Abstract

Regulatory roles of somatostatin analogs (SSAs) in catecholamine synthesis have not been elucidated. To clarify the actions of SSAs on catecholamine biosynthesis, we investigated the mutual interactions among SSAs including octreotide and pasireotide, steroids and BMPs using rat pheochromocytoma PC12 cells. