MM-1, a Novel c-Myc-associating Protein That Represses Transcriptional Activity of c-Myc*

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We have isolated the cDNA encoding a novel c-Myc-binding protein, MM-1, by the yeast two-hybrid screening of a human HeLa cell cDNA library. The protein deduced from the cDNA comprises 167 amino acids and was localized in the nucleus of introduced COS-1 cells. The MM-1 mRNA was highly expressed in human pancreas and skeletal muscle and moderately in other tissues. As for the c-Myc binding, glutathione S-transferase MM-1 expressed in Escherichia coli bound in vitro to c-Myc translated in reticulocyte lysate, and almost whole, the MM-1 molecule was necessary for the binding in the yeast two-hybrid system. The mammalian two-hybrid assays in hamster CHO cells revealed that MM-1 interacts in vivo with the N-terminal domain covering the myc box 2, a transcription-activating domain, of c-Myc. Furthermore, MM-1 repressed the activation of E-box-dependent transcription by c-Myc.

Human HeLa, monkey CV-1, monkey COS-I and hamster CHO cells were cultured in Dulbecco's modified Eagle's medium supplemented with 10% calf serum.

**Cloning of MM-1 by Two-hybrid System**

Saccharomyces cerevisiae HFC7 cells containing the lacZ gene driven by the GAL1 promoter were transformed first with pGBT-c-Myc. The transformant yeast cells were subsequently transformed with Human HeLa MATCHMAKER cDNA (CLONTECH), a cDNA library expressing the GALA activation domain fused to cDNAs from human HeLa cells. About 2 × 10^5 colonies were screened for ß-galactosidase expression, and the plasmid DNAs in the LacZ-positive cells were extracted by the procedure described in the protocols from CLONTECH. A plasmid thus obtained was named pGAD-9 and analyzed. Because the EcoRI-Xhol fragment insert of cDNA in pGAD-9 did not contain the ATG initiation codon, the Agt11 human placenta cDNA library (CLON-TECH) was further screened with the labeled insert of pGAD-9 as a probe. The longest cDNA obtained was inserted to the EcoRI site of pBluescript SK(-), and the construct was named PBS-MM-1.

**In Vitro Binding Assay**

GST-MM-1 and GST were purified from a 1,000-ml culture of Escherichia coli BL21(DE3) transformed with pGEX-MM-1 and pGEX-6P-1, respectively, as described previously (26). Two μg of the purified GST-MM-1 or GST were first applied to GST-Sepharose 4B (Amersham Pharmacia Biotec) in a buffer containing 20 mM Tris-HCl (pH 8.0), 150 mM NaCl, 0.5% Nonidet P-40, and 1 μM EDTA. The 35S-labeled c-Myc or its deletion mutants synthesized in vitro using pGEM-c-myc(3'-ATG) or pCDNA3-MYC deletions, respectively, as a template in the coupled transcription-translation system (Promega) were then applied to the column. After extensive washing of the column with the same buffer as above, the proteins bound to the resin were recovered, separated in a 7.5% polyacrylamide gel containing SDS, and visualized by fluorography.

**Plasmids**

Nucleotide sequences of oligonucleotides used were as follows: c-myc(GKPG)ATG, 5'-GGAAAATTCTGTTAACACCGGGAATGCCCTCACAGGTTAGCCTTC-3'; c-myc(3'-end), 5'-GGAAATTCAAGTTGAAAGC-3'; MM-1Bam(ATG), 5'-GGGGATGCTGATCTGCTCAGCA-3'; RVX, 5'-GAGCGATACAAATTCACAGCGGAGGG-3'; FLAG-A, 5'-CATGGAATCTACAGGAGGG-3'; and Hiroyoshi Ariga‡

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A Novel c-Myc-associating Protein

