A Guanine Nucleotide-binding Protein Participates in IgE Receptor-mediated Activation of Endogenous and Reconstituted Phospholipase A2 in a Permeabilized Cell System*

Vikram Narasimhan‡, David Holowka§, and Barbara Baird¶

From the ‡Section of Biochemistry, Molecular and Cell Biology, §Department of Chemistry, Cornell University, Ithaca, New York

Activation of phospholipase A2 (PLA2) by the aggregation of receptors for immunoglobulin E (IgE) can be studied in streptolysin O-permeabilized rat basophilic leukemia cells. Under these conditions, 40 μM guanosine 5′-O-(3-thio)triphosphate (GTPγS) stimulates PLA2 activity 5–6-fold when free Ca²⁺ concentrations are buffered at 10⁻⁷–10⁻⁵ M. Antigen-mediated cross-linking of receptors for IgE synergizes with low concentrations of GTPγS (0.1 μM) to cause similar stimulation. When the endogenous PLA2 activity is inactivated by chemical modification, we find that exogenously supplied PLA2 from porcine pancreas and Naja naja venom is also activated by the aggregation of cell-surface IgE receptors in these permeabilized cells. As with endogenous PLA2, GTPγS synergizes with IgE receptor-aggregation to activate exogenous PLA2 5–10-fold at 10⁻⁷–10⁻⁵ M free Ca²⁺. These data indicate that receptor-mediated activation of a guanine nucleotide-binding protein can shift the Ca²⁺ dependence of PLA2 activity resulting in greatly enhanced activity at physiological concentrations of intracellular free Ca²⁺. The partial reconstitution of various PLA2 forms into such a broken-cell system offers a new approach for studying the mechanisms of G-protein-mediated activation of PLA2.

Emerging paradigms to explain stimulus-secretion coupling in a variety of cells have included receptor-mediated activation of cellular phospholipases. In addition to a possible role for the well-documented activation of cellular phospholipase C (PLC) in the stimulation of exocytosis (1, 2), there is increasing evidence implicating the activation of cellular phospholipase A2 (PLA2). In particular, an important role has been suggested for the production of arachidonic acid and its metabolites in stimulus-secretion coupling in rat mast cells (3), human basophils (4), and rat basophilic leukemia cells (5). The activation of PLA2 within cells primarily results in the increased hydrolysis of the sn-2 acyl linkage of phosphatidylcholine (PC) and, to a lesser extent, phosphatidylethanolamine (6). The fatty acid at the 2-position of PC is largely arachidonic acid, and the activation of cellular PLA2 represents a major pathway for mobilization of cellular arachidonic acid. The arachidonic acid thus mobilized serves as the rate-limiting component in the synthesis of cyclooxygenase and lipoxygenase products in cells (7), and it has been shown to be capable of releasing calcium from intracellular stores (8) as well as activating Ca²⁺-dependent protein kinases (9). The activation of PLA2 occurs within minutes of receptor activation (10), but the mechanism by which receptors stimulate cellular PLA2 activities is not well understood.

A number of recent reports have suggested that the receptor-mediated activation of PLA2 in several cellular systems involves the activation of guanine nucleotide-binding proteins (G-proteins). These conclusions are based primarily on the findings that non-hydrolyzable GTP analogs, such as GTPγS, can stimulate PLA2 activities in permeabilized cell preparations (11, 12) and that receptor-stimulated arachidonic acid production in a variety of cell systems is susceptible to certain bacterial toxins known to modify subsets of cellular G-proteins (11, 42). Studies by Jelsema and Axelrod (13, 14) have indicated that the light-dependent activation of PLA2 in isolated rod outer segments can be mediated by the free βγ subunits of the visual G-protein transducin.

