considerably stronger soma depolarizing currents (3–8 nA, 3–10 nA) has been reported to give long-lasting synaptic enhancement, expressed as an increased EPSP[25,26]. These larger soma currents probably depolarized the dendritic tree more efficiently than in our current injection experiments. The conjunction paradigm used by Kelso et al.[27], which gave EPSP increase, also elicited a strong depolarization as judged from the continuous synaptically induced discharge at 75–100 Hz. Taken together, these results suggest that the conjunction effect is not generated at the soma, but more distally, possibly at, or close to, the dendritic synapses.

Dendritic depolarization coupled to synaptic activation seem to be a common element for development of conjunction-induced changes in hippocampal and cerebellar synapses, although the direction of the change differs[28].

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Phospholipase C activation via a GTP-binding protein in tumoral islet cells stimulated by carbamylcholine[1]

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Summary. Carbamylcholine and GTP act synergistically in stimulating the production of [^{3}H]inositol-1-phosphate by digitonized tumoral islet cells (RINm5F line) prelabeled with myo-[2-^{3}H(N)]inositol. The response to these two agents is similar to that evoked by GTPγS. These findings suggest that a GTP-binding regulatory protein couples the occupancy of muscarinic receptors to activation of phospholipase C in pancreatic islet cells.
Key words. Phospholipase C; GTP-binding protein; carbamylcholine.

Cholinergic neurotransmitters stimulate phospholipase C in pancreatic islet cells, leading to the hydrolysis of phosphoinositides, formation of inositol 1,4,5-trisphosphate and diacylglycerol, redistribution of intracellular Ca^{2+}, activation of protein kinase C, and eventual stimulation of insulin release (see Malaisse[2] for review). The results of the present study suggest that a GTP-binding regulatory protein couples, in tumoral islet cells, the occupancy of muscarinic receptors to the activation of phospholipase C.

Tumoral pancreatic islet cells (RINm5F line) were cultured, harvested and counted as previously described[3]. They were preincubated for 120 min at 37 °C in a bicarbonate-buffered medium[4] containing D-glucose (2.8 mM), bovine albumin (2.5 mg/ml), K_2HPO_4 (0.1 mM) and myo-[2-^{3}H(H)]myoinositol (4.7 μM). The cells were then washed thrice, resuspended in the same buffer except for the absence of tritiated inositol and presence of 1.0 mM unlabeled myoinositol ($16 \cdot 10^6$ cells/180 μl), and mixed with 0.6 ml of an imidazole buffer (20 mM; pH 7.0) containing 0.5 mg/ml digitonin. 20 s later, the cells were centrifuged for 20 s (Beckman Microfuge) and, after removal of the supernatant, resuspended in 0.5 ml of the same medium as that used for the determination of inositol phosphate metabolism in lysed 7315c tumor cells[5]. Aliquots of the digitonized cell suspension (30 μl) were mixed with an equal volume of the same medium containing, as required, carbamylcholine, GTP or GTPγS. After 10-min incubation at 37 °C, the reaction was halted by adding 1.5 ml of a mixture of $CHCl_3/CH_3OH/HCl$ (12 N) (2/1/0.01, v/v/v) and 0.44 ml of KCl (57 mM). After centrifugation (1 min, 800 × g) an aliquot (0.6 ml) of the upper aqueous phase was mixed with 2.0 ml H_2O, neutralized with 0.17 ml of Tris (0.3 M), and applied to a Dowex AG1X8 column (1.0 ml, 200–400, formate form) for separation of inositol phosphates[6]. The radioactive content of the lipids extracted from the pellet of digitonized cells amounted to 5.17 ± 0.24 fmol/10^3 cells and, over 10 min incubation, the basal production of [^{3}H]-inositol 1-phosphate averaged 15.6 ± 1.7 amol/10^3 cells (n = 15 in both cases), these results being expressed by refer-

Effect of carbamylcholine, GTP and GTPγS on [^{3}H]inositol 1-phosphate production by prelabeled digitonized RINm5F cells