AGGACGACGACGATGACAAGGAACTAGTCCCGGGCTCGAGCT-3

FLAG-B, 5'-CGAGCCCGGGACTAGTTCCTTGTCATCGTCGTCCTTG-

TAGTCCATGGTAC-3

MM-1EcoTTC, 5'-GCAAATTCATGGGGGTTG-

ATGTCATGACT-3

MM-1Bam(Cla), 5'-GGGGATCCTCATCGATGTG-

GGAA-3

MM-1ATG-167, 5'-GGATCCAGTATGTGGAAGCCAAGGAC-

T-3

MM-1ATG-396, 5'-GGCTCGAGTGGTTGGATTTTCTCCATCTG-

3

VP16(XhoI)N, 5'-GGCTCGAGGCTCGACGGCCCCCCCGAC-3

VP16C(ApaI), 5'-GGGGGCCCCTACCCACCGTACTCGTCAAT-3

c-Myc1671(Xho), 5'-GGCTCGAGCTTTTAGCTCGTTCCTCCTCTG-3

c-Myc1875(Xho), 5'-GGCTCGAGCACAAGAGTTCCGTAGCTGTTC-3

GAL4 DNA-binding domain (GALBD): 5'-CGGAAGAGTAGTAACA-

AAGGTCA-3

GAL4 activation domain (GALAD), 5'-AATACCACTAC-

AATGGATG-3

PreScission sense, 5'-TCGGATCTGGAAGTT-3

OVEC-E(A), 5'-CGAGCCCACCACGTCGTGCCT-3

OVEC-E(B), 5'-CGACAGGCACCACGTCGTGCCTGCGACAGCT-3

pGBT-c-myc is an expressing vector in yeast for a fusion protein with GAL4BD and c-Myc.

The c-Myc cDNA was prepared by PCR using pGEM-c-myc(ATG) as a template and c-myc(GKPG)ATG and c-myc(end) as primers. The PCR reactions were carried out for first 5 min at 94 °C, then for 30 cycles of 1 min at 94 °C followed by 2 min at 55 °C, and finally for 3 min at 72 °C. The amplified fragment was digested with EcoRI and cloned to the EcoRI site of pGBT9. All the PCR in this study used the same conditions as above.

pGEX-MM-1—The BamHI-EcoRI fragment of the polymerase chain reaction product with MM-1(ATG) and RVX primers on pBS-MM-1 template was inserted to the respective site of pGEX-5X-1 (Amersham Pharmacia Biotech).

pSV-FLAG—The 5'-ends of the oligonucleotides FALG-A and FLAG-B were phosphorylated by T4 polynucleotide kinase. The two oligonucleotides were annealed and inserted to pSV2b. The two oligonucleotides were annealed and inserted to pSV2b.
ing sites from SpeI to XhoI in pGBT9 were then inserted to the respective sites of the construct above.

*pGEX-6P-MM-1—*The EcoRI fragment of the polymerase chain reaction product using MM-1(EcoTTC) and RVX primers on the pBS-MM-1 template was inserted to the respective site of pGEX-6P-1 (Amersham Pharmacia Biotech).

*pSV-FLAG-MM-1—*The KpnI-ApaI fragment of pSV-FLAG-MM-1 was inserted to the EcoRI site of pSV-FLAG.

*pCMV-F-MM-1—*The KpnI-ApaI fragment of pSV-FLAG-MM-1 was inserted to the respective site of pcDNA3 (Invitrogen).

**pACT-MM-1, pACT-MM-1-M, pACT-MM-1-C, and pACT-MM-1-D**—The laminin1-EcoRI fragments of polymerase chain reaction products on the pBS-MM-1 template using the following combinations of primers were inserted to the respective site of pACT2: MM-1Bam(AG) and RVX for pACT-MM-1; MM-1ATG-167 and MM-1ATG-396 for pACT-MM-1-M; MM-1Bam(Cla) and RVXpACT-MM-1-C, MM-1ATG-167 and RVX for pACT-MM-1-C, and MM-1Bam(AG) and MM-1ATG-396 for pACT-MM-1-D.

