A 120-kDa protein that is tyrosine-phosphorylated upon antigen receptor ligation in B lymphocytes has been identified as the product of the c-cbl protooncogene. Tyrosine phosphorylation of Cbl depends on the efficient association of membrane immunoglobulin heavy chains with the Igα/β heterodimer but is unimpaired in splenic B cells from the Xid mouse. Cross-linking of membrane IgM and membrane IgG, but not of CD40, leads to the tyrosine phosphorylation of Cbl. In receptor-ligated B lymphocytes, p120<sup>cbl</sup> associates with an 85-kDa protein that has been identified as the 85-kDa subunit of phosphatidylinositol 3-kinase.

The antigen receptor on B lymphocytes is made up of membrane immunoglobulins associated with the Igα/β heterodimer (1, 2). This heterodimer serves to link the receptor with associated Src family kinases such as Blk, Lyn, Fyn, and Fgr (3–6), and also with the Syk tyrosine kinase (7, 8). Tyrosine phosphorylation appears to be an obligatory event (9) in the initiation of signal transduction pathways that promote B lymphocyte proliferation and differentiation. A number of signaling events downstream of this receptor depend on the interaction of membrane immunoglobulin heavy chains with the associated Igα/β heterodimer (10–12), while some are initiated independently of these associated glycoproteins (13). Activated protein tyrosine kinases are presumed to participate in triggering the Ras pathway, in activating PI<sup>3</sup>-kinase following antigen receptor ligation. An alternative pathway by which antigen-selected B lymphocytes may be induced to proliferate is mediated by T lymphocyte-derived cytokines and the triggering of CD40 on B cells by its ligand on activated T cells (24–26). Cross-linking of CD40 can lead to the activation of tyrosine and serine/threonine kinases, the activation of PI 3-kinase, the activation of phospholipase Cγ isozymes, and the nuclear translocation of the NF-κB transcription factor. While the molecular consequences of activating B lymphocytes via the antigen receptor and by CD40-mediated signaling are similar, the mechanisms by which these individual pathways are activated by these different ligands may well be distinct.

Cbl is the cellular homolog of the v-Cbl oncoprotein (27, 28) and is a predominantly cytosolic protein, which contains 17 proline-rich motifs potentially capable of binding a range of SH3 domains. Tyrosine phosphorylation of Cbl has been described in response to receptor occupancy of a number of receptors including the antigen receptor on T cells, the erythropoietin receptor, the granulocyte/macrophage colony-stimulating factor receptor, the Fcy receptor, the colony-stimulating factor-1 receptor, and the epidermal growth factor receptor (29–32). Tyrosine phosphorylation of Cbl has also been observed in v-src- and v-abl-transformed cells (32, 33), and this modification may be a critical event in mitogenic signaling.

We describe here the identification of Cbl as a prominent substrate for tyrosine phosphorylation in antigen-receptor-ligated B lymphocytes. This phosphorylation event requires the efficient interaction of membrane immunoglobulin heavy chains with the Igα/β heterodimer, and is unimpaired in splenic B cells from the Xid mouse. Following receptor ligation, Cbl is seen to associate with an 85-kDa phosphoprotein, identified as the 85-kDa subunit of PI 3-kinase. Our studies suggest that a major role of Cbl in B cells may be the recruitment and activation of PI 3-kinase following antigen receptor ligation.

**Experimental Procedures**

Cells—Cell lines used included WEHI 231 (IgM, immature B), BAL 17 (IgM, mature B), and A20.25 (IgG<sub>2a</sub>, mature B), as well as transfectants of A20.25 described below. The source for WEHI 231 cells was described earlier (34). BAL 17 cells were kindly provided by Dr. W. E. Paul. A20.25 transfectants expressing wild type human IgM and the YS/VV transmembrane human IgM mutant were kindly provided by Drs. A. Abbas and R. Mitchell (10). Splenic B cells from CBA/CaHN-xid<sup>+</sup> mice (Jackson Laboratory, Bar Harbor, ME) were purified as described in Ref. 17.

Antisera—Antibodies to Cbl (Santa Cruz), Shc (Upstate Biotechnology Inc.), Grb2 (Santa Cruz), phosphotyrosine (Zymed), and the p85 subunit of phosphatidylinositol 3-kinase (Santa Cruz) were obtained from commercial sources. Anti-Btk was obtained as described earlier (17).

