The antagonistic interactions between adenosine A1 and dopamine D1 receptors were studied in a mouse Ltk- cell line stably cotransfected with human adenosine A1 receptor and dopamine D1 receptor cDNAs. In membrane preparations, both the adenosine A1 receptor agonist N6-cyclopentyladenosine and the GTP analogue guanyl-5′-y1 imidodiphosphate induced a decrease in the proportion of dopamine D1 receptors in a high affinity state. In the cotransfected cells, the adenosine A1 agonist induced a concentration-dependent inhibition of dopamine-induced cAMP accumulation. Blockade of adenosine A1 receptor signal transduction with the adenosine A1 receptor antagonist 1,3-dipropyl-8-cyclopentylxanthine or with pertussis toxin pretreatment increased both basal and dopamine-stimulated cAMP levels, indicating the existence of tonic adenosine A1 receptor activation. Pretreatment with pertussis toxin also counteracted the effects of low concentrations of the A1 agonist on D1 receptor-agonist binding. The results suggest that adenosine A1 receptors antagonistically modulate dopamine D1 receptors at the level of receptor binding and the generation of second messengers.

It has been shown that the binding characteristics of one type of G protein-coupled receptor can be altered by the stimulation of another type of G protein-coupled receptor in crude membrane preparations (1). Such intramembrane interactions have been postulated to represent direct interactions between the receptor molecules and/or to involve G proteins or other mobile molecules associated with the membrane (1). There is increasing evidence suggesting that antagonistic intramembrane interactions between specific subtypes of adenosine and dopamine receptors constitute an important integrative mechanism in the basal ganglia (2, 3). Adenosine A1 and A2A receptors antagonistically and specifically modulate the binding characteristics of dopamine D1 and D2 receptors, respectively (2, 3). In membrane preparations from rat striatum, the stimulation of A2A receptors decreases the affinity of D2 receptors for agonists (4). On the other hand, the stimulation of A1 receptors was shown to decrease the proportion of D1 receptors in the high affinity state, without modifying the dissociation constants of high and low affinity D1 agonist-binding sites (5).

The A1 receptor agonist had the same effect as that induced by the GTP analogue Gpp(NH)p. It was hypothesized that A1 receptor stimulation might uncouple the striatal D1 receptor from the G protein (5). There is evidence that the antagonistic A2A-D2 and A1-D1 intramembrane interactions are involved in the motor depressant effects of adenosine receptor agonists and the motor stimulant effects of dopamine receptor antagonists, such as caffeine (2–5).

The same changes in the binding characteristics of striatal D2 receptors after A2A receptor stimulation have been obtained in membrane preparations from a mouse fibroblast cell line (Ltk-) stably cotransfected with the dog A1 receptor and human D2 (long-form) receptor cDNAs (6). In these transfection studies, it was also found that activation of adenyl cyclase was not involved in the intramembrane A2A-D2 interaction (6). Altogether, these results showed that stably cotransfected cell lines constitute a valuable model to study the mechanistic aspects involved in the intramembrane receptor-receptor interactions. In the present work, this methodology has been applied to study the antagonistic interaction between A1 and D1 receptors. The first aim of the study was to demonstrate the existence of an antagonistic A1-D1 intramembrane interaction in mammalian cells stably cotransfected with A1 receptor and D1 receptor cDNAs. The second aim was to demonstrate the existence of a functional antagonistic interaction between A1 and D1 receptors in the cotransfected cells by means of cAMP accumulation experiments. Finally, the third aim of the study was to find a functional significance of the antagonistic A1-D1 intramembrane interaction.

