Although the identity of the protein tyrosine kinases that mediate the activation of several protein kinases, leading to the secretion of variety of immunomodulatory molecules such as nitric oxide and proinflammatory cytokines. In this study, we have examined the role of the α isoenzyme of protein kinase C (PKC) in the regulation of LPS-initiated signal transduction in macrophages. To this end, we have stably overexpressed a dominant-negative (DN) version of PKC-α (DN PKC-α) in the murine macrophage cell line RAW 264.7. Clones overexpressing DN PKC-α were indistinguishable from the parental line with respect to morphology and growth characteristics. At the functional level, DN PKC-α overexpression strongly inhibited LPS-induced interleukin-1α mRNA accumulation, and to a lesser extent inducible nitric oxide synthase and tumor necrosis factor-α expression. DN-PKC-α overexpression did not cause a general unresponsiveness to LPS, as secretion of the matrix metalloproteinase-9 was up-regulated in our DN PKC-α-overexpressing clones. Moreover, LPS-induced phosphorylation and degradation of IκBα, NF-κB activation, as well as p38 mitogen-activated protein kinase and Jun N-terminal kinase phosphorylation, were not affected by DN PKC-α overexpression. Collectively, these data provide evidence that PKC-α regulates selective LPS-induced macrophage functions involved in host defense and inflammation.

Mononuclear phagocytes are multipotential cells that can be modulated to perform a variety of functions including secretion of nitric oxide (NO) and proinflammatory cytokines, which are important mediators in host defense and inflammation. In this regards, LPS, a major component of the cell wall of Gram-negative bacteria, is one of the most potent and best characterized modulator of macrophage function. Binding of LPS to the cell surface CD14 molecule triggers multiple intracellular signaling events, including TNF-α and IL-1 secretion, NO production, and tumoricidal activity (9, 13, 17, 18).

PKC was first characterized as a Ca2+-dependent and phospholipid-dependent protein serine/threonine kinase that requires diacylglycerol for activity (19). Subsequently, it has been established that PKC is not a single entity, but rather a family of closely related isoenzymes comprising at least 12 different members (20). Differences in their structure, requirement for activity, subcellular localization, and substrate specificity suggest that in a given cell, the various PKC isoforms may exert specific functions (20, 21). Macrophages and mononuclear cells express the Ca2+-dependent isoenzymes α, β, and βII, the Ca2+-independent isoenzymes δ and ε, and the atypical isoenzyme ζ (10, 16, 22, 23). However, our current knowledge on their respective contribution to the regulation of macrophage function is limited and mainly concerns the regulation of nitric oxide production. In one study, differential down-regulation of PKC isoenzymes induced by phorbol ester treatment revealed that PKC-βII participates in LPS-induced iNOS gene expression and nitrite production in the J774 macrophage cell line (10). More recently, transient PKC isoforms transfection studies in the RAW 264.7 macrophage cell line showed that iNOS gene expression is also regulated by PKC-ε, but in contrast to the pathway regulated by PKC-βII, the PKC-ε-dependent pathway is apparently not involved in the LPS response (24).

Elucidation of the role of a particular PKC isoenzyme in cellular regulation is complicated by the concomitant expression of several isoenzymes and by the lack of isoenzyme-specific activators or inhibitors. In the present study, we have investigated the role of PKC-α in the regulation of LPS-induced functions by overexpressing a kinase-deficient mutant of this isoenzyme in the murine macrophage line RAW 264.7. Such catalytically inactive mutants, which behaves as a dominant-negative molecule, acts by competing with the corresponding endogenous isoenzyme (21, 25). Using this approach, we obtained evidence that PKC-α activity regulates selective LPS-induced macrophage functions involved in host defense and inflammation.

**EXPERIMENTAL PROCEDURES**

**cDNAs and Expression Vectors**—The wild type human PKC-α cDNA (26) was obtained from the American Type Culture Collection (Rockville, MD). A dominant-negative version of the gene, DN PKC-α (K368D), was created by site-directed mutagenesis using the Transformer System with the mutagenic primer AD-5 (5′-GATGCGAACCTGAATCTGATCCGAGGAGG-3′), as described by the manufacturer (Clontech, Palo Alto, CA). The sequence of this mutant was confirmed by sequence analysis. Replacement of the conserved lysine resi...
Protein Kinase C-α and LPS-induced Macrophage Functions

