gutierrez, M. L., and Giacca, M. (1994) J. Virol. 72, 7080–7098

11. Deb, A., Zamanian-Daryoush, M., Xu, Z., Kaderesi, S., and Williams, B. R. G. (2001) EMBO J. 20, 2487–2496

12. Benkiran, M., Neurenti, C., Chun, B. F., Smith, S. M., Samuel, C. E., Guardino, A., and Jiang, K. T. (1997) EMBO J. 16, 611–624

13. Kumar, K. U., Srivastava, S. P., and Kaufman, R. J. (1999) Mol. Cell. Biol. 19, 1116–1125
14. Parker, L. M., Fierro-Monti, I., and Mathews, M. B. (2001) *J. Biol. Chem.* **276**, 32522–32530
15. Patel, R. C., and Sen, G. C. (1998) *EMBO J.* **17**, 4379–4390
16. Coulidge, C. J., and Patton, J. G. (2000) *Nucleic Acids Res.* **28**, 1407–1417
17. Goh, K. C., deVeer, M. J., and Williams, B. R. G. (2000) *EMBO J.* **19**, 4292–4297
18. Feng, G., S. Chong, K., Kumar, A., and Williams, B. R. (1992) *Proc. Natl. Acad. Sci. U. S. A.* **89**, 5447–5451
19. Brand, S. R., Kubayashi, R., and Mathews, M. B. (1997) *J. Biol. Chem.* **272**, 8388–8395
20. Sharp, T. V., Moonan, F., Romashko, A., Joshi, B., Barber, G. N., and Jagus, R. (1998) *Virology* **250**, 302–315
21. Yang, Y. C., and Yin, T. (1995) *Ann. N. Y. Acad. Sci.* **762**, 31–41
22. Heinrich, P. C., Behrmann, I., Muller-Newen, G. G., Schaper, F., and Graeve, L. (1998) *Biochim. J.* **334**, 297–314
23. Calkhoven, C. F., Muller, C., and Leutz, A. (2000) *Genes Dev.* **14**, 1920–1932
24. Towle, C. A., Mankin, H. J., Arruch, J., and Treadwell, B. V. (1984) *Biochem. Biophys. Res. Commun.* **121**, 134–140
25. Trepicchio, W. L., Wang, L., Bozza, M., and Deren A. J. (1997) *J. Immunol.* **159**, 5661–5670
26. Nanduri, S., Rahman, F., Williams, B. R., and Qin, J. (2000) *EMBO J.* **19**, 5567–5574
27. Jeffrey, I. W., Kaderetz, S., Meurs, E. F., Metzger, T., Bachmann, M., Schwemmele, M., Hovazessian, A. G., and Clemens, M. J. (1985) *Exp. Cell Res.* **218**, 17–27
28. Tian, B., and Mathews, M. B. (2001) *J. Biol. Chem.* **276**, 9936–9944
C114 Is a Novel IL-11-inducible Nuclear Double-stranded RNA-binding Protein That Inhibits Protein Kinase R
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