**EXPERIMENTAL PROCEDURES**

**Transfection and Maintenance of Fibroblast Ltk- Cells—**Cells from the mouse fibroblast Ltk- cell line previously transfected with the human D1 receptor cDNA (7) were used. The expression vector pZEM-3 (8) containing the full coding sequence of the human D1 receptor in front of mouse metallothionein promoter I had been cotransfected with the plasmid prSV-neo, which confers resistance to neomycin and Geneticin (G418). Metallothionein promoter I allows transcriptional induction by including zinc sulfate in the cell culture (8). Nevertheless, a clone expressing a relatively high level of D1 receptor mRNA and protein was obtained (D1 cells) without zinc-mediated induction (7). The D1 cells were cotransfected with the human adenosine A1 receptor cDNA (A1 cells). The expression vector pcDNA3 (Invitrogen) containing the full coding sequence of the human A1 receptor (gift from M. Lohse) (9, 10) in front of enhancer-promoter sequences from the immediate-early gene of the human cytomegalovirus was cotransfected with a hygromycin resistance plasmid (pHyg; gift from G. Vassart) with the calcium phosphate precipitation method as described in detail (6). The expression of the A1 receptor was verified by Northern blot and radioligand binding techniques (see below), and a clone expressing similar levels of A1 and D1 receptors was selected. The cotransfected cells were then plated in 96-well plates containing increasing concentrations of agonists, with the adenosine A1 receptor (1,3-dipropyl-8-cyclopentylxanthine; PTX, pertussis toxin; CPA, N6-cyclopentyladenosine) and D1 receptor (6-cyclopentyladenosine) antagonists (11). The accumulation of cAMP was measured using a cAMP assay kit (Amersham). The results were expressed as percentages of control values, which were normalized to 100%.

**ACKNOWLEDGMENTS**

This work was supported by grants from the Swedish Research Council, the Marianne and Marcus Wallenberg Foundation, CIRIT (Generalitat de Catalunya), and Åke Wibergs Stiftelse and by BIOMED 2 Program BMH4-CT96-0238. 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.

§ To whom correspondence should be addressed. Tel.: 46-8-7287081; Fax: 46-8-3379411.
D1 antagonist-binding sites (A1D1 cells) was chosen for further experiments. A1D1 cells were cultured routinely at 37 °C with 5% CO2 in Dulbecco’s minimal essential medium with 4.5 mg/ml glucose and 0.11 mg/ml sodium pyruvate supplemented with 10% fetal calf serum, 2 mM glutamine, 100 units/ml penicillin, 100 units/ml streptomycin, 200 μg/ml G418, 250 μg/ml hygromycin B, and 1.0% agarose gel, and transferred to a nitrocellulose membrane. Blots were hybridized with 32P-labeled adenosine A1 receptor cDNA by nick translation. Following hybridization, the membrane was washed and exposed to Kodak XAR-5 film with an intensifying screen at −70 °C. The optical density of the bands was measured by computer-assisted densitometric analysis (IBAS image analyzer).

**Membrane Preparation**—The D1 and A1D1 cells were petri dishes with a cell scraper. Harvested cells were washed twice with ice-cold phosphate-buffered saline and centrifuged at 2000 rpm for 5 min. The pellet was sonicated in 10 mM sodium dodecyl sulfate and resuspended in the incubation buffer containing adenosine deaminase (Boehringer Mannheim; 10 units/ml). The homogenate was centrifuged at 3000 rpm for 10 min at 4 °C; the precipitated nucleic fraction was discarded, and the supernatant was incubated for 30 min at 37 °C (to activate adenosine deaminase and to remove endogenous adenosine) and centrifuged at 20,000 rpm for 40 min at 4 °C. The membrane pellet was then resuspended by sonication in the incubation buffer without adenosine deaminase (final protein concentration of −0.2 mg/ml). In the experiments with [3H]HISCH 23390 (NEF Life Science Products), the incubation buffer was 50 mM Tris-HCl (pH 7.4) containing 120 mM NaCl, 5 mM KCl, 2 mM CaCl2, and 1 mM MgCl2. In the experiments with 3H]DPCPX, [3H]NEF Life Science Products, the incubation buffer was 50 mM Tris-HCl (pH 7.4) containing 2 mM MgCl2. **Purification**—Adenosine A1 receptor mRNA was obtained with the Northern blot analysis and the A1 receptor density (log Bmax values) obtained from the saturation experiments with [3H]DPCPX in membrane preparations from the different clones (Fig. 1). The non specific binding was <5% of the total binding. The D1 cells did not show any significant [3H]DPCPX-specific binding. A clone with similar concentrations of A1 and D1 binding sites (A1D1 cells) was chosen for the subsequent experiments. The Bmax and KD values for [3H]DPCPX binding in the A1D1 cells were 4.0 ± 0.4 pmol/mg of protein and 2.0 ± 0.1 nM (means ± S.E., n = 4), respectively (Fig. 2). The determined Kd value is in close agreement with the values previously reported for membrane preparations from Chinese hamster ovary cells and Escherichia coli cells expressing human A1 receptor subunits (9, 10, 14). For comparison, the Bmax for [3H]DPCPX binding in membrane preparations from rat striatum have been reported to be ~1 pmol/mg of protein and 1 nM, respectively (15).