Increment in inositol 1-phosphate production (amol/10^3 cells per 10 min)	
Carbamylcholine (1.0 mM)	1.56 ± 0.56 (15)
GTP (10 μM)	1.52 ± 0.68 (9)
GTP (10 μM) + carbamylcholine (1.0 mM)	8.56 ± 1.52 (9)
GTPγS (10 μM)	9.98 ± 0.73 (9)

ence to the specific activity of the preincubation medium. As shown in the table, carbamylcholine (1.0 mM) and GTP (10 μM), when tested separately, caused a modest but significant ($p < 0.05$) increase in [^{3}H]inositol 1-phosphate production. Such a production was markedly increased in the simultaneous presence of carbamylcholine and GTP. The increment in [^{3}H]inositol 1-phosphate production recorded in the presence of both agents was much higher ($p < 0.005$) than that computed by summing their individual effects, and represented 86 ± 16% (n = 9) of the paired increment evoked by a stable analog of GTP (GTPγS). The production of [^{3}H]-inositol 1-phosphate, 1,4-bisphosphate and 1,4,5-trisphosphate was also stimulated either by carbamylcholine, in intact RINm5F cells, or by GTPγS in a subcellular particulate fraction derived from these cells (data not shown).

The present results provide direct evidence to support the participation of a GTP-binding protein in the control of phospholipase C activity in pancreatic islet cells. Since we have previously reported[7] that neither of the two regulatory proteins Ns and Ni, which were both recently identified in islet cells[8,9], seem to affect phospholipase C activity in such cells, the GTP-binding protein mediating the activation of the latter enzyme by cholinergic neurotransmitters is likely to represent a novel regulatory protein. This proposal is consistent with recent studies[10,11] indicating the participation of a) guanine nucleotide-dependent regulatory protein(s), such as the *ras*-encoded p21 protein[11], in the stimulation of phospholipase C, although none of these previous studies deal with the activation of the latter enzyme by cholinergic agents.

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Somatostatin immunoneutralization overcomes the inhibitory effects of quipazine and pargyline on growth hormone secretion in domestic fowl

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Summary. The inhibitory effects of pargyline and quipazine on chicken growth hormone secretion were overcome by passive immunoneutralization of endogenous somatostatin (SRIF)-14 or SRIF-28(1–14)-like immunoreactivity. Administration of the specific antisera to control birds pretreated with 0.9% NaCl elevated the basal plasma GH concentrations. These results suggest that peptides with SRIF-14 or SRIF-28(1–14)-like immunoreactivity tonically inhibit GH secretion and are at least partially responsible for the inhibitory effects of pargyline and quipazine on GH release in immature domestic fowl.
Key words. Somatostatin; growth hormone; serotonin.

The release of pituitary growth hormone (GH) is inhibited by hypothalamic factors, somatostatins (SRIFs), that are secreted into hypophysial blood in response to neural information concerning the internal or external environment[1]. Both somatostatin-14 and SRIF-28 have been located in the avian hypothalamus[2] and both inhibit GH secretion in birds[3]. At least two other somatostatin moieties have been located in the avian hypothalamus[4] and peptides with SRIF-28(1–14) immunoreactivity, distinct from SRIF-14 and SRIF-28, are also likely to be present, since chickens immunized against SRIF-28(1–14) have elevated plasma GH concentrations[5]. These hypophysiotrophic factors may be released in response to increased serotoninergic activity, since hypothalamic serotonin turnover is inversely related to the plasma GH level[6] and the in vitro GH releasing activity of the hypothalamus is reduced following in vivo administration of serotoninergic drugs to fowl[7,8]. Drugs that enhance serotoninergic activity, including precursors (tryptophan and 5-hydroxytryptophan), receptor agonists (e.g. quipazine), re-uptake inhibitors (e.g. imipramine) or inhibitors of serotonin degradation (e.g. pargyline and clorgyline) all reduce plasma GH concentrations in fowl, while inhibitors of serotonin synthesis (e.g. parachorophenylalanine or a deficiency of dietary tryptophan), or antagonists of serotonin receptors (e.g. methysergide and cyproheptadine) block the effects of serotoninergic drugs or increase circulating GH concentrations[6–10]. Since serotonin directly affects SRIF-14 release from the rat hypothalamus[11] and as the inhibitory effects of quipazine on hypothalamus-induced GH secretion can be suppressed, in vitro, by the addition of SRIF-14 antisera to the incubation media[12], the serotoninergic inhibition of in vivo GH secretion in birds may thus be SRIF-mediated. This possibility has been investigated in the present study, by determining the effects of somatostatin immunoneutralization on GH secretion in birds pretreated with quipazine or pargyline.

Material and methods. Specific antisera, raised in rabbits against a synthetic cylic SRIF-14-glutaradehyde-human serum albumin conjugate (product No. AB 25) and against synthetic Tyr-soma-