ArgBP2γ Interacts with Akt and p21-activated Kinase-1 and Promotes Cell Survival*

Received for publication, January 4, 2005, and in revised form, March 2, 2005
Published, JBC Papers in Press, March 22, 2005, DOI 10.1074/jbc.M500097200

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Akt/protein kinase B is a major cell survival pathway through phosphorylation of proapoptotic proteins Bad and Bax and of additional apoptotic pathways linked to Forkhead proteins glycogen synthase kinase-3β and ASK1. To further explore the mechanism by which Akt regulates cell survival, we identified an Akt interaction protein by homologous splicing is identified (1997) J. ArgBP2γ, consensus SH 3 domains of Akt. It also interacts with Akt via the SH3 domain of Akt. Expression of Bad or DN Bad or SH3 domain-truncated mutant Bad overrides Akt-induced cell death, causing cell death; HA, hemagglutinin; GST, glutathione S-transferase; TUNEL, terminal deoxynucleotidyltransferase-mediated dUTP nick-end labeling; SoHo, sorbin homology; SH, Src homology; HEK, human embryonic kidney.

These data indicate that ArgBP2γ is a physiological substrate of Akt, functions as an adaptor for Akt and PAK1, and plays a role in Akt/PAK1 cell survival pathway.

Akt, also named protein kinase B (PKB)1 or RAC kinase, is a family of phosphatidylinositol 3-kinase-regulated serine/threonine kinases. Three members of Akt have been identified, Akt1/ PKBα, Akt2/PKBβ, and Akt3/PKBγ (1–7), all of which are activated by growth factors in a phosphatidylinositol 3-kinase-dependent manner (8–13). Full activation of the Akt requires their phosphorylation at Thr308 (Akt1), Thr309 (Akt2), or Thr320 (Akt3) in the activation loop and Ser473 (Akt1), Ser474 (Akt2), or Ser472 (Akt3) in the C-terminal activation domain (14). Akt1, one of the most studied isoforms, which was originally designated as Akt, has been shown to be an important regulator of programmed cell death. The kinase, for mediators have the Akt most widely expressed in the Akt, the proline family members and metabolic syndrome of the transcription factors to combine to direct targets of Forkhead proteins, causing expression of proteins promoting cell death and cell cycle arrest (17). Other major Akt substrates include MDM2, IκB kinase, 21Cup-1/WAF1, p27Kip1, ASK1, estrogen receptor, androgen receptor, TSC2, and XIAP (18–30).

In addition to acting as a kinase toward many substrates involved in its function, Akt forms complexes with other proteins that are not substrates but rather act as modulators of Akt activity and function. Several such Akt interaction proteins have been identified, including TCL1, CTPM, APPL, and TRB3. TCL1 is an oncprotein that interacts with the pleckstrin homology domain of Akt. It activates Akt by increasing Akt oligomerization and then promotes Akt nuclear translocation (31, 32). By contrast, CTPM has been shown to interact with the C-terminal regulatory region of Akt and inhibit phosphorylation of Akt on Ser473, leading to a decrease of Akt kinase activity (33). TRB3 is a mammalian homolog of Dro sophila tribbles and inhibits insulin-stimulated Akt activation by physical interaction with Akt (34). APPL is an adaptor protein that contains a pleckstrin homology domain, a phosphotyrosine-binding domain, and a leucine zipper motif and binds to both Akt and p110 catalytic subunit of phosphatidylinositol 3-kinase. However, the function of APPL is currently unknown (35). Furthermore, Hsp90 and Hsp27 also form a complex with Akt and induce Akt activation (36, 37). It has also been shown that Akt interacts with JIP1 scaffold protein to

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This article has been withdrawn by the authors. The same data were used to represent different experimental conditions. Specifically, parts of the GST-BAD panel from Fig. 6A were reused in the GST-BAD panel from Fig. 6B. Additionally, portions of the p-BAD-S112, p-BAD-S136, and HA-BAD panels from Fig. 6C were reused in Fig. 6D. The authors state that the reuse of images does not affect the overall conclusions of this work.

* This work was supported by NCI, National Institutes of Health Grants CA77429, CA77935, CA89242, and CA107078 and Department of Defense Grants DAMD17-02-20671 and DAMD17-05-1-0021. The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

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inhibit excitotoxin-induced JNK 1/2 activity in an Akt kinase-independent manner, thus providing a novel mechanism for Akt antiapoptotic function (38).