**pSV-FLAG-VP16-c-Myc (pSV-FV-c-Myc) and Its Deletion Constructs—*The EcoRI-XhoI fragments of the polymerase chain reaction products using the following combinations of templates and primers were inserted to the respective site of pSV-FLAG-VP16C: GALBD and c-Myc1875(Xho) Primers on pCMV-GAL-c-Myc for pSV-FV-c-Myc; PreScission sense and c-Myc1875(Xho) primers on pGEX-6P-c-Myc1 for pSV-FV-c-Myc1; GALBD and c-Myc1875(Xho) primers on pCMV-GAL-c-Myc for pSV-FV-c-Myc1ZIP; PreScission sense and c-Myc1875(Xho) primers on pGEX-6P-c-Myc111 for pSV-FV-c-Myc111; GALBD and c-Myc1671(Xho) primers on pCMV-GAL-c-Myc for pSV-FV-c-Myc111ZIP; PreScission sense and c-Myc1875(Xho) primers on pGEX-6P-c-Myc111 for pSV-FV-c-Myc111; PreScission sense and c-Myc1875(Xho) primers on pGEX-6P-c-Myc66 for pSV-FV-c-Myc66; GALBD and c-Myc1875(Xho) primers on pCMV-GAL-c-Myc for pSV-FV-c-Myc111; c-Myc(EcoD) and c-Myc1671(Xho) primers on pGEM-c-myc(AG) for pSV-FV-c-Myc111; c-Myc111(EcoD) and c-Myc1875(Xho) primers on pGEM-c-myc(AG) for pSV-FV-c-Myc111; c-Myc(Eco147) and c-Myc1875(Xho) primers on pGEM-c-myc(AG) for pSV-FV-c-Myc111; GALAD and c-Myc1875(Xho) primers on pGAD-GHX-c-myc12 for pSV-FV-c-Myc117.

**p4xE-SVP-Luc—**The oligonucleotides OVEC-E(A) and OVEC-E(B) were annealed, tandemly tetramerized, and inserted to the SacI-SalI sites of pSV-Luc.

**pcDNA2-c-Myc147, pcDNA3-c-Myc147ZIP, pcDNA3-c-Myc147MI, and pcDNA3-c-Myc147MI—**The EcoRI-XhoI fragment of the respective deletion construct of pSV-FLAG-VP16-c-Myc was inserted to the EcoRI-XhoI sites of pcDNA3.

**Indirect Immunofluorescence**

COS-1 cells were transfected with pFLAG-MM-1 or pEF-c-myc (26) by the calcium phosphate precipitation technique (27). Forty-eight h after transfection, the cells were fixed with the solution containing acetone-methanol (3:7) and reacted with a mouse anti-FLAG monoclonal antibody (M2, Eastman Kodak Co.) or an anti-c-Myc monoclonal antibody (C-33, SantaCruz). The cells were then reacted with an fluorescein isothiocyanate-conjugated anti-rabbit IgG and observed with a fluorescence microscope.

**Luciferase Assay**

CV-1 cells subconfluent in a 6-cm dish were transfected with various amounts of effector plasmids expressing the wild type or mutants of MM-1 and c-Myc in addition to 1 µg of pCMV-β-gal and 1 µg of p4xE-SVP-Luc by the calcium phosphate precipitation method. Forty-eight h after transfection, cell extracts were prepared by adding a solution containing 25 mM Tris-phosphate (pH 7.8), 2 mM dithiothreitol, 10% glycerol, 1% Triton X-100, and 2 mM 1,2-diaminocyclohexane-N,N,N’,N’-tetraacetic acid (Promega). After standardization of the protein concentration on the BCA assay (Pierce), 40 µg of protein was converted to the luciferase assay as above.

**Mammalian Two-hybrid Assay**

CHO cells were transfected with 2 µg of effector plasmids expressing the wild type or mutants of MM-1 and c-Myc fused to GALBD or VP16 in addition to 1 µg of pCMV-β-gal and 1 µg of pH17-MX-Luc-Luc and followed by luciferase assay as above.