**Competition Experiments of the Adenosine A1 Agonist CPA Versus the Adenosine A1 Antagonist [3H]DPCPX**—Competition experiments of the adenosine A1 agonist CPA versus the adenosine A1 antagonist [3H]DPCPX in membrane preparations from A1D1 cells showed a significantly better fit for two binding sites than for one binding site (F test, p < 0.05). K11, K12, and R1 values (in medians and, in parentheses, the interquartile
range) were estimated to 4.2 (22.1) nM, 163.0 (145.2) nM, and 8.0% (5.8), respectively. The determined $K_D$ values obtained by nonlinear regression analysis were 4.9 pmol/mg of protein and 1.8 nM, respectively.

**Saturation Experiments with the Dopamine D_1 Antagonist \(^{3}H\)SCH 23390—**No significant differences were obtained between the D_1 and A_1D_1 cells regarding the $B_{max}$ and $K_D$ values for the D_1 binding sites labeled with \(^{3}H\)SCH 23390. The $B_{max}$ values for the D_1 and A_1D_1 cells were 4.2 ± 0.2 and 4.6 ± 0.3 pmol/mg of protein (means ± S.E., respectively. The $K_D$ values for the D_1 and A_1D_1 cells were 2.6 ± 0.3 and 2.4 ± 0.2 nM (means ± S.E., n = 4), respectively. The nonspecific binding was <5% of the total binding. The A_1 agonist CPA did not significantly alter \(^{3}H\)SCH 23390 binding in A_1D_1 cell membranes ($B_{max} = 4.4 ± 0.1$ pmol/mg of protein and $K_D = 2.2 ± 0.2$ nM (means ± S.E.) (Fig. 3).

**Competition Experiments of Dopamine Versus the Dopamine D_1 Antagonist \(^{3}H\)SCH 23390—**Competition experiments of dopamine versus the dopamine D_1 antagonist \(^{3}H\)SCH 23390 in membranes from both D_1 and A_1D_1 cells showed a significantly better fit for two binding sites than for one binding site ($F$ test, $p < 0.05$). Similar $K_H$ and $K_L$ values were obtained in membrane preparations from D_1 and A_1D_1 cells, and the proportion of D_1 receptors in the high affinity state ($R_H$ values) was ~10% in both cases (Fig. 4 and Table I). In the presence of Gpp(NH)p (100 μM), a significantly better fit for one binding site ($R_H = 0$) was obtained in most of the membrane preparations from either D_1 or A_1D_1 cells, with IC_{50} values very similar to the $K_L$ values obtained in the absence of Gpp(NH)p. The same effect as that induced by Gpp(NH)p was obtained in the presence of the A_1 agonist CPA (1–100 nM) in membrane preparations from A_1D_1 cells. On the other hand, CPA (0.1 and 10 μM) was ineffective in membrane preparations from D_1 cells (Fig. 4 and Table I). Pretreatment of the A_1D_1 cells with PTX counteracted the effect of a low concentration of CPA (10 nM), but it did not counteract the effect of 10 μM CPA or 100 μM Gpp(NH)p (Fig. 5 and Table I). The degree of PTX-induced \(^{32}P\)ADP-ribosylation was markedly reduced in membrane preparations from PTX-pretreated A_1D_1 cells compared with nonpretreated cells (Fig. 6).