In the present report, we have identified an Akt interacting protein, ArgBP2γ, that functions as an adaptor for Akt and PAK1 and is phosphorylated by Akt. In addition, ArgBP2γ activates PAK1 by direct interaction with PAK1 and mediates Akt-induced PAK1 activation and Akt/PAK1 phosphorylation of Bad.

EXPERIMENTAL PROCEDURES

Yeast Two-hybrid Screening and Expression Constructs—Yeast two-hybrid system 3 was employed to identify Akt interaction protein(s) using the C-terminal regulatory region of Akt as bait following the manufacturer’s procedure (Clontech). A human fetal brain library (Clontech) was screened. Full-length cDNA of ArgBP2γ, isolated from a human skeletal muscle library, was subcloned into FLAG-tagged pGEX-4T1 vector. ArgBP2γ and Akt mutants were created with the QuickChange multiple site-directed mutagenesis kit (Stratagene). The cytomegalovirus-based expression constructs encoding HA-tagged Akt and Myc-tagged PAK1 were transfected with pcDNA3 or FLAG-ArgBP2γ. The cells were seeded in 60-mm Petri dishes at a density of 0.5 × 10^6 cells/dish. Following incubation overnight, the cells were transfected with 2 μg of DNA/dish using calcium phosphate or Lipofectamine Plus (Invitrogen).

Immunoprecipitation and Immunoblotting—Cells were lysed in a lysis buffer containing 20 mM Tris-HCl (pH 7.5), 137 mM NaCl, 15% (v/v) glycerol, 1% Nonidet P-40, 2 mM phenylmethylsulfonyl fluoride, 2 μg/ml aprotinin and leupeptin, 2 mM benzamidine, 20 mM NaF, 10 mM NaPPi, 1 mM sodium vanadate, and 25 mM β-glycerophosphate. Lysates were subjected to immunoprecipitation and immunoblotting analysis as previously described (30). Briefly, lysates were precleared with protein A-protein G (2:1) agarose beads. Following the removal of the beads by centrifugation, lysates were incubated with appropriate antibodies in the presence of protein-A-protein G (2:1) agarose beads for 2 h at 4 °C. After being washed, the immunoprecipitates were subjected to in vitro kinase assay. Protein expression was determined by probing Western blot of the immunoprecipitates or total cell lysates with the appropriate antibodies as noted in the figure legends.

GST Pulldown Assay—Glutathione-agarose beads coupled to GST alone, GST-SH3 domains of ArgBP2γ, or GST-Akt-pleckstrin homology, kinase domain, and -C-tail motif were incubated with whole cell lysate (~800 μg of protein) for 2 h at 4 °C. After being washed four times with lysis buffer, the beads were subjected to Western blot analysis with appropriate antibodies.

In Vitro Kinase Assays—Akt and PAK1 kinase assays were performed as previously described (13, 26). Briefly, reactions were carried out in the presence of 10 μCi of [γ-^32P]ATP and 3 μM cold ATP in 30 μl of buffer containing 20 mM Hepes (pH 7.4), 10 mM MgCl2, 2 mM MnCl2, 1 mM dithiothreitol. Histone H2B and myelin basic pro-
tein were used as exogenous substrate, respectively. After incubation at room temperature for 30 min, the reactions were stopped by adding protein loading buffer and separated in SDS-PAGE gels. Each experiment was repeated three times. The relative amounts of incorporated radioactivity were determined by autoradiography and quantified with a Phosphorimager (Amersham Biosciences).

**TUNEL Assay**—HeLa cells were transfected with appropriate plasmids as noted in the figure legends, seeded into 60-mm diameter dishes, and grown in Dulbecco's modified Eagle's medium supplemented with 10% fetal calf serum for 24 h. Following treatment with or without VP16, doxorubicin, or staurosporine, apoptotic cells were determined by terminal deoxynucleotidyltransferase-mediated dUTP nick-end labeling (TUNEL) using an in situ cell death detection kit (Roche Applied Science). These experiments were performed in duplicate.