DN PKC-α inhibits LPS-induced nitrite secretion

| Cells | Treatment (µg/ml LPS) |
|-------|-----------------------|
| 0     | A1 0.2 15.6           |
| 0     | A2 0.5 10.4           |
| 0     | B1 0.2 11.8           |
| 0     | B2 0.7 14.5           |
| 10    | A1 0.6 15.6           |
| 10    | A2 0.5 11.8           |
| 10    | B1 0.2 12.5           |
| 10    | B2 0.7 15.6           |

*These values represent the mean ± S.E. of one experiment performed in triplicate samples.

results were prepared essentially as described (40). Protein contents were determined using the BCA protein assay kit (Pierce) and the extracts were stored at 70 °C. EMSA were performed by incubating 32P-labeled NP-β-B consensus oligonucleotide (5'-'AGTTGAGGGGACTT-TCCACAGG-3', obtained from Promega) with 10 µg of nuclear extracts for 20 min at room temperature. The incubation mixture contained 3 µg of poly(dI-dC) in a binding buffer (10 mM Tris-HCl, 1 mM MgCl2, 0.5 mM EDTA, 0.5 mM dithiothreitol, 20 mM NaCl, 4% glycerol). The DNA-protein complexes were separated from free oligonucleotide by electrophoresis under nondenaturing conditions in 4% native polyacrylamide gels in a buffer containing 44.5 mM Tris, 44.5 mM borate, pH 8.0, and 1 mM EDTA. The specificity of binding was determined by competition with excess unlabeled oligonucleotide. After electrophoresis, gels were exposed to films at ~70 °C.

RESULTS

Generation of DN PKC-α Overexpressing RAW 264.7 Macrophages—Stable transfectants from two independent populations of RAW 264.7 macrophages electroporated with pCIN-DN PKC-α were selected in the presence of 500 µg/ml G418. Western blot analyses were performed on three clones selected from each independent population of transfectants to determine their PKC-α expression levels. The three clones from the first population (clones DN PKC-α B1, C2, and D1), and one clone from the second population (clone DN PKC-α A2) expressed immunoreactive PKC-α above endogenous levels (not shown). To determine whether DN PKC-α overexpression had any effect on LPS-induced responses, we measured the ability of these four DN PKC-α-overexpressing clones to secrete nitrite in response to LPS. As shown in Table I, LPS-induced nitrite secretion was inhibited in the four DN PKC-α-overexpressing clones (clones DN PKC-α B1, D1, A2, and C2) with respect to the RAW 264.7 cells transfected with the empty vector. Inhibition of LPS-induced nitrite production was likely a consequence of DN PKC-α overexpression, as LPS-induced nitrite secretion in three clones RAW 264.7 cells transfected with a construct containing the wild-type murine PKC-ζ cDNA (41) was similar to that of RAW 264.7 cells transfected with the empty vector (clones PKC-ζ A1, A2, B1) (Table I).

Clone DN PKC-α A2, with a 2-fold increase in immunoreactive PKC-α levels, and clone DN PKC-α C2, with a 10-fold increase in immunoreactive PKC-α levels (Fig. 1A), were selected for further analyses. Increased DN PKC-α levels in these clones was also demonstrated by measuring [3H]PDBu binding levels (42), which...
LPS induced the expression of these three genes in a dose-dependent manner (10 and 100 ng/ml) for 6 h. In control RAW 264.7 cells, we determined the levels of TNF-α in response to 10 ng/ml LPS (Fig. 3A, lanes 1–3). TNF-α secretion was slightly increased for clone A2 and was barely above basal levels for clone C2. Similar results were obtained with clones B1 and D1, both of which failed to secrete TNF-α in response to 100 ng/ml LPS (data not shown). Nitrite secretion (Fig. 3C) was reduced by approximately 60–70% for clone A2, and by 80–90% for clone C2 with respect to RAW 264.7 cells. Thus, DN PKC-α overexpression had a major inhibitory effect on LPS-induced TNF-α and NO production.

Overexpression of DN PKC-α Enhances LPS-stimulated MMP-9 Secretion—In addition to inflammatory cytokines and nitrite, LPS stimulates macrophages to secrete various hydrolases, including the matrix metalloproteinase MMP-9 (43). Based on data obtained with PKC inhibitors, it has been proposed that PKC exerts both positive and negative regulation on LPS-induced MMP-9 secretion in macrophages (39). To determine the role of PKC-α in this process, we measured the secretion of MMP-9 in the supernatants of control cells and of clones A2 and C2 after stimulation with either 10 or 100 ng/ml LPS (Fig. 3D). At 100 ng/ml LPS, IL-1α secretion was significantly increased for clone A2 and was barely above basal levels for clone C2. Similar results were obtained with clones B1 and D1, both of which failed to secrete IL-1α in response to 100 ng/ml LPS (data not shown). Nitrite secretion (Fig. 3C) was reduced by approximately 60–70% for clone A2, and by 80–90% for clone C2 with respect to RAW 264.7 cells. Thus, DN PKC-α overexpression had a major inhibitory effect on LPS-induced IL-1α and NO production.