**cAMP Accumulation Experiments—**In A_1D_1 cells, but not in D_1 cells (data not shown), CPA induced a significant concentration-dependent inhibition of cAMP accumulation induced by 30 μM forskolin and 0.1 μM dopamine (one-way ANOVA, $p < 0.001$ in both cases), with IC_{50} values (95% confidence intervals in parentheses) of 0.9 (0.2–2.8) nM and 0.8 (0.3–1.8) nM, respectively (Fig. 7). In A_1D_1 cells, dopamine induced a significant concentration-dependent increase in cAMP accumulation (Fig. 8). The effect of dopamine was significantly antagonized by CPA (30 nM) (bifactorial ANOVA, $p < 0.001$ for the factors dopamine and CPA) (Fig. 8). The EC_{50} values (95% confidence
intervals in parentheses) of the concentration-response curves of dopamine in the absence and presence of CPA, obtained by nonlinear regression analysis, were 0.2 (0.03–1.6) μM and 0.6 (0.02–14.9) μM, respectively. The maximal response values (95% confidence intervals in parentheses) in the absence and presence of CPA were 0.5 (0.4–0.6) pmol/50 μl and 0.3 (0.2–0.4) pmol/50 μl, respectively. On the other hand, the effect of dopamine was significantly potentiated by DPCPX (30 nM) (bifactorial ANOVA, p < 0.001 for the factors dopamine and DPCPX) (Fig. 8). The EC50 values (95% confidence intervals in parentheses) of the concentration-response curves of dopamine in the absence and presence of DPCPX were 0.4 (0.2–0.9) μM and 0.3 (0.09–0.8) μM, respectively. The maximal response values (95% confidence intervals in parentheses) in the absence and presence of DPCPX were 0.9 (0.8–0.9) pmol/50 μl and 1.2 (1.0–1.3) pmol/50 μl, respectively. Since they were independently analyzed, the basal levels of cAMP (dopamine concentration = 0) were not included in the ANOVA. cAMP basal levels were significantly increased by DPCPX (Student’s t test, p < 0.05), and they were not modified by CPA (Fig. 8). In PTX-pretreated A1D1 cells, the basal levels of cAMP were significantly higher than in the control experiment, without PTX pretreatment (0.41 ± 0.01 and 0.23 ± 0.01 pmol/50 μl, means ± S.E., respectively). CPA also induced a significant concentration-dependent inhibition of cAMP accumulation induced by a high concentration of dopamine (10 μM), and the cAMP accumulation induced by dopamine (10 μM) was significantly higher in PTX-pretreated cells (bifactorial ANOVA, p < 0.001 for the factors CPA and PTX) (Fig. 9). However, CPA was more effective in control cells. In PTX-pretreated cells, only a high concentration of CPA (10 μM) significantly antagonized cAMP accumulation induced by dopamine (10 μM) (post hoc one-way ANOVA, p < 0.05) (Fig. 9).

**DISCUSSION**

A mouse fibroblast Ltk− cell line stably cotransfected with human A1 and D1 receptor cDNAs was obtained, and a clone containing similar amounts of both receptors (≈4 pmol/mg of protein) was chosen (A1D1 cells). Both receptors were shown to be functional in cAMP accumulation experiments. It has been previously shown that dopamine induces a concentration-dependent increase in cAMP accumulation in Ltk− cells transfected with the human D1 receptor cDNA (D1 cells), but not in nontransfected cells (7). It was also shown that the effect of dopamine is mediated by D1 receptors since it was selectively counteracted by a D1 but not a D2 receptor antagonist (7). In the present experiments, dopamine-induced cAMP accumulation was also demonstrated in the A1D1 cells, with an EC50 value very similar to the Kd value obtained in the [3H]SCH 23390-dopamine competition experiments (≈0.3 μM). Furthermore, in A1D1 cells, the A1 agonist CPA counteracted the cAMP accumulation induced by dopamine or forskolin, with an IC50 value similar to the Kd value shown in [3H]DPCPX-CPA competition experiments (1 nM range). In addition, the A1 antagonist DPCPX was found to significantly increase the basal levels of cAMP and to potentiate dopamine-induced cAMP accumulation. Altogether, these results show the existence of a functional antagonistic interaction between A1 and D1 receptors in A1D1 cells. Nonlinear regression analysis indicated that the CPA- and DPCPX-mediated effects on dopamine-induced cAMP accumulation were additive.
Adenosine A1-Dopamine D1 Interaction

