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Effects of Adenosine (ADO) and A₁ and A₂ Ado Agonists on Calcium Uptake and cAMP Levels in Cultured Rat Mesangial Cells (MC)

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EFFECTS OF ADENOSINE (ADO) AND A_1 AND A_2 ADO AGONISTS ON CALCIUM UPTAKE AND cAMP LEVELS IN CULTURED RAT MESANGIAL CELLS (MC).

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ABSTRACT- MC exhibits A_1 and A_2 receptors with opposite actions on cAMP formation and $^{45}\text{Ca}^{2+}$ uptake. ADO 10^{-4} M activated both second messengers, but neither A_1 nor A_2 receptors seem to be involved in these ADO-induced effects.

There are some evidences about the existence of A_1 and A_2 ADO receptors in isolated glomeruli^{1,2} and A_1 ADO receptors in glomerular MC³. In this study, we tried to functionally identify A_1 and A_2 receptors in MC by the effects of the agonists R-PIA and NECA on changes in cAMP content in 5 μM forskolin (F)-pretreated MC (table 1). R-PIA induced a decrease in cAMP content that was inhibited in the presence of the A_1 antagonist PD116,948 (AT_1) whereas NECA induced an increase in cAMP that was only inhibited in the presence of the A_2 antagonist PD115,199 (AT_2). Thus, these results suggest that there are A_1 and A_2 -like ADO receptors in MC with opposite actions on cAMP formation.

ADO 10^{-4} M increased cAMP content in F-stimulated MC. However, unlike NECA, the response of ADO was evident within the first min of incubation (table 1) and it was not inhibited by the AT_2 . Thus, we suggest that the effect of ADO on cAMP levels is not mediated by an A_2 -like ADO receptor.

Since renal actions of ADO seem to depend on extracellular calcium⁴, we studied the effects of ADO and its agonists on calcium entry in MC. Activation of the A_1 receptor stimulates whereas activation of the A_2 inhibits $^{45}\text{Ca}^{2+}$ -uptake. ADO 10^{-4} M, as R-PIA, increased $^{45}\text{Ca}^{2+}$ -uptake (fig. 1). However, the receptor involved in the stimulation of $^{45}\text{Ca}^{2+}$ -uptake induced by R-PIA and that involved in the stimulation induced by ADO does not seem to be the same since AT_2 potentiated R-PIA effect but inhibited ADO response.

TABLE 1: Time-course of changes on cAMP content in F-pretreated MC induced by ADO and its analogues. Results are expressed as $\Delta\%$ F-treated MC (* $p < 0.01$). Data are $x \pm \text{SEM}$.

| Treatment/Time(min) | 1 | 2 | 5 |
|--------------------------------------|---------------|-----------------|----------------|
| R-PIA (10^{-6} M) | $-43 \pm 9^*$ | $-59 \pm 2.2^*$ | $-44 \pm 11^*$ |
| R-PIA+AT ₁ (10^{-6} M) | | -13 ± 10 | |
| NECA (10^{-6} M) | -3 ± 14 | $61 \pm 19^*$ | $63 \pm 17^*$ |
| NECA+AT ₂ (10^{-6} M) | | 10 ± 22 | |
| ADO (10^{-4} M) | $87 \pm 19^*$ | $108 \pm 28^*$ | $129 \pm 17^*$ |
| ADO+AT ₂ (10^{-6} M) | | $105 \pm 27^*$ | |

⁴⁵-Calcium uptake ($\Delta\%$)

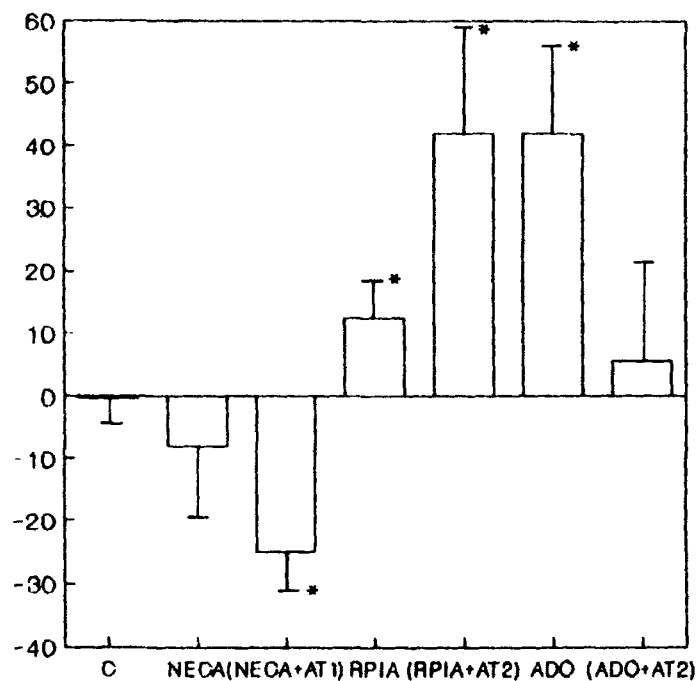


FIGURE 1: Effect of ADO (10^{-4} M) and the agonists ($1 \mu\text{M}$) and/or antagonists (10 nM) on $^{45}\text{Ca}^{2+}$ -uptake after 30 s of incubation. Data are $x \pm \text{SEM}$. * $p < 0.05$ related to basal uptake.

ADO 10^{-4} M have effects on cAMP production and on $^{45}\text{Ca}^{2+}$ -uptake in MC that can not be explained by the activation of classic A_1 or A_2 ADO receptors. Another kind of receptor or conformational state may be hypothesized.

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