Overexpression of DN PKC-α Enhances LPS-stimulated MMP-9 Secretion—In addition to inflammatory cytokines and nitrite, LPS stimulates macrophages to secrete various hydrolases, including the matrix metalloproteinase MMP-9 (43). Based on data obtained with PKC inhibitors, it has been proposed that PKC exerts both positive and negative regulation on LPS-induced MMP-9 secretion in macrophages (39). To determine the role of PKC-α in this process, we measured the secretion of MMP-9 in the supernatants of control cells and of clones A2 and C2 after stimulation with either 10 or 100 ng/ml LPS (Fig. 3D). At 100 ng/ml LPS, IL-1α secretion was significantly increased for clone A2 and was barely above basal levels for clone C2. Similar results were obtained with clones B1 and D1, both of which failed to secrete IL-1α in response to 100 ng/ml LPS (data not shown). Nitrite secretion (Fig. 3C) was reduced by approximately 60–70% for clone A2, and by 80–90% for clone C2 with respect to RAW 264.7 cells. Thus, DN PKC-α overexpression had a major inhibitory effect on LPS-induced IL-1α and NO production.

Overexpression of DN PKC-α Enhances LPS-stimulated MMP-9 Secretion—In addition to inflammatory cytokines and nitrite, LPS stimulates macrophages to secrete various hydrolases, including the matrix metalloproteinase MMP-9 (43). Based on data obtained with PKC inhibitors, it has been proposed that PKC exerts both positive and negative regulation on LPS-induced MMP-9 secretion in macrophages (39). To determine the role of PKC-α in this process, we measured the secretion of MMP-9 in the supernatants of control cells and of clones A2 and C2 after stimulation with either 10 or 100 ng/ml LPS (Fig. 3D). At 100 ng/ml LPS, IL-1α secretion was significantly increased for clone A2 and was barely above basal levels for clone C2. Similar results were obtained with clones B1 and D1, both of which failed to secrete IL-1α in response to 100 ng/ml LPS (data not shown). Nitrite secretion (Fig. 3C) was reduced by approximately 60–70% for clone A2, and by 80–90% for clone C2 with respect to RAW 264.7 cells. Thus, DN PKC-α overexpression had a major inhibitory effect on LPS-induced IL-1α and NO production.

Overexpression of DN PKC-α Enhances LPS-stimulated MMP-9 Secretion—In addition to inflammatory cytokines and nitrite, LPS stimulates macrophages to secrete various hydrolases, including the matrix metalloproteinase MMP-9 (43). Based on data obtained with PKC inhibitors, it has been proposed that PKC exerts both positive and negative regulation on LPS-induced MMP-9 secretion in macrophages (39). To determine the role of PKC-α in this process, we measured the secretion of MMP-9 in the supernatants of control cells and of clones A2 and C2 after stimulation with either 10 or 100 ng/ml LPS (Fig. 3D). At 100 ng/ml LPS, IL-1α secretion was significantly increased for clone A2 and was barely above basal levels for clone C2. Similar results were obtained with clones B1 and D1, both of which failed to secrete IL-1α in response to 100 ng/ml LPS (data not shown). Nitrite secretion (Fig. 3C) was reduced by approximately 60–70% for clone A2, and by 80–90% for clone C2 with respect to RAW 264.7 cells. Thus, DN PKC-α overexpression had a major inhibitory effect on LPS-induced IL-1α and NO production.