Table I

| Treatment | $R_H$ | $K_H$ | $K_i/IC_{50}$ |
|-----------|-------|-------|---------------|
| A₁D₁ cells |  |  |  |
| Control | 12.0 (3.9) | 0.2 (2.8) | 65.5 (4.1) |
| CPA, 0.1 μM | 14.5 (11.4) | 0.4 (0.9) | 61.0 (21.5) |
| CPA, 1 nM | 0.0 (0.0)* |  | 49.5 (13.0) |
| CPA, 10 nM | 0.0 (5.4)* |  | 52.3 (24.9) |
| CPA, 100 nM | 0.0 (0.0)* |  | 60.6 (10.9) |
| A₁D₁ cells |  |  |  |
| PTX control | 9.0 (13.0) | 0.3 (6.2) | 64.8 (47.6) |
| PTX + CPA, 10 nM | 12.5 (13.0) | 1.8 (5.5) | 64.7 (13.7) |
| A₂D₂ cells |  |  |  |
| PTX control | 10.3 (7.2) | 0.4 (2.7) | 62.1 (20.2) |
| PTX + CPA, 10 μM | 0.0 (0.0)* |  | 56.6 (23.1) |
| A₁D₁ cells |  |  |  |
| PTX control | 12.0 (6.9) | 0.7 (4.1) | 52.7 (9.8) |
| PTX + Gpp(NH)p, 100 μM | 0.0 (2.0)* |  | 45.4 (7.5) |
| D₁ cells |  |  |  |
| Control | 12.8 (1.3) | 0.2 (0.3) | 90.0 (18.1) |
| CPA, 0.1 μM | 12.7 (4.3) | 0.1 (0.9) | 87.0 (35.0) |
| D₁ cells |  |  |  |
| Control | 10.3 (5.8) | 0.3 (0.5) | 54.5 (22.3) |
| CPA, 10 μM | 11.7 (12.3) | 0.4 (2.5) | 58.4 (9.4) |
| D₁ cells |  |  |  |
| Control | 9.5 (6.0) | 0.4 (0.9) | 66.9 (37.4) |
| Gpp(NH)p, 100 μM | 0.0 (6.0)* |  | 63.8 (36.0) |

* $p < 0.01$ compared with control (Kruskal-Wallis and Mann-Whitney’s U tests).

cAMP accumulation were mainly due to changes in the maximal stimulation without changes in EC₅₀. This suggests that, in agreement with the results obtained from radioligand binding experiments, the A₁ receptor-mediated modulation of D₁ receptors does not involve changes in the affinity of D₁ receptors for agonists. This is in contrast to the A₂A-D₂ interaction (see the Introduction), where A₂A receptor stimulation induces a decrease in the affinity of D₂ receptors for agonists (4, 6).

The radioligand binding experiments carried out with membrane preparations from the cotransfected A₁D₁ cells showed results very similar to those obtained with rat striatal membrane preparations (5). The only difference was the lower proportion of D₁ receptors in the high affinity state (D₁H) in the A₁D₁ cells (~10%) as compared with the rat striatal membranes (~30%) (5). Since it has been previously shown that the density of D₁H correlates with the G protein content and with the endogenous dopamine levels (16), this difference might reflect either a low content of G proteins or the absence of a previous exposure of the D₁ receptors to dopamine. Both the GTP analogue Gpp(NH)p and CPA induced a significant reduction in the proportion of D₁H, Gpp(NH)p, but not CPA, was also effective in membrane preparations from control cells containing D₁ but not A₁ receptors, which demonstrates that the A₁ receptors are required for CPA to have an effect. Since D₁H represents the D₁ receptors coupled to the G protein, these results can be interpreted as an uncoupling of the D₁ receptor from its G protein induced by A₁ receptor stimulation.

PTX induces an uncoupling of the A₁ receptor from its G protein by inducing an ADP-ribosylation of the Gα subunit of the G_i (and G_o) protein family. This results in a reduction of the number of A₁ receptors in the high affinity state and in a blockade of A₁ receptor signal transduction (17–19). A₁D₁ cells were exposed to PTX to study the possible involvement of G_i proteins in the A₁ receptor-mediated uncoupling of the D₁ receptor from the G protein. As with the blockade of A₁ receptors with the A₁ antagonist DPCPX, PTX induced a significant increase in the basal levels of cAMP and potentiated dopamine-induced cAMP accumulation. This gives functional support for the blockade of A₁ receptor signal transduction by PTX in these experiments. It was found that PTX counteracted the effect of CPA (10 nM), but not of Gpp(NH)p, on D₁ receptor binding characteristics, suggesting that the G_i protein was, in fact, necessary for the intramembrane A₁-D₁ interaction. However, a higher concentration of CPA (10 μM), which is sufficient to
bind to the A1 receptor in the low affinity state in the A1D1 cells (see competitive inhibition curves of CPA versus [3H]DPCPX), could still uncouple D1 receptors from the Gs protein after PTX pretreatment. This effect of CPA was not reproduced in D1 cells, which shows that it is not a nonspecific effect, but is A1 receptor-mediated. Furthermore, in agreement with the radioligand binding experiments, a high concentration of CPA (10 μM) was still able to significantly decrease dopamine-induced cAMP accumulation after PTX pretreatment. The PTX-induced ribosylation, although very distinct, was not complete (see the SDS-polyacrylamide gel in Fig. 6). Therefore, it is still possible that stimulation of the low amount of A1 receptors in the high affinity state left after PTX pretreatment with the high concentration of CPA would be able to reproduce the same effect as the low concentration of CPA in PTX-nonpretreated cells. Nevertheless, the clear correlation between the results obtained with the radioligand binding and cAMP accumulation experiments suggests that the intramembrane A1-D1 interaction involved in the binding experiments is related to the A1-D1 interaction found at the adenyl cyclase level.