**RESULTS AND DISCUSSION**

**Cloning of a cDNA Encoding the c-Myc Binding Protein—**To screen cDNAs encoding c-Myc-associating proteins, the entire coding sequences of the c-myc cDNA were fused to the GALBD and introduced to S. cerevisiae HF7C cells. A human cDNA library prepared from HeLa cells and cloned in pGADGH was then introduced to the transformant yeast cells, and the clones resistant to His marker were selected. Among a total of 2 × 10^6 transformant cells, 17 colonies were His-positive, and 15 of the 17 His-positive colonies yielded a high expression of β-galactosidase activity. Restriction enzyme analyses revealed that the cDNA carried in the 15 colonies were of 2 classes. The cDNA of one class, named No. 9, did not contain the initiation codon ATG, and another cDNA library prepared from human placenta and cloned in agt11 was hence screened by hybridization with a labeled No. 9 cDNA. Two cDNA clones thus obtained contained the same coding sequence, and the protein coded by the longer cDNA was termed MM-1 (Myc Modulator -1) and further characterized.

The MM-1 cDNA comprised 1,029 nucleotides with a stop codon in-frame at the nucleotide 285 upstream from the first ATG at 418 (Fig. 1A). It was therefore determined that MM-1 cDNA encodes 167 amino acids starting from the nucleotide 12. There exists a putative leucine zipper structure from amino acid 28 to 49. It is not clear at present whether MM-1 makes complexes with other proteins via the leucine zipper, but no homodimer of MM-1 was observed with the purified recombinant MM-1 (data not shown). The EST data base search revealed several cDNA clones homologous to the MM-1 cDNA including accession numbers W25318, AA287397, and...
These clones were obtained via Genome Systems Inc., and the nucleotide sequences of the inserts were determined (Fig. 1B). The clone W25318 contained 10 original nucleotides followed by the same 589 nucleotides as in the MM-1 cDNA from 441 to 1029, and the sequence at the junction between the W25318 original 10 nucleotides and the following nucleotides common to W25318 and MM-1 was TAAG, which is a consensus sequence of donor/acceptor sites for splicing. Since a stop codon, TAA, thus appeared at the junction, the ATG at the nucleotide 457 referred to the MM-1 cDNA is a putative initiation site for the clone W25318. Both the clones AA287397 and H03166 are probably derived from different splicing of the same gene as MM-1 (Fig. 1B). These two clones did not contain stop codons in-frame upstream from the ATG at the nucleotide 457, and the clones hence may not contain the complete coding sequences.

The expression of MM-1 was examined in various human tissues by Northern blot analyses (Fig. 2). At least four distinct bands were detected corresponding to the sizes of 0.7, 1.15, 2.9, and 4.4 kb. The 0.7-kb mRNA was vigorously expressed in all the tissues examined. The 1.15-kb mRNA corresponding to the size of the MM-1 cDNA cloned here was strongly expressed in pancreas, weakly in kidney, skeletal muscle, and placenta and faintly in liver and lung (Fig. 2). To verify the cellular localization of MM-1, an expression vector for MM-1 fused to FLAG was transfected to monkey COS-I cells. Two days after transfection, the cells were fixed, reacted with an anti-FLAG monoclonal antibody (M2; Kodak), and visualized with an fluorescein isothiocyanate-conjugated antimouse antibody. Magnification is shown in the figure.

Association of MM-1 with c-Myc—To examine the interaction between MM-1 and c-Myc, GST-MM-1 or GST was expressed in E. coli and applied to a glutathione-Sepharose column. The 35S-labeled c-Myc synthesized in vitro in the coupled transcription-translation system (Promega) was then applied to the column, and the labeled protein bound to the GST-MM-1 or GST on the column was separated in a gel and visualized (Fig. 4A, lanes 1–3). The result showed that the labeled c-Myc bound to GST-MM-1 but not to GST, and the direct binding between MM-1 and c-Myc was thus suggested. To assess the binding domain of MM-1 with c-Myc, the wild type and deletion mutants of MM-1 were fused to the GALAD, the wild type c-Myc were fused to the GALBD, and the interaction of the fusion proteins was assayed in yeast. All the deletion mutants of MM-1 except for Δ13, deleting 13 amino acids from the N terminus, entirely lost or hardly retained the binding activity to c-Myc (Fig. 4B). The binding activity of MM-1 to c-Myc was hence suggested to require nearly the whole molecule of MM-1, probably because the appropriate stereostructures of the rather small molecule is important for the interaction. To determine the binding domain on the c-Myc side, similar assays applying the yeast two-hybrid system were first attempted. The background GAL4 activity, however, varied among the wild type and deletion mutants of c-Myc when the proteins were fused to GALBD, and the assays did not work when the c-Myc variants were fused to GALAD and used as a bait. We hence examined the c-Myc domains for interaction with MM-1 by in vitro binding assays. The deletion mutants of c-Myc as well as the wild type protein were synthesized and used for in vitro binding assay. The mutant protein lacking Myc-box II (ΔMII) or the amino acids 1 to 147 lost the binding activity, whereas the mutant deleted of Myc-box I (ΔMI) or leucine zipper (ΔZIP) retained the binding activity (Fig. 4A, lanes 4–15). The binding activity of c-Myc to MM-1 was further tested by the mammalian two-hybrid assays, which were successfully applied to see the interaction of c-Myc with p107, RB, or TBP (21, 28). c-Myc and its deletion mutants were fused to the VP16 activation domain (VP16AD), whereas MM-1 was fused to GALBD. Hamster CHO cells were transfected with the expression vectors for MM-1-GALBD and c-Myc or its mutants and fused to VP16AD in addition to pHE17-MX-Luc, which contains 6xGAL4, and the HTLV-1 promoter was linked to the luciferase gene. First, for testing the effect of the transactiva-
tion domain of c-Myc in this system, the cells were transfected
with wild type, or the segment N-containing transactivation
domain of c-Myc was fused to VP16AD together with pHE17-
MX-Luc. These Myc constructs gave no luciferase activities in
the absence of MM-1-GALBD because of the lack of the DNA
binding domain to GAL4 (data not shown). In the cells intro-
duced with GALBD-MM-1 and c-Myc-VP16AD (the wild type
Myc fused to VP16AD), the luciferase activity was seven
times as high as that in the cells with GALBD-MM-1 and
VP16AD, indicating that MM-1 interacted with c-Myc
in vivo (Fig. 4C). Among the deletion mutants of c-Myc, the activity
was lost for ΔS, ΔMI, Δ6, Δ147, and Δ177, whereas ΔMI, ΔZIP, ΔN,
Δ43, and Δ103 still retained the activity (Fig. 4C). Deletion
of ZIP to ΔMI, ΔS, and ΔMII had little effect (Fig. 4C, ΔMIΔZIP, ΔSΔZIP, and ΔMIIΔZIP, respectively). The results indicate that
MM-1 binds in vivo to the domain around myc box II from the
amino acid 104 to 166 but not to the basic-helix-loop-helix-leucine zipper of c-Myc in CHO cells. Similar results were
obtained when the same plasmids were transfected to human
HeLa cells (data not shown).

Transcriptional Repression Activity of MM-1 to c-Myc—To verify the effect of MM-1 on the transcription activity of c-Myc,
We have here described MM-1, a new partner protein of c-Myc. MM-1 is a nuclear protein like c-Myc and binds to the N-terminal domain of c-Myc covering Myc box II and possessing transcriptional activation activity. Binding between MM-1 and c-Myc was observed both in vitro and in vivo in yeast and transfected mammalian cells. The search through the EST data base implied the presence of several splicing forms of the transcript from the MM-1 gene. In the Northern blot analyses, at least 4 distinct bands were detected, and the 0.7-kb mRNA was ubiquitously expressed in various human tissues. The 1.15-kb mRNA corresponding to the cDNA we obtained here was also expressed in several tissues but, except in pancreas, to much weaker levels than the 0.7-kb mRNA. The 0.7-kb mRNA may correspond to the clone W25318 (see Fig. 1B), which lacks only 13 amino acids from the N terminus of the MM-1 cDNA. We hence constructed a Δ13 by deleting the N-terminal 13 amino acids from the wild type MM-1 and tested the mutant for biological functions. No difference was observed between Δ13 and the wild type MM-1 in terms of the activities of c-Myc binding and transcriptional repression (data not shown).

MM-1 was thus suggested to repress the transcriptional activity of c-Myc through association with c-Myc. To verify this further, c-Myc mutants lacking the MM-1 binding activity but still sustaining transcriptional activity were desirable. Such mutants, however, could not be constructed, because the regions of c-Myc for both MM-1 binding and transcriptional activities are overlapped. The c-Myc mutants ΔS and ΔMII, which lost the MM-1 binding activity (Fig. 4), hardly activated the E-box-dependent transcription (Fig. 5A). The result with an MM-1 mutant lacking the c-Myc binding activity (Fig. 5B) supported the suggestion above. The lack of c-Myc binding activity resulted in the loss of the repression activity on the transcriptional activity of c-Myc.

The region around Myc box II of c-Myc associating with MM-1 is known to be essential for c-Myc to sustain the activities of transcription, cell transformation, and apoptosis induction (1–4). The region has also been reported to be bound by p107, Bin1, TBP, or α-tubulin (19–25) to modulate the functions of c-Myc. Among the binding proteins, p107 and TBP bind to the epitope around Myc box II, the amino acids from 100 to 148 (21) overlapping the MM-1 binding domain, the amino acids from 104 to 166, p107 (19–21) as well as Bin1 (22) is classified as a tumor suppressor protein and represses the transcription or transforming activity of c-Myc as MM-1 does.

Two mechanisms have been considered to explain the transcriptional inhibitory activity of p107 to c-Myc. One is that p107 recruits cyclinA/Cdk2 to phosphorylate Ser-62 in c-Myc, and Thr-58 is subsequently phosphorylated to lead the downmodulation of the c-Myc transcriptional activity (21). This was based on the fact that the c-Myc transcriptional activity was not inhibited by p107 in several Burkitt lymphoma cells in which mutations were frequently found at the Ser-62 and Thr-58 of c-Myc (19, 21). The conflicting observation, on the other hand, was reported that p107 similarly inhibited the transcriptional activity of both the wild type and mutated c-Myc in Burkitt lymphoma cells (29), proposing another mechanism that p107 competitively interferes with the binding of positive regulatory factors including TBP. Since MM-1 shares similar functions with p107, the same mechanism may exist for the negative regulation of c-Myc transcriptional activity by MM-1. Further examination of the interaction among c-Myc, MM-1, TBP, p107, and possibly other associating proteins yet unidentified is required to assess such possibilities.
After the submission of this manuscript, two other groups reported that MM-1 may be a human homologue of GIM5 or PFD5, a subunit of the complex promoting the formation of functional actin or tubulin (30, 31). Relationships among c-Myc, MM-1, and the complex have not been clarified.