A convenient experimental system to study the receptor-mediated activation of PLA2 in secretory cells is the RBL-2H3 subline (15). This cell line appears to be of mucosal mast cell lineage (16) and expresses FccRI, the high-affinity cell surface receptor for the Fc portion of immunoglobulin E (15, 17, 18). Aggregation of these receptors by any one of a variety of means results in cellular degranulation and the accompanying secretion of histamine and other mediators of the immediate hypersensitivity response (15, 19). Early biochemical events following the aggregation of IgE receptors on RBL cells include (i) increased hydrolysis of polyphosphoinositides (20, 21); (ii) a rise in the cytoplasmic free ionized calcium levels (22); (iii) an increased influx of calcium across the plasma membrane (23, 24); and (iv) increased cellular PLA2 activity (10, 23).

In this report we describe the IgE receptor-mediated, guanine nucleotide-dependent activation of both cellular and exogenously introduced PLA2 in permeabilized RBL-2H3...
cells. The results reported here indicate that at least some forms of both intracellular and secreted PLAr enzymes can be activated by a process that involves cellular G-proteins. This experimental system should allow further investigation of the mechanism for G-protein-mediated activation of PLAr.

**EXPERIMENTAL PROCEDURES**

**Assay for PLAr in Permeabilized Cells**—RBL cells of subline 2H3 were maintained and harvested as described (14). Cells were sonicated overnight with 5 μg/106 cells of monoclonal anti-2,4-dinitrophenol (DNP)-specific IgE (H1;26.82.18) (25) and then washed and resuspended in GAME buffer (135 mM potassium glutamate, 20 mM HEPES, 5 mM NaCl, 5 mM Na2ATP, 7 mM MgCl2, 1 mM EGTA, pH 7.4) that had [Ca2+]i adjusted with CaCl2 as monitored by a calcium-sensitive electrode. Cells (105/ml) were permeabilized for 5 min at 37°C with 0.15 IU/ml streptolysin O (Burroughs-Wellcome), and permeabilization was monitored by ethidium bromide fluorescence (26, 27).

For measurements of PLAr activity, exogenous substrate was prepared by driving a mixture of 1-stearoyl-2-[3H]arachidonoyl-L-3-phosphatidylcholine ([3H]PC, 1 mg/mmole), 

**PLA2 activity with endogenous substrate was measured after labeling of cellular lipids with [3H]arachidonic acid ([3H]AA). [3H]AA (0.1 μCi/ml) with 0.1 mg/ml carrier PC) was added to 1 ml of permeabilized cells along with appropriate nucleotide analogs and/or antigen (DNPz,-BSA, Ref. 28). Following incubation at 37°C for 10 min the reactions were terminated by addition of 3 ml of isopropanol, n-heptane, 1 M acetic acid (40:10:1) and vortexed for 30 s. 1 ml of n-heptane was then added to each reaction and the resultant phases clarified by centrifugation (2000 × g, 5 min). 1.5 ml of the supernatant from this centrifugation was counted in 10 ml of Liueiscint (National Diagnostics) to determine the release of [3H] label from phospholipid substrate.

PLAr activity with endogenous substrate was measured after labeling of cellular lipids with [3H]arachidonic acid ([3H]AA). [3H]AA (0.1 μCi/ml) Du Pont-New England Nuclear) was added to adherent RBL cells, and the cells were cultured at 37°C for an additional 16-20 h. The cells were then harvested, permeabilized, and assayed as described above.

**Inactivation of Cellular PLAr by p-Bromaoctophenone (PBA)**—Cells were harvested as described above and resuspended in a modified Tyrode’s buffer (135 mM NaCl, 20 mM HEPES, 5 mM KCl, 2 mM MgCl2, 1.8 mM CaCl2, 5.6 mM glucose) containing a saturated solution of PBA crystals (Fisher, 240 mesh) and centrifuged (2000 × g, 5 min). 1 ml of the supernatant from this centrifugation was counted in 10 ml of Liueiscint (National Diagnostics) to determine the release of [H] label from phospholipid substrate.

**Preparation of Exogenous PLAr**—Porcine pancreas and Naja naja PLAr stock solutions (Sigma) were extensively dialyzed against GAME buffer (pCa 8) at 4°C, diluted 1:10, and stored at 4°C. For some experiments the PLAr was chemically inactivated by exposure to PBA as described elsewhere (29, 30). Briefly, 10 μM stock PLAr in GAME buffer was incubated with 50 μM PBA for 2 h at 37°C. The reaction was extensively dialyzed against GAME buffer (pCa 8) at 4°C, diluted 1:10, and stored at 4°C.