In summary, three main findings have been obtained in this work. The first finding is that in membrane preparations from stably cotransfected A1D1 cells, the stimulation of A1 receptors induces an uncoupling of the D1 receptor from its G protein. This intramembrane A1-D1 interaction has the same characteristics as that previously found in rat striatum (5). The demonstration of this interaction in an artificial and very different cellular type and cellular environment strongly suggests that these kind of intramembrane receptor-receptor interactions (1) represent a generalized functionally important mechanism in mammalian cells. The second finding is a functional antagonistic A1-D1 interaction at the adenyl cyclase level. Although previously shown in homogenates of rat striatum (20), this is

![FIG. 6. Effects of PTX on the [32P]ADP-ribosylation of G proteins in membrane preparations from A1D1 cells. PTX ADP-ribosylates G proteins with molecular masses of 39–41 kDa. [32P]ADP-ribosylation is markedly reduced in A1D1 cells previously exposed to PTX compared with controls. The positive control (+) contained whole rat brain; the negative control (−) contained buffer. PTX and C (control) represent A1D1 cells previously pretreated or not with PTX, respectively.](http://www.jbc.org/)

![FIG. 7. Counteracting effects of the adenosine A1 agonist CPA on the cAMP accumulation induced by forskolin (30 μM) and dopamine (0.1 μM) in A1D1 cells. Results are expressed as means ± S.E. (n = 6, in triplicate/experiment). Basal cAMP accumulation levels for forskolin and dopamine experiments were 1.2 ± 0.1 and 1.3 ± 0.1 pmol/50 μl (means ± S.E.), respectively.](http://www.jbc.org/)

![FIG. 8. Counteracting effect of the adenosine A1 agonist CPA (30 nM) and potentiating effect of the A1 antagonist DPCPX (30 nM) on the cAMP accumulation induced by dopamine in A1D1 cells. Results are expressed as means ± S.E. (n = 6, in triplicate/experiment).](http://www.jbc.org/)

![FIG. 9. Counteracting effects of the adenosine A1 agonist CPA on the cAMP accumulation induced by dopamine (10 μM) in A1D1 cells after PTX pretreatment. Results are expressed as means ± S.E. (n = 3, in triplicate/experiment). Basal cAMP accumulation levels for control and PTX-pretreated cells were 0.2 ± 0.02 and 0.4 ± 0.04 pmol/50 μl (means ± S.E.), respectively. * and **, significantly different compared with 0 CPA (p < 0.05 and p < 0.01, respectively).](http://www.jbc.org/)
the first time that such an interaction has been demonstrated at the cellular level. Finally, the third finding is the correlation between the results obtained with the radioligand binding and cAMP accumulation experiments, suggesting that the intramembrane A1-D1 interaction involved in the binding experiments is related to the A1-D1 interaction found at the adenylyl cyclase level. Similar interactions are likely to occur in nerve cells that express both A1 and D1 receptors, such as the γ-aminobutyric acidergic strionigral-striointopeducular neurons (21).