Lymphocyte Activation—Anti-IgM and anti-iG stimulation of B cells was performed as described earlier (17). Anti-CD40 stimulation was performed incubating 2 × 10<sup>7</sup> BAL 17 B cells in 200 μl of serum-free RPMI medium at 37 °C with anti-mouse CD40 at a concentration known to induce proliferation (2 μg/ml, Serotech).

Immunoprecipitations, anti-phosphotyrosine immunoblots, and in...
vitro kinase assays were performed as described previously (17, 34).

GST-Grb2 Association with Cbl—Glutathione S-transferase fusion proteins including Grb2 and a mutant Grb2 protein in which the N-terminal SH3 domain is non-functional (a tryptophan to lysine substitution in codon 36) were kindly provided by Dr. Bruce Mayer. Lysates from non-stimulated and stimulated A20.25 B cells were made using 1% Nonidet P-40 in 20 mM Tris, pH 7.5, 150 mM NaCl, and 2 mM phenylmethylsulfonyl fluoride. Binding to immobilized GST fusion proteins, elution, and analysis on polyacrylamide SDS gels was performed as described earlier (34). Cbl associated with Grb2 was revealed by an immunoblot assay.

Assay for PI 3-Kinase Activity in Anti-Cbl, Anti-phosphotyrosine, and Anti-p85 Immunoprecipitates—The assay was performed essentially as described (35). Briefly anti-Cbl, anti-PY, and anti-p85 immunoprecipitates were incubated with micellar phosphatidylinositol (0.2 mg/ml) in 25 mM MOPS, pH 7.0, 5 mM MgCl2, 1 mM EDTA, 150 μM unlabeled ATP, and 25 μCi of [γ-32P]ATP in a total reaction volume of 50 μl. After a 20-min incubation at 37 °C, the reaction was stopped using 100 μl of 1:1 CH3OH:HOAc. Labeled phospholipid was extracted with 200 μl of CHCl3 and was dried under N2. Thin layer chromatography was performed overnight with H2O/glacial acetic acid-propand (34:1:65).

RESULTS

Cbl Is Tyrosine-phosphorylated following Membrane IgM or Membrane IgG Cross-linking of B Cells—Membrane immunoglobulins were cross-linked on an IgM-expressing B cell line (WEHI 231) and an IgG-expressing B cell line (the 4J subclone of A20.25, which also expresses a transfected human IgM mutant; Ref. 10) using anti-mouse IgM and IgG, respectively. Lysates from stimulated cells contained a 120-kDa tyrosine-phosphorylated protein (Fig. 1, upper panel), which was depleted by predearing with anti-Cbl, but not by control antibodies. Depletion of Cbl was confirmed by an immunoblot assay (lower panel). Tyrosine phosphorylation of Cbl is seen as early as 10 s after cross-linking and peaks at about 5 min. Similar results were observed with the surface IgM-positive BAL 17 line and untransfected A20.25 cells.

In Fig. 2A, Cbl tyrosine phosphorylation is apparent from the 30-s time point. In a slightly longer exposure, phosphorylation was apparent from the 10-s time point. Tyrosine-phosphorylated proteins with a slightly slower mobility than the major Cbl band probably represent Cbl species phosphorylated on multiple sites. These bands were depleted by anti-Cbl as seen in Figs. 1 and 2A. Similar bands were observed on anti-Cbl immunoblots of lysates from activated B cells (data not shown). The tyrosine-phosphorylated 70-kDa species seen both in Figs. 1 and 2A, exactly comigrates with, and probably represents, tyrosine-phosphorylated Syk. Phosphorylation of Cbl is observed soon after the cross-linking of membrane immunoglobulins but is not observed after cross-linking CD40 (Fig. 2B), although both stimuli can independently contribute to the initiation of similar signaling pathways.

Cross-linking of a Transmembrane IgM Mutant Fails to Initiate the Tyrosine Phosphorylation of Cbl—Mutations in the transmembrane domain of membrane IgM have been demonstrated to impair signal transduction. A Tyr/ Ser → Val/Val mutation (10) in human membrane IgM expressed in a murine B cell line (A20.25) has been examined in a number of studies. While cross-linking of a wild type human IgM transfectant leads to the effective initiation of intracellular signaling, this mutant human membrane IgM associates poorly with the murine Igα/β heterodimer and is compromised in terms of its ability to initiate a calcium flux (10) or to lead to the tyrosine phosphorylation of a number of unidentified cellular proteins (11, 12). We immunoprecipitated Cbl following cross-linking of the above A20.25 transfectants either with anti-mouse IgG or anti-human IgM. As seen in Fig. 3 (upper panel), cross-linking of the Y54V/V mutant human IgM does not lead to the efficient tyrosine phosphorylation of Cbl.