**Measurements of PLC and PLD Activities in Permeabilized Cells**—Measurements of PLC and phospholipase D (PLD) activities toward exogenous substrate were performed using substrate prepared as described above except that 1-stearoyl-2-arachidonoyl-3-[3H]choline phosphatidylcholine (1.5-2.0 μCi/mmole) was added as the radiolabeled substrate. The release of [3H] label as phosphocholine or choline was determined as described elsewhere (31). Inositol-specific PLC activity was assayed as described above.

**RESULTS**

**Guanine Nucleotide-stimulated PLAr Activity in Permeabilized RBL Cells**—Permeabilization of RBL cells is effected by exposure to the cholesterol-binding bacterial toxin, streptolysin O (26-28), which yields relatively large pores >120 Å in diameter (32). This permeabilized cell system has been previously reported to retain the activation of cellular PLC in response to the aggregation of IgE receptors (27). In the presence of EGTA-containing buffers these pores permit strong buffering of the free cytoplasmic Ca2+ concentration ([Ca2+]i; Ref. 28). We found that these permeabilized cells also retain PLAr activity. Exogenous sn-2-[3H]arachidonoyl-phosphatidylcholine ([3H]-AA-PC) was initially used as a substrate for the cellular enzyme(s) because of its chemical homogeneity and because potential interference from endogenous phosphatidylinositol-specific PLAr activities would be minimized. The exogenous substrate consists of small unilamellar vesicles consisting of radiolabeled PC with carrier styrbayan PC.

**FIG. 1A (open circles) shows endogenous PLAr activity as represented by release of [3H]AA from the exogenous substrate in the presence of the permeabilized RBL cells. This activity is highly Ca2+-dependent with little observed at [Ca2+]i between 0.01 and 1 μM (pCa = 8-6). The addition of GTPyS to permeabilized RBL cells results in a marked stimulation of the endogenous PLAr activity at low [Ca2+]. Maximal stimulation obtained with 40 μM GTPyS is 5-6-fold when [Ca2+]i is maintained between 0.1 and 10 μM (Fig. 1A, closed circles). At higher [Ca2+]i (100-1000 μM), GTPyS has a smaller effect on PLAr activity with only 1.4-2-fold stimulation observed.

Data from other experiments (not shown) provided further information about the measured activities. The observed
PLA₂ activities appear to be intracellular because no detectable basal PLA₂ activity is observed with biosynthetically labeled intact cells in the presence of millimolar [Ca²⁺], whereas permeabilized RBL cells display a significant basal PLA₂ activity under similar conditions (Table I). Furthermore, we do not observe any detectable antigen-stimulated PLA₂ activity in intact cells as measured by the hydrolysis of exogenous substrate (data not shown). The concentration of GTP-S required for half-maximal stimulation of PLA₂ activity in permeabilized cells is ~0.5 μM. Other nucleotide analogs including 5'-adenylyl imidodiphosphate and adenosine 5'-O-(2-thio)di phosphate do not affect the cellular PLA₂ activity. Up to 65% of the ⁳H label released from [⁴H]AA-PC in the presence or absence of GTP-S migrates as arachidonic acid in thin-layer chromatography analysis (6), and, in the presence of the cyclooxygenase inhibitor indomethacin (1 mM), this amount is increased to 85%. The observed release of [⁴H] does not appear to arise from cellular PLC or PLD activities because the use of sm-3 [⁴H]choline-PC as a substrate does not result in any significant release of radioactive label as choline or phosphocholine. The fractional release of ³H label from exogenous [⁴H]AA-PC is small (<1% of the total; see Fig. 1) because of large excess of substrate was employed to ensure adequate accessibility to the cellular PLA₂. However, the rate of release was found to be linear with time at 37 °C for incubation periods between 5 and 20 min, and similar incubations at 25 °C resulted in no significant release (data not shown).