Overexpression of DN PKC-α Enhances LPS-stimulated MMP-9 Secretion—In addition to inflammatory cytokines and nitrite, LPS stimulates macrophages to secrete various hydrolases, including the matrix metalloproteinase MMP-9 (43). Based on data obtained with PKC inhibitors, it has been proposed that PKC exerts both positive and negative regulation on LPS-induced MMP-9 secretion in macrophages (39). To determine the role of PKC-α in this process, we measured the secretion of MMP-9 in the supernatants of control cells and of clones A2 and C2 after stimulation with either 10 or 100 ng/ml LPS (Fig. 3D). At 100 ng/ml LPS, IL-1α secretion was significantly increased for clone A2 and was barely above basal levels for clone C2. Similar results were obtained with clones B1 and D1, both of which failed to secrete IL-1α in response to 100 ng/ml LPS (data not shown). Nitrite secretion (Fig. 3C) was reduced by approximately 60–70% for clone A2, and by 80–90% for clone C2 with respect to RAW 264.7 cells. Thus, DN PKC-α overexpression had a major inhibitory effect on LPS-induced IL-1α and NO production.

Overexpression of DN PKC-α Enhances LPS-stimulated MMP-9 Secretion—In addition to inflammatory cytokines and nitrite, LPS stimulates macrophages to secrete various hydrolases, including the matrix metalloproteinase MMP-9 (43). Based on data obtained with PKC inhibitors, it has been proposed that PKC exerts both positive and negative regulation on LPS-induced MMP-9 secretion in macrophages (39). To determine the role of PKC-α in this process, we measured the secretion of MMP-9 in the supernatants of control cells and of clones A2 and C2 after stimulation with either 10 or 100 ng/ml LPS (Fig. 3D). At 100 ng/ml LPS, IL-1α secretion was significantly increased for clone A2 and was barely above basal levels for clone C2. Similar results were obtained with clones B1 and D1, both of which failed to secrete IL-1α in response to 100 ng/ml LPS (data not shown). Nitrite secretion (Fig. 3C) was reduced by approximately 60–70% for clone A2, and by 80–90% for clone C2 with respect to RAW 264.7 cells. Thus, DN PKC-α overexpression had a major inhibitory effect on LPS-induced IL-1α and NO production.
translocation to the nucleus where it binds to specific DNA sequences (14, 44). This process is initiated with IκB phosphorylation by the IκB kinase, IKK-α, on specific serine residues (45, 46), followed by its ubiquitination and degradation. To investigate whether DN PKC-α overexpression affected this pathway, we measured the kinetics of LPS-induced IκBα phosphorylation and degradation by immunoblotting analysis. In both control cells (Fig. 5A, lanes 1–5) and clone C2 (lanes 6–10), IκBα phosphorylation was maximal within 10–20 min following the addition of LPS. Decline in phosphorylated IκBα levels was observed between 20 and 30 min post-stimulation. Kinetics of IκBα degradation were also similar in control cells (Fig. 5B, lanes 1–5) and in clone C2 (lanes 6–10), with a sharp decline occurring between 10 and 20 min after LPS stimulation. Consequently, the kinetics of NF-κB nuclear translocation were similar in LPS-stimulated control cells and in clone C2 as determined by electrophoretic mobility shift assay (Fig. 6). Similar to clone C2, both clones B1 and D1 showed normal kinetics of LPS-induced NF-κB nuclear translocation (data not shown). Thus, DN PKC-α overexpression did not interfere with LPS-induced IκBα phosphorylation and degradation and with NFκB nuclear translocation in RAW 264.7 cells.

DISCUSSION

A role for PKC in the regulation of LPS-inducible events in macrophages has been suggested from the observations that exposure of macrophages to LPS activates PKC (9–16) and that pretreatment of macrophages with either PKC inhibitors or...
phorbol esters inhibits LPS-induced TNF-\(\alpha\), IL-1, and MMP-9 secretion, NO production, and tumoricidal activity (9, 13, 17, 18, 39). However, our knowledge on the contribution of particular PKC isoenzymes is limited and relies mainly on indirect evidence. The present study was aimed at investigating the role of PKC-\(\alpha\) in the regulation of LPS-induced macrophage functions. To this end, we have stably overexpressed a dominant-negative mutant of this isoenzyme in the murine macrophage line RAW 264.7. Our main finding is that overexpression of DN PKC-\(\alpha\) had selective effects on LPS-initiated signal transduction, suggesting that PKC-\(\alpha\) activity is required for the modulation of specific macrophage function by LPS. In particular, IL-1\(\alpha\) and NO production were significantly inhibited in DN PKC-\(\alpha\)-overexpressing cells.