Tyrosine Phosphorylation of Cbl Is Unimpaired upon Cross-linking of Membrane IgM Expressed by Splenic B Cells from Xid Mice—The catalytic activation of Src family kinases is known to occur in the first minute after B cell antigen receptor cross-linking (20), while the activation of Syk (20) and Btk peaks a few minutes later (19, 20). The dependence of Cbl tyrosine phosphorylation on the Igα/β heterodimer and the time course of Cbl phosphorylation suggest that antigen receptor-associated Src family kinases and Syk probably play a role in this tyrosine phosphorylation event. Xid mice harbor a point mutation in the PH domain of Btk (36, 37). In response to antigen receptor ligation, splenic B cells from Xid mice appear to initiate signal transduction in a manner similar to B cells from wild type mice, but the Xid B cells, in contrast to wild type B cells, fail to enter S phase following stimulation (23). While Xid B cells are defective in terms of T-independent responses, they respond normally to protein antigens. Splenic B cells from gene-targeted mice, which fail to synthesize any Btk, cannot be functionally distinguished from Xid B cells (22), suggesting that the Xid point mutation completely disrupts Btk function. Receptor ligation of Xid B cells, however, leads to the efficient tyrosine phosphorylation of Cbl (Fig. 4), suggesting that the phosphorylation of Cbl occurs independently of Btk.
Shc-Grb2-Cbl Complexes in Lysates from Activated B Lymphocytes

Cbl contains multiple proline-rich stretches, which presumably constitute sites for SH3 interactions, and also contains a number of tyrosine residues, which, if phosphorylated, could serve as sites for SH2 binding. While the N-terminal SH3 domain of Grb2 has been demonstrated to associate with Cbl in lysates from T lymphocytes (29), the significance of this association remains unclear. One possibility could involve the recruitment of Cbl to the antigen receptor via Shc and Grb2. While it has been suggested that Shc-Grb2-SOS complexes contribute to the recruitment of SOS to the membrane in activated T cells (38), this remains an unresolved issue. Recruitment of Grb2-SOS to the membrane may depend on its association in activated T cells with a 36-kDa membrane-associated phosphoprotein (39). Complex formation between T cell recep-

**Fig. 2.** Time course of tyrosine phosphorylation following receptor ligation of BAL 17 B cells. Lysates were prepared 10 s (10”), 30 s (30”), 1 min (1’), 3 min (3’), 5 min (5’), and 15 min (15’) after activation. Additional lysates at the 5-min time point were precleared either with anti-Cbl or with preimmune IgG. Details as in legend to Fig. 1. B: Cbl is tyrosine-phosphorylated after antigen receptor ligation but not following CD40 cross-linking. BAL 17 B cells were either not stimulated (N) or were stimulated with anti-IgM for 5 min (S1), anti-CD40 for 30 s (S2), or anti-CD40 for 5 min (S3). In leftmost four lanes, total lysates were separated on SDS-PAGE. In rightmost four lanes, anti-Cbl immunoprecipitates were separated. Proteins were visualized by an anti-phosphotyrosine immunoblot.

**Fig. 3.** Cross-linking of a transmembrane IgM mutant that associates poorly with the Igα/Igβ heterodimer compromises the tyrosine phosphorylation of Cbl. A20.25 cells expressing transfected wild-type human IgM (A20 WT) or a transmembrane YS/VV mutant (A20/4J) were individually either not stimulated (N) or cross-linked with anti-human IgM (αμ) or anti-mouse IgG (αγ). Lysates were immunoprecipitated with anti-Cbl and were separated on SDS-PAGE, followed by an immunoblot analysis using anti-phosphotyrosine antibody (upper panel). Immunoprecipitated Cbl was quantified (lower panel) by reprobing with anti-Cbl.

**Fig. 4.** Cbl is efficiently tyrosine-phosphorylated following receptor ligation in Xid splenic B cells. Splenic B cells were purified from CBA/CaH-N-xidJ mice and were either not stimulated (N) or cross-linked with anti-IgM (S). Total lysates and anti-Cbl immunoprecipitates were separated on SDS-PAGE and tyrosine-phosphorylated proteins revealed by an immunoblot assay.
tor-associated ITAMs and Shc may be relatively inefficient (40). We wished to ascertain whether the formation of a complex between Shc, Grb2, and Cbl could be demonstrated in activated B lymphocytes. We were able to confirm, as described previously (41), the formation of Shc-Grb2 complexes after B cell activation (Fig. 5A) and also the association of fusion proteins containing an intact N-terminal SH3 domain of Grb2 with Cbl from B cell lysates (Fig. 5B). While these data suggest that Shc-Grb2-Cbl complexes may well be formed in activated B cells, in our hands we were able to observe an in vivo association between Grb2 and Cbl only in three murine pre-B cell lines.2 Although we could detect phosphorylated Shc species in anti-Cbl immunoprecipitates from lysates of activated B cells (data not shown), we were unable, in any of the three activated B cell lines tested, to demonstrate an interaction in vivo between Grb2 and Cbl. However, Shc-Grb2-Cbl complexes are readily observed in activated human B cell lines.3

The band that has been labeled as Shc in the lower panel of Fig. 5A is inferred to be the phosphorylated form of p52 Shc. Anti-Shc immunoblots detect the p52 and p46 species of Shc in B cells but fail to reveal p66. Although the p46 form of Shc is also phosphorylated in activated B cells, the band representing it is probably obscured in Fig. 5A by rabbit IgG detected by the second antibody.

In Receptor-ligated B Cells, Cbl Associates with the 85-kDa Subunit of Phosphatidylinositol 3-Kinase—Since Cbl is tyrosine-phosphorylated in response to receptor ligation, we wished to ascertain if Cbl is specifically associated with any proteins after antigen receptor cross-linking. Given the knowledge that Cbl associates constitutively with Src family kinases via the SH3 domains of the latter (29, 31) and with Syk by a poorly understood mechanism (31), one of the approaches that was used to identify proteins associated with Cbl was an in vitro kinase assay on Cbl immunoprecipitates of detergent lysates from non-activated and activated B cells. As seen in Fig. 6, phosphorylation of Cbl as revealed by this assay is increased after receptor ligation. In addition, a prominent 85-kDa phosphoprotein was seen to be associated specifically with Cbl immunoprecipitated from lysates of activated B cells, but not from non-activated B cell lysates. Since this protein was of the predicted size for the 85-kDa subunit of phosphatidylinositol 3-kinase, we examined lysates of B cells before and after activation for Cbl-associated PI-3 kinase as well as for Btk. Lysates were immunoprecipitated from non-activated and activated B cells with anti-Cbl antibodies and were analyzed for associated PI-3 kinase using antibodies specific for the p85 subunit in an immunoblot assay. The same filter was also probed with anti-Btk but no significant association of Btk with Cbl was observed (data not shown). As seen in Fig. 7A, p85 was seen to be associated with Cbl only in activated B cells.2

2 T. J. Kim and S. Pillai, unpublished observations.

3 H. Band, personal communication.
PI 3-Kinase and p120cdl Associate in Receptor-ligated B Cells

**DISCUSSION**

Since the tyrosine phosphorylation of Cbl is an early event downstream of the engagement of a number of mitogenic receptors, we sought to identify proteins that specifically associate with Cbl after the initiation of signal transduction. A number of proteins associate constitutively with Cbl usually via SH3 domain-mediated interactions. These proteins include Ssrc family kinases, Grb2, and Nck (39, 21, 42). We have demonstrated here that an 85-kDa protein specifically associates with Cbl following anti-IgM exposure. As seen in Fig. 7B, a dramatic increase in Cbl-associated phosphatidylinositol 3-kinase activity was observed in activated B cell lysates.

Three different cell lines representing distinct stages of differentiation were used in all the studies described above (other than those examining membrane IgM mutants). Most experiments were performed with all three cell lines, although in some only two of the three lines were used. No functional differences between these cell lines was observed in any of the above studies.

**REFERENCES**

1. Reth, M. (1992) Annu. Rev. Immunol. 10, 97–121
2. Chatterjee, J. C., Bodey, W., Campbell, K., Chien, N., Friedman, J., Hardwood, A., Jensen, W., Pleiman, C., and Clark, M. C. (1993) Cell Biol. 82, 85–106
3. Burkhardt, A. L., Brunswick, M., Bolen, J. R., and Mond, J. J. (1993) Proc. Natl. Acad. Sci. U. S. A. 88, 7410–7414
4. Yamanashi, Y., Kakiuchi, T., Mizuguchi, J., Yamamoto, T., and Toyoshima, K. (1991) Science 251, 192–194
5. Campbell, M. A., and Sefton, B. M. (1992) Proc. Natl. Acad. Sci. U. S. A. 88, 8613–8619
6. Wechsler, R. J., and Monroe, J. G. (1995) J. Immunol. 154, 3324–3424
7. Hutchcroft, J. E., Harrison, M. L., and Geahlen, R. L. (1992) J. Biol. Chem. 267, 113–1113
8. Yamada, T., Taniguchi, T., Yang, C., Yasue, S., Saito, H., and Yamamura, H. (1993) Eur. J. Biochem. 213, 455–459
9. Gold, M. R., Law, D. A., and DeFranco, A. L. (1990) Nature 345, 810–813
10. Shaw, A. C., Mitchell, R. N., Weaver, Y. K., Campos-Torres, J., Abbas, A. K., Jensen, W., Pleiman, C., and Clark, M. C. (1993) Immunol. Rev. 132, 85–106
11. Grupp, S. A., Campbell, K., Mitchell, R. N., Cambier, J. C., and Abbas, A. K. (1993) J. Biol. Chem. 268, 25776–25779
12. Sanchez, M., Misulovin, Z., Burkhardt, A. L., Mahajan, S., Costa, T., Franke, R., Bolen, J. B., and Nussenzwick, M. (1993) J. Exp. Med. 178, 1049–1055
14. Law, D. A., Chan, V. W. F., Datta, S. K., and DeFranco, A. L. (1993) Curr. Biol. 3, 645–657

15. Rowley, R. B., Burkhardt, A. L., Chao, H.-G., Matsuda, G. R., and Bolen, J. B. (1995) J. Biol. Chem. 270, 11590–11594

16. Kurosaki, T., Takakura, T., Yamanashi, Y., Inazu, T., Taniguchi, T., Yamamoto, T., and Yamamura, H. (1994) J. Exp. Med. 179, 1725–1729

17. Aoki, Y., Kim, Y.-T., Stillwell, R., Kim, T. J., and Pillai, S. (1995) J. Biol. Chem. 270, 15658–15663

18. Siderorenko, S. P., Law, C.-L., Chandran, K. A., and Clark, E. A. (1995) Proc. Natl. Acad. Sci. U.S.A. 92, 359–363

19. Aoki, Y., Isselbacher, K. J., and Pillai, S. (1994a) Proc. Natl. Acad. Sci. U.S.A. 91, 10606–10609

20. Saouaf, S. J., Mahajan, S., Rowley, R. B., Kut, S. A., Fargnoli, J., Burkhardt, A. L., Tsukada, S., Witte, O. N., and Bolen, J. B. (1994) Proc. Natl. Acad. Sci. U.S.A. 91, 9524–9528

21. deWeers, M., Brouns, G. S., Hinshelwood, S., Kincon, C., Schuurman, R. K. B., Hendriks, R. W., and Bont, J. (1994) J. Biol. Chem. 269, 23857–23860

22. Khan, W. N., Alit, F. W., Gerstein, R. M., May, A. A., Larsson, I., Rathbun, G., Davidson, L., Muller, S., Kantor, A. B., Herzenberg, L. A., Rosen, F. S., and Sideras, P. (1995) Immunity 3, 283–299

23. Lindsberg, M.-L., Brunowik, M., Yamasuda, H., Lees, A., Inman, J. J., June, C. H., and Mond, J. J. (1991) J. Immunol. 147, 3774–3779

24. Uckun, F. M., Schievan, G. L., Dibridik, I., Chandan-Langlie, M., Uetting, M., and Ledbetter, J. A. (1991) J. Biol. Chem. 266, 17478–17485

25. Ren, C., Lemos, T., Yu, M. S., and Geha, R. (1994) J. Exp. Med. 179, 673–680

26. Lamanach-Girard, A. C., Chiles, T. C., Parker, D. C., and Rothstein, T. L. (1993) J. Exp. Med. 177, 1215–1219

27. Langdon, W. Y., Hartley, J. W., Kinken, S. P., Ruscotti, S. K., and Morse, H. C., III (1989) Proc. Natl. Acad. Sci. U.S.A. 86, 1168–1172