*In Vivo*[^32P]PI Labeling—COS7 cells were co-transfected with FLAG-ArgBP2γ, wild type, and constitutively active Akt or p38αN3A and labeled with [32P]Pi (0.5 mCi/ml) in phosphate- and serum-free minimum essential medium for 4 h. Cell lysates were subjected to immunoprecipitation with anti-FLAG antibody (Sigma). The immunoprecipitated proteins were separated by SDS-PAGE and transferred to membrane. The phosphorylated ArgBP2γ band was examined by autoradiography.

**RESULTS**

**Identification of Akt/PKBα-binding Protein ArgBP2γ**—In an attempt to identify protein(s) specifically interacting with Akt1, the C-terminal regulatory domain of Akt1 (410–480 amino acids), the most diverse region between three isoforms of Akt, was used as bait in a yeast two-hybrid screening. A human fetal brain cDNA library was used in this screen because Akt1 is highly expressed in brain (1, 9). A total of 32 clones that specifically interacted with the bait were identified. Sequence analysis revealed that two of the clones contained overlapping sequences of a cDNA (Fig. 1A). The largest clone as radiolabeled probe. Sequence alignment analysis showed that ArgBP2γ belongs to a newly defined vinexin adaptor protein family (41). These experiments were performed in duplicate.

**Domains of ArgBP2γ bind to proline-rich motifs in Akt, but have no effect on Akt activation.** A, Western blot of GST-ArgBP2γ and FLAG-Akt1, the C-terminal regulatory domain of Akt1 (410-480 amino acids), the most diverse region between three isoforms of Akt, was used as bait in a yeast two-hybrid screening. A human fetal brain cDNA library was used in this screen because Akt1 is highly expressed in brain (1, 9). A total of 32 clones that specifically interacted with the bait were identified. Sequence analysis revealed that two of the clones contained overlapping sequences of a cDNA (Fig. 1A). The largest clone as radiolabeled probe. Sequence alignment analysis showed that ArgBP2γ belongs to a newly defined vinexin adaptor protein family (41).

**Definition of Domains Involved in Akt-ArgBP2γ Interaction**—Sequence alignment analysis showed that ArgBP2γ belongs to a newly defined vinexin adaptor protein family (41). Although the function of the SoHo domain is currently unclear, the SH3 domain is known to bind to proline-rich sequences containing the PXPF core sequence. As the C-terminal region of Akt1, which was used as the bait for yeast two-hybrid screen, contains two proline-rich motifs, we examined whether SH3 domains of ArgBP2γ are required for interaction with Akt. Fig. 2A shows that Akt was detected in the ArgBP2γ, but not ArgBP2γ-SH3, immunoprecipitate. We next performed GST pulldown assay to determine which SH3 domain(s) of ArgBP2γ interacts with Akt and which motif of the C terminus of Akt binds to ArgBP2γ. Cell lysates were incubated with GST fusion proteins derived from different regions of Akt and ArgBP2γ that were immobilized on GSH beads. GST alone was used as a control. After stringent washes, the GST-Akt pulldown products and GST-ArgBP2γ bound proteins were subjected to immunoblotting analysis with anti-ArgBP2γ or anti-Akt antibody, respectively. As illustrated in Fig. 2, B and C, the C-terminal regulatory region of Akt interacts with the first and second SH3 domains of ArgBP2γ.

As SH3 domain binds to the PXPF motif and Akt contains two proline-rich regions (424PFKP427 and 467PHFP470) within its C terminus (1, 2), we next defined the ArgBP2γ binding sites...
of Akt. Akt-P424A, Akt-P467A, and Akt-P424/467A were created by converting proline(s) to alanine(s). GST pulldown assay showed that mutation of either Pro234 or Pro467 abrogated interaction with ArgBP2γ, indicating that both proline-rich motifs are required for binding to the SH3 domain of Akt (Fig. 2D). Further, in vitro Akt kinase assay was performed with anti-phospho-Ser 473 Akt antibody and showed that ArgBP2γ has no significant effect on Akt phosphorylation at Ser473 (Fig. 2E and data not shown).