Non-hydrolyzable GTP Analog and the IgE Receptor Synergistically Activate Cellular PLA₂—Aggregation of IgE receptors on RBL cells can be effectively achieved by sensitization of the cell-surface receptors with a DNP-specific monoclonal IgE followed by exposure of the cells to DNP-conjugated bovine serum albumin (DNP₂₅ BSA; Ref. 28). Addition of this antigen (optimally 0.1 μg/ml DNP₂₅ BSA) to streptolysin O-permeabilized RBL cell preparations stimulates cellular PLA₂ activity 2.5-fold at [Ca²⁺] of 0.1 to 1 μM (Fig. 1B). At the highest levels of [Ca²⁺] employed (i.e. 1 mM), no effect of antigen addition on PLA₂ activity is observed.

In order to assess whether the effect of antigen on PLA₂ activity involves the activation of a G-protein, we tested the PLA₂ activity in the presence of low levels of GTP-S. Low concentrations of GTP-S (0.1 μM) alone have little stimulatory effect on PLA₂ activity at [Ca²⁺] of 0.1 to 1 μM, and no effect of GTP-S at this concentration is seen when [Ca²⁺] = 1 mM (Fig. 1B). Addition of antigen together with 0.1 μM GTP-S results in the marked 5-6-fold stimulation of PLA₂ activity at [Ca²⁺] of 0.1–1 μM (Fig. 1B), while no effect of antigen and GTP-S is observed at the highest [Ca²⁺].

It is notable that the effect of antigen and GTP-S on PLA₂ activity is significantly more than the sum of the effects of either agent added alone (Fig. 1B). All the stimulatory effects of antigen added alone or with GTP-S (0.1 μM) described above could be inhibited (>80%) by the addition of 100 μM GDP·S (data not shown). These data suggest that a cellular G-protein mediates at least a part of the IgE receptor-mediated stimulation of cellular PLA₂ activity that is induced by the aggregation of IgE receptor complexes. Furthermore, the antigen-stimulated stimulation of cellular PLA₂ in permeabilized cells appears to be optimal in the range 0.1–1 μM [Ca²⁺], which is similar to the activation of the PLA₂ observed at higher concentrations of GTP-S in the absence of antigen (Fig. 1A).

Similar experiments were performed with permeabilized cells that had been biosynthetically labeled with [⁴H]AA. The resulting incorporation of this label into a variety of endogenous phospholipids gives rise to a more heterogeneous substrate than the exogenous [⁴H]AA-PC employed in the experiments of Fig. 1 (33). However, a larger percentage of labeled phospholipids could be hydrolyzed under the stimulating conditions, probably because they were generally more accessible to the activated PLA₂. As shown in Table I, release of [⁴H] AA from endogenous biosynthetically labeled phospholipids is highly Ca²⁺-dependent. Separate addition of 0.1 μM GTP-S or antigen causes small increases in the [⁴H]AA release, while their simultaneous addition results in a synergistic activation of release in the range of [Ca²⁺] = 0.1–1 μM. These results are consistent with those shown in Fig. 1B. Similar to the data shown in Fig. 1A, maximal GTP-S-dependent release of [⁴H] AA in the absence of antigen is observed with 40 μM GTP-S. This stimulation requires permeabilization of the cells (data not shown).

Exogenous PLA₂ from Heterologous Sources Can Reconstitute Cellular G-protein-PLA₂ Coupling—In order to explore the mechanism for the effect of cellular G-proteins on PLA₂ activity, we introduced purified exogenous PLA₂ into permeabilized RBL cell preparations together with the exogenous [⁴H]AA-PC substrate. Measurement of exogenous PLA₂ activity against a negligible background of endogenous cellular PLA₂ activities was possible if the cells were pretreated with the histidine-modifying agent PBA prior to permeabilization. The pretreatment of intact RBL cells with PBA has been shown previously to inhibit cellular PLA₂ activity by >95% (5). We observe that pretreatment of RBL cells with PBA (2 mM, 20 min, 37 °C) completely inhibits the stimulation of cellular PLA₂ active in permeabilized cells with or without GTP-S (40 μM) at [Ca²⁺] between 0.1 and 1000 μM (Fig. 2A).