28. Blake, T. J., Shapiro, M., Morse, H. C., III, and Langdon, W. Y. (1991) Oncogene 6, 635–657

29. Donovan, J. A., Wange, R. L., Langdon, W. Y., and Samelson, L. E. (1994) J. Biol. Chem. 269, 22921–22924

30. Odai, H., Saeki, K., Iwanami, T., Hanazono, Y., Tanaka, T., Mitiaki, K., Yazaki, Y., and Hirai, H. (1995) J. Biol. Chem. 270, 10800–10805

31. Marcilla, A., Rivero-Lecano, O. M., Agarwal, A., and Robbins, K. C. (1995) J. Biol. Chem. 270, 9115–9120

32. Tanaka, S., Neff, L., Baron, R., and Levy, J. B. (1995) J. Biol. Chem. 270, 14347–14351

33. Andoniou, C. E., Thien, C. B. F., and Langdon, W. Y. (1994) EMBO J. 13, 4515–4523

34. Aoki, Y., Isselbacher, K. J., Cherayil, B. J., and Pillai, S. (1994b) Proc. Natl. Acad. Sci. U.S.A. 91, 4204–4208

35. Serunian, L. A., Auger, K. R., and Cantley, L. C. (1991) Methods Enzymol. 211, 78–87

36. Thomas, J. D., Sideras, P., Smith, C. I. E., Vorechovsky, I., Chapman, V., and Paul, W. E. (1993) Science 261, 355–358

37. Rawlings, D. J., Safran, D. C., Tsukada, S., Large, D. A., Grimaldi, J.-C., Cohen, L., Mohr, R. N., Bazan, J. F., Howard, M., Copeland, N. G., Jenkins, N. A., and Witte, O. N. (1993) Science 261, 358–361

38. Ravichandran, K. S., Lee, K. K., Songyang, Z., Cantley, L. C., Burn, P., and Burakoff, S. J. (1993) Science 262, 902–905

39. Sieh, M., Batzer, A., Schlesinger, J., and Weiss, A. (1994) Mol. Cell. Biol. 14, 4435–4442

40. Osman, N., Lucas, S. C., Turner, H., and Canter, D. (1995) J. Biol. Chem. 270, 13981–13986

41. Smit, L., deVries-Smits, A. M. M., Bos, J. L., and Borst, J. (1994) J. Biol. Chem. 269, 20209–20212

42. Gold, M. R., Chan, V. W. F., Turck, C. W., and DeFranco, A. L. (1992) J. Immunol. 149, 2012–2022

43. Yamashita, Y., Fukui, T., Wongsasrit, B., Kinoshita, Y., Ichimori, Y., Toyoshima, K., and Yamamoto, T. (1992) Proc. Natl. Acad. Sci. U.S.A. 89, 1118–1122

44. Rivero-Lecano, O. M., Sameshima, J. H., Marcilla, A., and Robbins, K. C. (1994) J. Biol. Chem. 269, 17363–17366

45. Songyang, Z., Shoelson, S. E., Chaudhuri, M., Gish, G., Gison, T., Haser, W. G., King, F., Roberts, T., Ratnoffsky, S., Lechleider, R. J., Neel, B. G., Birge, R. B., Fajardo, J. E., Chou, M. M., Hanauska, F., Schaffhause, B., and Cantley, L. C. (1993) Cell 72, 767–778

46. Tuveson, D. A., Carter, R. H., Sottlof, S. P., and Fearon, D. T. (1993) Science 260, 896–899

47. Nakashima, H., Brewer, K. A., and Exton, J. H. (1993) J. Biol. Chem. 268, 13–16

48. Hu, Q., Klippel, A., Muslin, A. J., Fantl, W. J., Williams, L. T. (1995) Science 268, 100–102

49. Valius, M., and Kazlausas, A. (1993) Cell 73, 321–334

50. Meisner, H., Conway, B. R., Hartley, D., and Czech, M. P. (1995) Mol. Cell. Biol. 15, 3571–3578

51. Fuzakawa, T., Reedquist, K. A., Trub, T., Soltoff, S., Panchamourthy, G., Druker, B., Cantley, L. C., Shoelson, S. E., and Band, H. (1995) J. Biol. Chem. 270, 19141–19150

52. Vartibekian, L., Daley, G. Q., Jackson, P., Baltimore, D., and Cantley, L. C. (1991) Mol. Cell. Biol. 11, 1107–1113
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