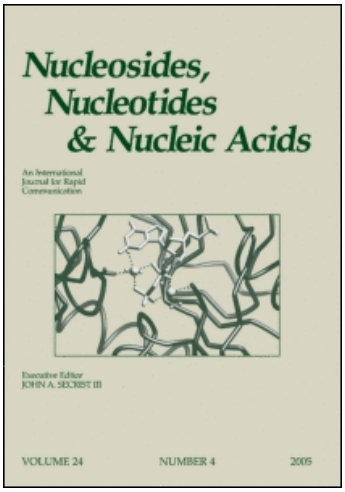

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Effects of Adenosine (ADO) and A_1 and A_2 Ado Agonists on Calcium Uptake and cAMP Levels in Cultured Rat Mesangial Cells (MC)

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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 $^{45}Ca^{2}+$ 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 MC[3]. 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 calcium[4], 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 $^{45}Ca^{2}+$-uptake. ADO 10^{-4} M, as R-PIA, increased $^{45}Ca^{2}+$-uptake (fig. 1). However, the receptor involved in the stimulation of $^{45}Ca^{2}+$-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 Δ% F-treated MC (* $p < 0.01$). Data are x ± SEM.

Treatment/Time(min)	1	2	5
R-PIA (10^{-6} M)	-43 ± 9*	-59 ± 2.2*	-44 ± 11*
R-PIA+AT_1 (10^{-6} M)		-13 ± 10	
NECA (10^{-6} M)	-3 ± 14	61 ± 19*	63 ± 17*
NECA+AT_2 (10^{-6} M)		10 ± 22	
ADO (10^{-4} M)	87 ± 19*	108 ± 28*	129 ± 17*
ADO+AT_2 (10^{-6} M)		105 ± 27*	

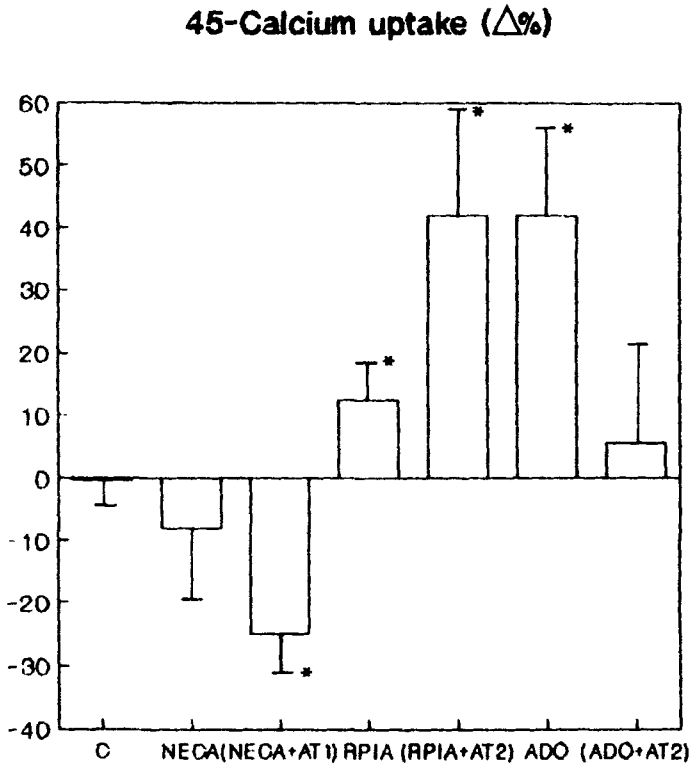

FIGURE 1: Effect of ADO (10^{-4} M) and the agonists (1 μM) and/or antagonists (10 nM) on $^{45}Ca^{2+}$-uptake after 30 s of incubation. Data are x ± SEM. *$p < 0.05$ related to basal uptake.

ADO 10^{-4} M have effects on cAMP production and on $^{45}Ca^{2}$+-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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