**Akt Phosphorylates ArgBP2γ**

ArgBP2γ contains four putative Akt phosphorylation sites (Ser232, Thr234, Ser305, and Thr379), which we next determined whether ArgBP2γ is phosphorylated. Expression proteins containing each putative Akt phosphorylation site of ArgBP2γ were bacterially expressed and labeled with [32P]orthophosphate for 4 h. Immunoprecipitates were prepared with anti-FLAG antibody and separated by SDS-PAGE. Following transfer, the membrane was incubated with [32P]orthophosphate for 4 h. Immunoprecipitates were subjected to kinase assay using myelin basic protein as a substrate. As shown in Fig. 2F, the first and third Akt phosphorylation serine/threonine sites to alanines. Fig. 5A and 5B show that the first and third SH3 domains of ArgBP2γ function as docking sites for Akt and PAK1. Akt-P467A shows that Akt phosphorylates ArgBP2γ in vitro and in vivo. A, in vitro kinase assay. HEK293 cells were transfected with the indicated Akt expression plasmids and immunoprecipitated with anti-HA antibody. The immunoprecipitates were subjected to in vitro kinase assay using the GST-fused putative Akt phosphorylation site of ArgBP2γ as substrate. B, in vivo [32P]orthophosphate labeling. COS7 cells were transfected with the indicated plasmids and incubated with [32P]orthophosphate for 4 h. Immunoprecipitates were prepared with anti-FLAG antibody and separated by SDS-PAGE. Following transfer, the membrane was exposed to a film (top) and detected with anti-FLAG antibody (bottom).

**ArgBP2γ Interacts with and Activates PAK1**

We next determined whether Akt activation of PAK1 mediated by ArgBP2γ depends on their binding. A deletion mutation of ArgBP2γ (ArgBP2γΔSH3) that binds neither to PAK1 nor Akt was created by truncation of its C-terminal three SH3 domains (Figs. 2A and 4B). The kinase assay revealed that ArgBP2γΔSH3 not only failed to activate PAK1 but also inhibited constitutively active Akt-induced PAK1 activation (Fig. 5B). Because Akt phosphorylates ArgBP2γ, the effect of Akt phosphorylation of ArgBP2γ on PAK1 activation was evaluated by in vitro PAK1 kinase assay in the cells transfected with Akt and nonphosphorylatable ArgBP2γ-4A, prepared by converting the Akt phosphorylation serine/threonine sites to alanines. Fig. 5B
shows that the nonphosphorylatable ArgBP2γ/4A failed to induce PAK1 activation even though SH3 domains of ArgBP2γ/4A were intact. Moreover, ArgBP2γ/4A considerably reduced constitutively active Akt-stimulated PAK1 activation. Taken collectively, we concluded that ArgBP2γ mediates Akt activation of PAK1 and that SH3 domains of ArgBP2γ are critical for PAK1 activation induced by Akt and/or ArgBP2γ. Furthermore, Akt activation of PAK1 in the intact cell requires phosphorylation of ArgBP2γ by Akt, which may result in the conformation change of ArgBP2γ that leads to exposing the SH3 domains to interaction with PAK1.

ArgBP2γ Induces Bad Phosphorylation and Regulates Akt and PAK1 Phosphorylation of Bad—Previous studies demonstrate that PAK1 promotes cell survival through phosphorylation of Bad at Ser112 and Ser136 (42, 43) and that the antiapoptotic function of Akt is mediated by phosphorylation of Bad at Ser136 (15, 16). As ArgBP2γ is an adaptor for Akt and PAK1 and is phosphorylated by Akt, we next examined the effects of ArgBP2γ on Bad phosphorylation by PAK1 and Akt using in vitro kinase assay. As shown in Fig. 6A, ectopic expression of wild type ArgBP2γ enhanced PAK1 phosphorylation of Bad. In
addition, the coexpression of constitutively active Akt and PAK1, especially in combination with wild type ArgBP2/H9253, further elevated Bad phosphorylation (Fig. 6, A and B). However, Akt/PAK1-induced Bad phosphorylation was reduced by expression of either nonphosphorylatable or SH3 domain deletion mutant ArgBP2γ (Fig. 6B), suggesting that ArgBP2γ has a role in regulation of Akt and PAK1 phosphorylation of Bad through its interaction with Akt and PAK1 in a phosphorylation-dependent manner.

To investigate the effects of ArgBP2γ on Akt1/PAK1 phosphorylation of Bad intact cells, HEK293 cells were transfected with HA-Bad and different forms of ArgBP2γ with or without PAK1 and Akt. HA-Bad immunoprecipitates were subjected to Western blot analysis with anti-phospho-Bad-Ser112 and Ser136 antibodies. As shown in Fig. 6C, co-expression of PAK1 with wild type ArgBP2γ induced Bad phosphorylation at Ser112 and Ser136 to a similar level of constitutively active PAK1. Consistent with previous findings (15, 16, 42, 43), ectopic expression of constitutively active Akt induced phosphorylation of Bad only at Ser136, whereas constitutively active PAK1 phosphorylated Bad at both Ser112 and Ser136. However, co-expression of wild type ArgBP2γ, Akt, and PAK1 significantly induced Bad phosphorylation at Ser112 and Ser136, whereas expression of either nonphosphorylatable or SH3 domain-truncated ArgBP2γ failed to enhance and, indeed, inhibited the Bad phosphorylation induced by PAK1 and constitutively active Akt (Fig. 6, C and D). These data indicate that Akt and PAK1 phosphorylation of Bad is positively regulated by ArgBP2γ.

ArgBP2γ Reduces Cell Death Induced by Ectopic Expression of Bad or DNA Damage—We next examined the effects of ArgBP2γ on Bad-induced programmed cell death. HEK293 cells were transiently transfected with Bad, Bad/ArgBP2γ/H9253, or pcDNA3 vector alone. TUNEL assay was performed after 48 h of the transfection. Triple experiments revealed that Bad-transfected HEK293 cells underwent apoptosis. However, ArgBP2γ partially inhibited the apoptosis induced by Bad (Fig. 7A). Further, the effect of ArgBP2γ on PAK1 antiapoptotic function was further investigated. Ectopic expression of PAK1 alone partially inhibited Bad-induced apoptosis. Co-expression of ArgBP2γ and PAK1, however, exhibited more antiapoptotic
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There is no effect than that of expression of either ArgBP2γ or PAK1 alone. Moreover, nonphosphorylatable ArgBP2γ-4A and SH3 domain-truncated ArgBP2γ had no significant effect on PAK1-inhibited apoptosis (Fig. 7B). Ectopic expression of wild type, but not nonphosphorylatable, ArgBP2γ also exhibited antiapoptotic effects on DNA damage agent-induced programmed cell death, which includes VP16, doxorubicin, and staurosporine (Fig. 7C).

DISCUSSION

In the present study, we identified an Akt interaction protein, ArgBP2γ, that functions as an adaptor protein that binds to Akt and PAK1. ArgBP2γ is a physiological substrate of Akt and mediates Akt activation of PAK1 and phosphorylation of Bad in an interaction- and phosphorylation-dependent manner. In addition, we observed that ArgBP2γ interacts with other isoforms of Akt, including Akt2 and Akt3 (data not shown), even though the C terminus of Akt1, the most diverse region among three isoforms of Akt, was used as bait for yeast two-hybrid screening.

ArgBP2γ contains four Akt phosphorylation consensus sites, three of which are highly phosphorylated by Akt and the other (Ser205) with a lower phosphorylation level (2). However, nonphosphorylatable ArgBP2γ-4A, but not ArgBP2γ-3A, abrogates the function of ArgBP2γ in regulation of Akt and PAK1 signaling. This suggests that Akt phosphorylation of four serine/threonine sites of ArgBP2γ is required for its normal cellular function. A recent study has demonstrated that CTMP binds to the C-terminal region of Akt and inhibits Akt kinase activity by decreasing phosphorylation of Ser473 of Akt (33). Unlike CTMP, however, ArgBP2γ has no effect on Akt activation even though it interacts with the C-terminal region of Akt.

In addition to the N-terminal serine/threonine-rich region, a major characteristic of ArgBP2γ is that it contains a novel SoHo domain and three SH3 domains. Based on sequence analysis, ArgBP2γ belongs to a recently identified protein family that includes vinexin and CAP/ponsin (41). This protein family belongs to a recently identified adaptor protein family that includes VP16, doxorubicin, and staurosporine (Fig. 7D).

Previous studies have demonstrated that Bad is a primary target of Akt and PAK1 and is phosphorylated by Akt at Ser146 and by PAK1 at Ser112 and Ser136, which results in reduced interaction between Bad and Bel-2 or Bel-2x, and increased association of Bad with 14–3–3 (50). We demonstrated in this study that ArgBP2γ overrides Bad- and DNA damage-induced cell death. As an adaptor protein, ArgBP2γ enhances PAK1 and Akt phosphorylation of Bad at both Ser112 and Ser136, indicating that ArgBP2γ could play an important role in Akt/PAK1 cell survival pathway.