In the presence of these PBA-treated, permeabilized RBL cells and [⁴H]AA-PC, the addition of GTP-S (40 μM) stimulates the activity of exogenously supplied purified PLA₂ from porcine pancreas or the N. naja snake venom. The stimulation is maximally 5-fold at [Ca²⁺] = 1 μM when PLA₂ from either N. naja (Fig. 2A) or porcine pancreas (not shown) is added. Similar to the data shown in Fig. 1A, maximal GTP-S-dependent release of [⁴H] AA in the absence of antigen is observed with 40 μM GTP-S. This stimulation requires permeabilization of the cells (data not shown).

**Table I**

| µCa | Buffer | GTP-S³ | Antigen | Antigen + GTP-S |
|-----|--------|--------|---------|-----------------|
| 0.1 μM | 0.08 ± 0.03 | 0.08 ± 0.03 | 0.08 ± 0.03 | 0.11 ± 0.03 |
| 0.5 μM | 1.00 ± 0.03 | 1.00 ± 0.04 | 1.00 ± 0.04 | 1.03 ± 0.04 |
| 1.00 ± 0.04 | 1.00 ± 0.04 | 1.00 ± 0.04 | 1.00 ± 0.04 | 1.00 ± 0.04 |
| 5.00 ± 0.04 | 5.00 ± 0.04 | 5.00 ± 0.04 | 5.00 ± 0.04 | 5.00 ± 0.04 |

*Numbers represent percentage of total incorporated ³H label released in 10 min. The total incorporated ³H label was 62,000 ± 5,000 cpm/sample. The data represent the results from one experiment with each sample performed in triplicate (± S.D.).

The treatment of permeabilized cells with antigen and GTP-S was performed as described under "Experimental Procedures." Antigen (DNP₂₅ BSA) was used at a final concentration of 0.1 μg/ml.
DNP,,-BSA) in permeabilized RBL cells prepared from
of exogenous PLAz from both sources >10-fold (Fig. 1).
addition of 0.1 nM PLAz (data not shown). However, the simultaneous we have no way of determining the specific activity of the
PLAz derived from either porcine pancreas (Fig. 2B) or N. number of factors contributing to this difference, but since
this activity is stimulated by the addition of antigen. This totered using both biosynthetically labeled endogenous phos-
when [Ca²⁺] is maintained between 0.1 and 100
permeabilization of RBL cells allows manipulation of
DNP₂⁻BSA was added to the permeabilized cells before addition of
GTPyS (40 µM final concentration) in appropriate GAME buffer
activity in the absence (open circles) or presence of GTPyS (40 µM,
closed circles). A relative PLA₂ activity of 100 corresponds to the
release of 770-890 dpm/sample in three experiments. B, exogenous
porcine pancreatic PLA₂ (100 nM PLA₂) was added to the permeabil-
cells. Antibodies (0.1 µg/ml) and GTPyS (0.1 µM) were added prior
to incubation with substrate as indicated: no addition (open circles),
GTPyS (open triangles) or buffer only (closed triangles) and incubation with
substitute.
percentages of label hydrolyzed may be explained by differences in the amount of substrate that is accessible to the PL\(\alpha\) and/or G-protein components. It is possible, for example, that only exogenous \([\text{H}]\text{AA-PC}\) that becomes incorporated into the cellular membranes can serve as a substrate for the activated PL\(\alpha\). Despite these differences the results obtained with both methods lead to the same conclusion, that activation of PL\(\alpha\) enzymes by antigen-mediated cross-linking of Ig\(\varepsilon\) receptors is enhanced synergistically by GTP\(\gamma\)S, implicating the involvement of a G-protein in the antigen-stimulated pathway. It is notable that this activation is seen to occur maximally at [Ca\(^{2+}\)] in the expected range for a physiologically relevant process (0.1–1 \(\mu\)M) can be inhibited by GDP\(\beta\)S. We found that added GTP does not cause a similar synergistic response with antigen, possibly because significant amounts of GTP and/or GDP remain associated with the unwashed permeabilized cells used in our experiments.