Previous studies on the iNOS gene revealed that at least two PKC isoenzymes regulate its expression. Based on the differential down-regulation of PKC isoenzymes by phorbol esters, it has been suggested that PKC-\(\beta\)II may participate in LPS-induced iNOS gene expression and nitrite production (10). More recently, transient transfection studies in RAW 264.7 cells provided evidence that PKC-\(\epsilon\) regulates a pathway that promotes iNOS gene expression in response to phorbol esters (24). Interestingly, this PKC-\(\epsilon\)-dependent pathway is apparently not involved in the LPS response. Our finding that DN PKC-\(\alpha\) overexpression inhibited LPS-induced nitrite secretion and reduced iNOS mRNA accumulation indicated that PKC-\(\alpha\) also regulates NO production. Collectively, these observations raise the possibility that iNOS expression is regulated by multiple PKC-dependent pathways, which may be activated by distinct stimuli. Considering the multiple levels of regulation for iNOS expression (53, 54), it is conceivable that particular PKC isoenzymes act at distinct steps along the intracellular cascades leading to NO production.

The regulation of IL-1\(\alpha\) and TNF-\(\alpha\) production in macrophages by particular PKC isoenzymes is not well known. Kovacs et al. (17) previously reported that preincubation of murine peritoneal macrophages with the PKC inhibitor H7 reduced in a dose-dependent manner the expression of IL-1\(\alpha\) mRNA after stimulation with LPS. The potent inhibition of LPS-induced IL-1\(\alpha\) mRNA accumulation in cells overexpressing DN PKC-\(\alpha\) suggests that PKC-\(\alpha\) is one of the PKC isoenzymes that regulate IL-1\(\alpha\)-gene expression. The effect of DN PKC-\(\alpha\) overexpression on LPS-induced TNF-\(\alpha\) production was less important than TNF-\(\alpha\)-protein secretion and TNF-\(\alpha\)-mRNA accumulation were reduced by approximately 50% in clone C2, which expresses the highest levels of DN PKC-\(\alpha\). Thus, based on the previous demonstration that H7 potently inhibited LPS-induced TNF-\(\alpha\)-gene expression in murine macrophages (17), our data suggest that PKC isoenzyme(s) other than PKC-\(\alpha\) regulate LPS-induced TNF-\(\alpha\)-expression.

Macrophages secrete various matrix metalloproteinases whose function is the remodelling of extracellular matrices (55). Expression of MMP-9 (43) in RAW 264.7 cells is inducible by LPS and is subjected to both positive and negative regulation by PKC (39). It was thus of interest to determine whether overexpression of DN PKC-\(\alpha\) would affect MMP-9 production. In contrast to IL-1\(\alpha\), TNF-\(\alpha\), and nitrite secretion, we found that LPS-induced MMP-9 secretion was significantly enhanced in DN PKC-\(\alpha\) overexpressing cells. This observation suggests that PKC-\(\alpha\) is one of the isoenzyme that negatively regulates LPS-stimulated MMP-9 expression. Negative regulation of gene expression by particular PKC isoenzymes has been recently described in the mast cell line RBL-2H3, where overexpression of either PKC-\(\alpha\) or PKC-\(\epsilon\) specifically and effectively inhibited receptor-dependent cytosolic phospholipase A2 activity and arachidonic acid metabolite release (56). Importantly, up-regulation of MMP-9 production demonstrates that DN PKC-\(\alpha\)-overexpression did not inhibit all LPS responses in RAW 264.7 cells.

NF-\(\kappa\)B, an ubiquitous transcription factor, is one of the major intracellular mediators of LPS-induced responses (14, 44). In resting cells, dimeric NF-\(\kappa\)B are complexed to a member of the I\(\kappa\)B family of inhibitory proteins which masks the NF-\(\kappa\)B nuclear localization signal. Upon cell stimulation, I\(\kappa\)B is phosphorylated on specific serine residues by IKK-\(\alpha\) (45, 46), ubiquitinated, and proteolytically degraded, allowing NF-\(\kappa\)B dimers to translocate to the nucleus and bind to consensus DNA sequences (44). A role for PKC in the regulation of NF-\(\kappa\)B activation pathway has been evidenced by the demonstration that PKC-\(\zeta\) associates with an I\(\kappa\)B kinase activity and that overexpression of a dominant-negative mutant of PKC-\(\zeta\) blocked NF-\(\kappa\)B activation (57–59). Since LPS-induced I\(\kappa\)B phosphorylation and degradation and NF-\(\kappa\)B activation take place normally in DN PKC-\(\alpha\)-overexpressing clones, it is likely that PKC-\(\alpha\) is not involved in the activation of this pathway. Considering that NF-\(\kappa\)B plays an important role in the transcriptional activation of TNF-\(\alpha\)-gene expression (14), this suggestion would be consistent with the minor effect of DN PKC-\(\alpha\)-overexpression on LPS-induced NF-\(\kappa\)B activation.
expression on LPS-induced TNF-α expression. Regarding the regulation of iNOS expression, there is evidence that activation of NF-κB alone is not sufficient for its induction. Indeed, while LPS can activate NF-κB in macrophages derived from either LPS-responsive or LPS-hyporesponsive mice, induction of iNOS or TNF-α takes place only in macrophages from LPS-responsive mice (60). Recently, Xie (61) identified a novel LPS-response element (LRERα) within the iNOS promoter which may work in concert with NF-κB in regulating transcriptional activation. It will thus be of interest to determine whether a LRERα binding activity is induced in our DN PKC-α overexpressing RAW 264.7 cells. In contrast to the IL-1β promoter region, very little is known on the regulatory elements present upstream the IL-1α gene. A recent analysis of the human IL-1α promoter region failed to demonstrate the presence of an NF-κB-binding site but revealed the presence of a LPS-inducible AP-1-binding site (62), indicating that NF-κB does not participate in the transcriptional activation of IL-1α. This finding is consistent with the previous report that macrophages from mice lacking the p50 subunit of NF-κB are activators of Raf-1