Acknowledgments—We thank Michael Greenberg for GST-Bad and the DNA Sequencing Facility at the H. Lee Moffitt Cancer Center for sequencing ArgBP2γ.

REFERENCES

1. Jones, P. F., Jakubowicz, T., Pitossi, F. J., Maurer, F., and Hemmings, B. A. (1990) Cell 61, 417–425
2. Bellacosa, A., Testa, J. R., Staal, S. P., and Tsichlis, P. N. (1991) Science 254, 897–927
3. Nakatani, K., Sakaue, H., Thompson, D. A., Weigel, R. J., and Roth, R. A. (1991) Biochem. Biophys. Res. Commun. 176, 526–534
4. Liu, A-X., Testa, J. R., Hamilton, T. C., Jove, R., Nicosia, S. V., and Cheng, J. Q. (1995) Eur. J. Biochem. 230, 471–481
5. Datta, S. R., Brunet, A., and Greenberg, M. E. (1999) Genes Dev. 13, 2905–2927
6. Datta, S. R., Dudek, H., Tao, X., Masters, S. F., Hu, G., and Greenberg, M. E. (1997) Cell 91, 231–241
7. del Pesoa, L., González-García, M., Pagea, C., Herreraa, R., and Nuneza, G. (1997) Science 278, 687–689
8. Burgering, B. M. T., and Coffer, P. J. (1999) Nature 376, 599–602
9. Cross, D. A., Alessi, D. R., Cohen, P., and Rixon, S. (1997) Nat. Cell Biol. 1, 221–230
10. Sato, T., Hasegawa, S., Tanaka, M., Ono, Y., Kameyama, K., Haga, T., and Yoshioka, N. (1999) Biochem. Biophys. Res. Commun. 256, 885–902
11. Liang, J., Zubovitz, J., Petrocelli, T., Kotchetkov, R., Han, K., Slingerland, J. M. (2002) Mol. Cell 10, 785–789
12. Zhou, B. P., Liao, Y., Xia, W., Zou, Y., Spohn, B., and Hung, M. C. (2001) Cell 106, 857–868
13. Zhou, B. P., Liao, Y., Xia, W., Zou, Y., Spohn, B., and Hung, H. C. (2002) Nat. Cell Biol. 3, 241–246
14. Cross, D. A., Alessi, D. R., Cohen, P., and Rixon, S. (1997) Biochem. Biophys. Res. Commun. 236, 421–427
15. Liu, A-X., Testa, J. R., Hamilton, T. C., Jove, R., Nicosia, S. V., and Cheng, J. Q. (1998) Cancer Res. 58, 2973–2977
16. Datta, S. R., Brunet, A., and Greenberg, M. E. (1999) Genes Dev. 13, 2905–2927
17. Datta, S. R., Dudek, H., Tao, X., Masters, S. F., Hu, G., and Greenberg, M. E. (1997) Cell 91, 231–241
18. del Pesoa, L., González-García, M., Pagea, C., Herreraa, R., and Nuneza, G. (1997) Science 278, 687–689
19. Brunet, A., Bonni, A., Zigmond, M. J., Lin, M. Z., Joo, P., Hu, L. S., Anderson, M. J., Arden, K., Bennis, J., and Greenberg, M. E. (1999) Cell 96, 857–868
20. Zhou, B. P., Liao, Y., Xia, W., Zou, Y., Spohn, B., and Hung, M. C. (2001) Nat. Cell Biol. 3, 241–246
21. Zhou, B. P., Liao, Y., Xia, W., Zou, Y., Spohn, B., and Hung, M. C. (2001) Nat. Cell Biol. 3, 241–246
22. Zigliotto, G., Motti, M. L., Brunì, P., Melillo, R. M., D’Alessio, A., Califano, D., Vinci, F., Chiappetta, G., Tischli, P., Bellacosa, A., Fusco, A., and Santoro, M. (2001) Mol. Cell 7, 1126–1134
23. Liang, J., Zubovitz, J., Petrocelli, T., Kotchetkov, R., Connor, M. K., Han, K., Chu, S., James, Y., and Abraham, R. T. (2000) Cancer Res. 60, 3504–3513