Although our results strongly implicate a role for G-proteins in the receptor-mediated activation of cellular PL\(\alpha\), the nature of the endogenous G-protein in RBL cells responsible for the activation of endogenous PL\(\alpha\) remains to be elucidated. We have found that pretreatment of cells with either pertussis toxin (100 ng/ml, 3 h) or choleragen toxin (1 \(\mu\)g/ml, 3 h) prior to permeabilization does not affect the ability of antigen (or GTP\(\gamma\)S) to activate either the endogenous or exogenous PL\(\alpha\) activities in these permeabilized cells, suggesting that neither \(G_{\alpha}\), \(G_{\beta}\), nor \(G_{\gamma}\) is involved. Choleragen toxin pretreatment of RBL cells also does not alter receptor activated, inositol-specific PLC activity that is assayed after cell permeabilization (28). In experiments with intact RBL cells, Ig\(\varepsilon\) receptor-mediated activation of PL\(\alpha\) and PLC has been found to be insensitive to pretreatment with pertussis toxin (Ref. 16 and Footnote 2). We have recently shown that the pretreatment of RBL cells with choleragen toxin potentiates the antigen-stimulated Ca\(^{2+}\) influx into intact RBL cells (28), indicating that Ig\(\varepsilon\) receptors may stimulate Ca\(^{2+}\) influx and PL\(\alpha\) via distinct G-proteins.

Several different pathways have been proposed to account for the receptor-mediated activation of PL\(\alpha\) in various cell types, including those involving elevated cytosolic Ca\(^{2+}\) (34), protein kinase C (35), calcium-binding proteins (36, 37), and protein synthesis (38). The synergistic effect of antigen and GTP\(\gamma\)S on endogenous PL\(\alpha\) activity in the permeabilized cell system occurs under conditions where the Ca\(^{2+}\) levels are strongly buffered at 0.1 \(\mu\)M and thus does not appear to require the elevation of [Ca\(^{2+}\)]. Soluble mediators are unlikely to play a critical role in PL\(\alpha\) activation in the permeabilized cell system since supernatants from GTP\(\gamma\)S-stimulated cells do not possess the ability to activate exogenous PL\(\alpha\). We have found that pretreatment of cells with cycloheximide and cme to inhibit protein synthesis does not alter the antigen-stimulated PL\(\alpha\) activity. Exposure of permeabilized RBL cells to the protein kinase C-activating phorbol ester, tetradecanoyl phorbol acetate (100 nm), does not significantly elevate cellular PL\(\alpha\) activity under conditions where GTP\(\gamma\)S and antigen strongly stimulate cellular PL\(\alpha\) (data not shown). This indicates that the activation of protein kinase C is not sufficient for the activation of PL\(\alpha\) in this system. Thus, our data are most consistent with either a direct interaction of relevant G proteins with endogenous PL\(\alpha\) or an indirect interaction that is mediated by other as yet unidentified cellular component(s).

Our ability to reconstitute GTP\(\gamma\)S- and antigen-stimulated PL\(\alpha\) activities in the permeabilized PBA-treated cells using secreted forms of PL\(\alpha\) is further evidence that the stimulated release of \([\text{H}]\text{AA}\) observed in untreated permeabilized cells is catalyzed by endogenous PL\(\alpha\). As with the endogenous PL\(\alpha\) activity, the exogenous PL\(\alpha\) activity that is dependent on stimulation by GTP\(\gamma\)S and antigen at low [Ca\(^{2+}\)] can be detected with either exogenous (Fig. 2) or endogenous (Table II) substrates. Our results are consistent with previous observations that anti-porcine pancreatic PL\(\alpha\) antibodies can inhibit cellular forms of PL\(\alpha\) that appear to co-localize with the ras protein in ras-transformed cells (39).