REFERENCES
1. Zoli, M., Agnati, L. F., Hedlund, P., Li, X. M., Ferré, S., and Fuxe, K. (1993) *Mol. Neurobiol.* 7, 293–334
2. Ferré, S., Fuxe, K., von Euler, G., Johansson, B., and Fredholm, B. B. (1992) *Neuroscience* 51, 501–512
3. Ferré, S., Fredholm, B. B., Morelli, M., Popoli, P., and Fuxe, K. (1997) *Trends Neurosci.* 20, 482–487
4. Ferré, S., von Euler, G., Johansson, B., Fredholm, B. B., and Fuxe, K. (1992) *Proc. Natl. Acad. Sci. U. S. A.* 89, 7238–7241
5. Ferré, S., Popoli, P., Giménez-Llort, L., Finman, U.-B., Martínez, E., Scotti de Carolis, A., and Fuxe, K. (1994) *Neuroreport* 6, 73–76
6. Dasgupta, S., Ferré, S., Kull, B., Hedlund, P., Finman, U.-B., Ahlberg, S., Arenas, E., Fredholm, B. B., and Fuxe, K. (1996) *Eur. J. Pharmacol.* 316, 325–331
7. Liu, Y. F., Civelli, O., Zhou, Q.-Y., and Albert, P. R. (1992) *Mol. Endocrinol.* 6, 1815–1824
8. Uhler, M. D., and McKnight, G. S. (1987) *J. Biol. Chem.* 262, 15202–15207
9. Townsend-Nicholson, A., and Shine, J. (1992) *Mol. Brain Res.* 16, 365–370
10. Libert, F., Van Sande, J., Lefort, A., Czernilofsky, A., Dumont, J. E., Vassart, G., Eansinger H. A., and Mendla, K. D. (1992) *Biochem. Biophys. Res. Commun.* 187, 919–926
11. Chomczynski, P., and Sacchi, N. (1987) *Anal. Biochem.* 162, 156–159
12. Fredholm, B. B., Proctor, W., Van der Ploeg, I., and Dunwiddie, T. V. (1989) *Eur. J. Pharmacol.* 172, 249–262
13. Nordstedt, C., and Fredholm, B. B. (1990) *Anal. Biochem.* 187, 231–234
14. Jockers, R., Linder, M. E., Hahnenegger, M., Nanoff, C., Bertin, B., Strasberg, A. D., Marullo, S., and Freissmuth, M. (1994) *J. Biol. Chem.* 269, 32077–32084
15. Cunha, R. A., Constantino, M. D., Sebastiao, A. M., and Ribeiro, J. A. (1995) *Neuroreport* 6, 1583–1588
16. Hervé, D., Trouvé, F., Blane, G., Głowinski, J., and Tassin, J.-P. (1992) *Neuroscience* 46, 687–700
17. Kurose, H., Katada, T., Amano, T., and Ui, M. (1983) *J. Biol. Chem.* 258, 4870–4875
18. Hsa, J. A., Moss, J., Hewlett, E. L., and Vaughan, M. (1984) *J. Biol. Chem.* 259, 1086–1090
19. Cote, T. E., Frey, E. A., and Sekura, R. D. (1984) *J. Biol. Chem.* 259, 8690–8698
20. Abbracchio, M. P., Colombo, F., Di Luca, M., Zaratin, P., and Cattabeni, F. (1987) *Pharmacol. Res. Commun.* 19, 275–286
21. Ferré, S., O’Connor, W. T., Svenningsson, P., Bjorklund, L., Lindberg, J., Tinner, B., Strumberg, I., Goldstein, M., Ogren, S. O., Ungerstedt, U., Fredholm, B. B., and Fuxe, K. (1996) *Eur. J. Neurosci.* 8, 1545–1553
Adenosine $A_1$ Receptor-mediated Modulation of Dopamine $D_1$ Receptors in Stably Cotransfected Fibroblast Cells
Sergi Ferré, Maria Torvinen, Katerina Antoniou, Eva Irenius, Olivier Civelli, Ernest Arenas, Bertil B. Fredhol and Kjell Fuxe

*J. Biol. Chem.* 1998, 273:4718-4724.
*doi: 10.1074/jbc.273.8.4718*

Access the most updated version of this article at [http://www.jbc.org/content/273/8/4718](http://www.jbc.org/content/273/8/4718)

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 21 references, 6 of which can be accessed free at [http://www.jbc.org/content/273/8/4718.full.html#ref-list-1](http://www.jbc.org/content/273/8/4718.full.html#ref-list-1)