29. Dan, H. C., Sun, M., Yang, L., Feldman, R. I., Sui, X. M., Ou, C. C., Nellist, M., Yeung, R. S., Halley, D. J., Nicosta, S. V., Pledger, W. J., and Cheng, J. Q. (2002) J. Biol. Chem. 277, 35364–65670
30. Dan, H. C., Sun, M., Kaneko, S., Feldman, R. I., Nicosta, S. V., Wang, H-G., Tsang, B. K., and Cheng, J. Q. (2004) J. Biol. Chem. 279, 5405–5412
31. Pekarsky, Y., Koval, A., Hallas, C., Bichi, R., Tesini, M., Malstrom, S., Russo, G., Tsichlis, P., and Croce, C. M. (2000) Proc. Natl. Acad. Sci. U. S. A. 97, 3028–3033
32. Laine, J., Kunstle, G., Obata, T., Sha, M., and Noguchi, M. (2000) Mol. Cell 6, 395–407
33. Maira, S. M., Galetic, I., Brazil, D. P., Kaech, S., Ingley, E., Thelen, M., and Hemmings, B. A. (2001) Science 294, 374–380
34. Mitsuuchi, Y., Johnson, S. W., Sonoda, G., Tanno, S., Golemis, E. A., and Testa, J. R. (1999) Oncogene 18, 4891–4898
35. Sato, S., Fujita, N., and Tsuruo, T. (2000) Proc. Natl. Acad. Sci. U. S. A. 97, 10382–10387
36. Kanishi, H., Matusuzaki, H., Tanaka, M., Takemura, Y., Kuroda, S., Ono, Y., and Kikkawa, U. (1997) FEBS Lett. 410, 493–498
37. Kim, A. H., Yano, H., Cho, H., Meyer, D., Monks, B., Margolis, B., Birnbaum, M. J., and Chao, M. V. (2002) Neuron 35, 697–709
38. Sells, M. A., Knaus, U. G., Bagrodia, S., Ambrose, D. M., Bokoch, G. M., and Chernoff, J. (1997) Curr. Biol. 7, 202–210
39. Bokoch, G. M., Wang, Y., Bohl, B. P., Sells, M. A., Quilliam, L. A., and Knaus, U. G. (1996) J. Biol. Chem. 271, 25746–25749
40. Wang, B., Golemis, E. A., and Kruh, G. D. (1997) J. Biol. Chem. 272, 17542–17550
41. Kikura, N., Ueda, K., and Amachi, T. (2002) Cell Struct. Funct. 27, 1–7
42. Tang, Y., Zhou, H., Chen, A., Pittman, R. N., and Field, J. (2000) J. Biol. Chem. 275, 9106–9109
43. Schurmann, A., Mooney, A. F., Sanders, L. C., Sells, M. A., Wang, H. G., Reed, J. C., and Bokoch, G. M. (2000) Mol. Cell. Biol. 20, 453–461
44. Kimura, A., Baumann, C. A., Chiang, S. H., and Saltiel, A. R. (2001) Proc. Natl. Acad. Sci. U. S. A. 98, 9098–9103
45. Edwards, D. C., Sanders, L. C., Bokoch, G. M., and Gill, G. N. (1999) Nat. Cell Biol. 1, 253–259
46. Frost, J. A., Swantek, J. L., Stippec, S., Yin, M. J., Gaynor, R., and Cobb, M. H. (2000) J. Biol. Chem. 275, 19693–19699
47. Frost, J. A., Sten, H., Shapiro, P., Lewis, T., Ahn, N., Shaw, P. E., and Cobb, M. H. (1997) EMBO J. 16, 6426–6438
48. Manser, E., Leung, T., Salihiuddin, H., Zhao, Z. S., and Lim, L. (1994) Nature 367, 40–46
49. Zhou, G. L., Zhuo, Y., King, C. C., Fryer, B. H., Bokoch, G. M., and Field, J. (2000) Mol. Cell. Biol. 20, 8058–8069
50. Kim, D., Dan, H. C., Park, S., Yang, L., Liu, Q., Kaneko, S., Ning, J., He, L., Yang, H., Sun, M., Nicosta, S. V., and Cheng, J. Q. (2005) Front. Biosci. 10, 975–984
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J. Biol. Chem. 2005, 280:21483-21490.
doi: 10.1074/jbc.M500097200 originally published online March 22, 2005

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September 20, 2016