Reconstitution experiments with well-characterized secreted forms of PL\(\alpha\) should allow further investigation of the mechanism by which G-proteins mediate the activation of this important class of cellular lipases. For example, a consensus tyrosine-X-glycine-X-glycine sequence involved in Ca\(^{2+}\) binding to both mammalian pancreatic and \(N.\) naja venom PL\(\alpha\) enzymes has been characterized (40, for review see Ref. 34). As a mechanism for G-protein action on PL\(\alpha\), our data are consistent with the possibility that the either the G-protein itself or an intermediary protein acts allosterically to enhance Ca\(^{2+}\) binding directly to the consensus Ca\(^{2+}\)-binding site. An alternative possibility is that the G-protein-activated species leads to the enhanced binding of PL\(\alpha\) to phospholipid substrate, thereby indirectly increasing the effective affinity of the PL\(\alpha\) enzyme for Ca\(^{2+}\). Such cooperativity between binding of Ca\(^{2+}\) and phospholipid substrate to distinct sites on the PL\(\alpha\) from mammalian pancreatic and snake venom sources has been reported (34, 41). The use of this novel experimental system to analyze the G-protein-mediated activation of site-directed mutant PL\(\alpha\) and purified intracellular PL\(\alpha\) forms should serve to provide greater insight into the role of specific structural features of PL\(\alpha\) enzymes involved in their cellular activation.

Acknowledgments—We thank Drs. R. Cerione and C. Fewtrell for helpful comments on the manuscript.

REFERENCES
1. Berridge, M. J. (1987) Annu. Rev. Biochem. 56, 159–193
2. Cockcroft, S., and Stutchfield, J. (1988) Phil. Trans. R. Soc. Lond. B Biol. Sci. 320, 247–265
3. Sullivan, I. J., and Parker, C. W. (1979) J. Immunol. 122, 431–436
4. Marone, G., Kagey-Sobotka, A., and Lichtenstein, L. M. (1979) J. Immunol. 123, 1669–1677
5. McGivney, A., Morita, Y., Crews, F. T., Hirata, F., Axelrod, J., and Siraganian, R. P. (1981) Arch. Biochem. Biophys. 212, 572–580
6. Billah, M. M., Lapentina, E., and Custrescasas, P. (1980) J. Biol. Chem. 255, 10297–10301
7. Irvine, R. F. (1982) Biochem. J. 204, 3–9
8. Beaumier, L., Faucher, N., and Naccache, P. H. (1987) FEBS Lett. 221, 289–292
9. McPhail, C. L., Clayton, C. C., and Snyderman, R. (1984) Science 224, 622–625
10. Garcia-Gutierrez, M., and Siraganian, R. P. (1986) J. Immunol. 136, 259–263
11. Burch, R. M., Luini, A., and Axelrod, J. (1986) Proc. Natl. Acad. Sci. U. S. A. 83, 7201–7205
12. Okano, Y., Yamada, K., Yano, K., and Nozawa, Y. (1987) Biochem. Biophys. Res. Commun. 145, 1967–1975
13. Jelsma, C. L. (1987) J. Biol. Chem. 262, 162–168
14. Jelsma, C. L., and Axelrod, J. (1987) Proc. Natl. Acad. Sci. U. S. A. 84, 3623–3627
15. Barsumian, E. L., Isersky, C., Petroni, M. G., and Siraganian, R. P. (1981) Eur. J. Immunol. 11, 317–323
16. Seldin, D. C., Adelman, S., Austen, K. F., Stevens, R. L., Hein, A., Caulfield, J. P., and Woolley, R. G. (1986) Proc. Natl. Acad. Sci. U. S. A. 82, 3871–3875
17. Kuleczky, A., Jr., and Metzger, H. (1974) J. Exp. Med. 140, 1676–1695
G-protein-mediated Activation of Phospholipase A2 in RBL Cells