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REFERENCES
1. Henriksson, M., and Lüscher, B. (1996) Adv. Cancer Res. 68, 109–182
2. Ryan, K. M., and Birnie, G. D. (1996) Biochem. J. 314, 713–721
3. Hoffman, B., Liebermann, D. A., Selvakumaran, M., and Nguyen, H. Q. (1996) Curr. Top. Microbiol. Immunol. 211, 17–27
4. Packham, G., and Cleveland, J. L. (1994) Mol. Cell. Biol. 14, 5741–5747
5. Lüscher, B., and Eisenman, R. N. (1990) Genes Dev. 4, 2025–2035
6. Blackwood, E. M., and Eisenman, R. N. (1992) Genes Dev. 6, 71–80
7. Eilers, M., Schirm, S., and Bishop, M. J. (1991) EMBO J. 10, 133–141
8. Gauthier, S., Meichle, A., and Eilers, M. (1994) Mol. Cell. Biol. 14, 3853–3862
9. Benvenisty, N., Leder, A., Kus, A., and Leder, P. (1992) Genes Dev. 6, 2513–2523
10. Schuldiner, O., Eden, A., Ben-Yosef, T., Yanuka, O., Simchen, G., and Benvenisty, N. (1996) Proc. Natl Acad. Sci. U. S. A. 93, 7143–7148
11. Rosenwald, I. B., Rhoads, D. B., Callanan, L. D., Isselbacher, K. J., and Schmidt, E. V. (1995) Proc. Natl Acad. Sci. U. S. A. 90, 6176–6178
12. Jones, R. M., Branda, J., Johnston, K. A., Polymenis, M., Gadd, M., Rustgi, A., Callanan, L., and Schmidt, E. V. (1996) Mol. Cell. Biol. 16, 4754–4764
13. Bello-Fernandez, C., Packham, G., and Cleveland, J. L. (1993) Proc. Natl Acad. Sci. U. S. A. 90, 7804–7808
14. Miltenberger, R. J., Sukow, K. A., and Farnham, P. J. (1995) Mol. Cell. Biol. 15, 2527–2535
15. Galaktionov, K., Chen, X., and Beach, D. (1996) Nature 382, 511–517
16. Shrivastava, A., Saleque, S., Kalpana, G. V., Artandi, S., Goff, S. P., and Calame, K. (1993) Science 262, 1889–1892
17. Gu, W., Bhatia, K., Magrath, I. T., Dang, C. V., and Dalla-Favera, R. (1994) Science 264, 251–254
18. Beijersbergen, R. L., Hijmans, E. M., Zhu, L., and Bernards, R. (1994) EMBO J. 13, 4080–4086
19. Hoang A. T., Lutterbach, B., Lewis, B. C., Yano, T., Chou, T. Y., Barrett, J. F., Raffeld, M., Hano, S. R., and Dang, C. V. (1995) Mol. Cell. Biol. 15, 4031–4042
20. Sakkamuro, D., Elliott, K. J., Wechsler-Reya, R., and Prendergast, G. C. (1996) Nat. Genet. 14, 69–77
21. Maheewaran, S., Lee, H., and Sonenschein, G. E. (1994) Mol. Cell. Biol. 14, 1147–1152
22. Hateboer, G., Timmers, H. T., Rustgi, A. K., Billaud, M., van’t Veer, L. J., and Bernards, R. (1993) Proc. Natl Acad. Sci. U. S. A. 90, 8489–8493
23. Negishi, Y., Nishita, Y., Saegusa, Y., Kakizaki, I., Galli, I., Kihara, F., Tamai, K., Miyajima, N., Iguchi-Ariga, S. M., and Ariga, H. (1994) Oncogene 9, 1133–1143
24. Graham, F. L., and Van der Eb, A. J. (1973) Virology 52, 456–467
25. Adnane, J., and Robbins, P. D. (1995) Oncogene 10, 381–387
26. Smith-Sørensen, B., Hijmans, E. M., Beijersbergen, R. L., and Bernards, R. (1998) J. Biol. Chem. 273, 5513–5518
27. Geissler, S., Siegers, K., and Schiebel, E. (1998) EMBO J. 17, 952–966
28. Vainberg, I. E., Lewis, S. A., Rommelaere, H., Ampe, C., Vandenkerckhove, J., Klein, H. L., and Cowan, N. C. (1998) Cell 93, 863–873