We thank Mireille Varin for technical assistance. We are grateful to S. Rees for the kind permission to use the pICN-4 expression vector, and P. Duplay, D. Malo, and H. Charest for helpful comments and discussions.

Acknowledgments—We thank Mireille Varin for technical assistance. We are grateful to S. Rees for the kind permission to use the pICN-4 expression vector, and P. Duplay, D. Malo, and H. Charest for helpful comments and discussions.

REFERENCES

1. Wright, S. D., Ramos, R. A., Tobias, P. S., Ulevitch, R. J., and Mathison, J. C. (1990) Science 249, 1431–1433
2. Ulevitch, R. J., and Tobias, P. S. (1995) Annu. Rev. Immunol. 13, 437–457
3. Weinstein, S. L., Gold, M. R., and DeFranco, A. L. (1991) Proc. Natl. Acad. Sci. U. S. A. 88, 4148–4152
4. English, B. K., Ihle, J. N., Myracle, A., and Yi, T. (1993) J. Immunol. 151, 272, 2774–2778
5. Meng, F., and Lowell, C. A. (1997) J. Immunol. 158, 108–110
6. Kolch, W., Holzhut, N., Davidova, J., Davidov, W. F., Rupp, A., Rose, J. S., and Mushinski, J. F. (1991) J. Immunol. 147, 3981–3987
7. Diaz-Guerra, M. J. M., Bodelon, O. G., Velasco, M., Whelan, R., Parker, P. J., and Bocca, L. (1990) J. Biol. Chem. 265, 32073–32079
8. Nishimura, T., Shapira, L., Takashiba, S., Champagne, C., Amar, S., and Van Dyke, T. (1994) J. Immunol. 153, 1818–1824
9. Fujihara, M., Connolly, N., Ito, N., and Suzuki, T. (1994) J. Immunol. 153, 2726–2728
10. Wang, C. S., Liu, H. C., Tsueman, E. I., and Baltimore, D. (1995) Cell 80, 321–330
11. Reimann, T., Buscher, D., Hipskind, R. A., Krautwald, S., Lohmann-Matthes, M.-L., and Bacescu, M. (1994) J. Immunol. 153, 5740–5749
12. Kolch, W., Heidecker, G., Koch, G., Hummel, R., Vahidi, H., Miscek, H., Finkenzeller, G., Marzi, D., and Rapp, U. R. (1993) Nature 364, 249–252
13. Cai, H., Smola, U., Wixler, V., Eisenmann-Tappe, I., Diaz-Meco, M. T., Moscat, J., Rapp, U., and Cooper, G. M. (1997) Mol. Cell. Biol. 17, 732–741

Downloaded from http://www.jbc.org/ by guest on July 19, 2018
Protein Kinase C-α Modulates Lipopolysaccharide-induced Functions in a Murine Macrophage Cell Line

Anik St-Denis, Frédéric Chano, Pierre Tremblay, Yves St-Pierre and Albert Descoteaux

J. Biol. Chem. 1998, 273:32787-32792.
doi: 10.1074/jbc.273.49.32787

Access the most updated version of this article at http://www.jbc.org/content/273/49/32787

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 66 references, 32 of which can be accessed free at http://www.jbc.org/content/273/49/32787.full.html#ref-list-1