18. Metzger, H., Alcaraz, G., Hohman, R., Kinet, J.-P., Pribluda, V., and Quarto, R. (1986) Annu. Rev. Immunol. 4, 419-470
19. Taurog, J. D., Mendoza, G. R., Hook, W. A., Siraganian, R. P., and Metzger, H. (1977) J. Immunol. 119, 1757-1761
20. Beaver, M. A., Rogers, J., Moore, J. P., Hesketh, T. R., Smith, G. A., and Metcalfe, J. C. (1984) J. Biol. Chem. 259, 7129-7136
21. Cunha-Melo, J. R., Dean, N. M., Moyer, J. D., Masayama, K., and Beaver, M. A. (1987) J. Biol. Chem. 262, 11455-11463
22. Beaver, M. A., Moore, J. P., Smith, G. A., Hesketh, T. R., and Metcalfe, J. C. (1984) J. Biol. Chem. 259, 7137-7142
23. Crews, F. T., Morita, Y., McGivney, A., Hirata, F., Siraganian, R. P., and Axelrod, J. (1981) Arch. Biochim. Biophys. 212, 561-571
24. Fewtrell, C., and Sherman, E. (1987) Biochemistry 26, 6995-7000
25. Liu, F. T., Bohn, J. W., Perry, E. L., Yamamoto, H., Molinaro, C. A., Sherman, L. A., Klinman, N. R., and Katz, D. H. (1986) J. Immunol. 124, 2728-2736
26. Howell, T. W., and Gomperts, B. D. (1987) Biochem. Biophys. Acta 927, 177-183
27. Ali, H., Cunha-Melo, J., and Beaver, M. A. (1989) Biochem. Biophys. Acta 1010, 88-99
28. Narasimhan, V., Holowka, D., Fewtrell, C., and Baird, B. (1988) J. Biol. Chem. 263, 19626-19632
29. Wolwerk, J. J., Pietersen, W. A., and de Haas, G. H. (1974) Biochemistry 13, 1446-1454
30. Roberts, M. F., Deems, R. A., Minvey, T. C., and Dennis, E. A. (1977) J. Biol. Chem. 252, 2406-2411
31. Yavin, E. (1976) J. Biol. Chem. 251, 1392-1397
32. Buckingham, L., and Duncan, J. (1983) Biochem. Biophys. Acta 729, 115-122
33. Garcia-Gil, M., and Siraganian, R. P. (1986) J. Immunol. 136, 3825-3828
34. Verheij, H. M., Slotooboom, A. J., and de Haas, G. H. (1981) Rev. Physiol. Biochem. Exp. Pharmacol. 91, 81-203
35. Gronich, J. H., Bonventre, J. V., and Nemenoff, R. A. (1988) J. Biol. Chem. 263, 16645-16651
36. Wong, P. Y.-K., and Cheung, W. Y. (1979) Biochem. Biophys. Res. Commun. 90, 473-480
37. Moskowitz, N., Andres, A., Silva, W., Shapiro, L., Schook, W., and Punzkin, S. (1985) Arch. Biochem. Biophys. 241, 413-417
38. Aderem, A., Scott, W. A., and Cohn, Z. A. (1986) J. Exp. Med. 163, 139-154
39. Bar-Sagi, D., Suhan, J. P., McCormick, F., and Feramisco, J. R. (1988) J. Cell Biol. 106, 1649-1658
40. Renetseder, R., Brunie, S., Dijkstra, B. W., Drent, J., and Sigler, P. B. (1985) J. Biol. Chem. 260, 11627-11634
41. Pietersen, W. A., Vidal, J. C., and de Haas, G. H. (1974) Biochemistry 13, 1439-1445
42. Nakamura, T., and Ut M. (1985) J. Biol. Chem. 260, 3584-3593
A guanine nucleotide-binding protein participates in IgE receptor-mediated activation of endogenous and reconstituted phospholipase A2 in a permeabilized cell system.
V Narasimhan, D Holowka and B Baird

J. Biol. Chem. 1990, 265:1459-1464.

Access the most updated version of this article at http://www.jbc.org/content/265/3/1459

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 0 references, 0 of which can be accessed free at http://www.jbc.org/content/265/3/1459.full.html#ref-list-1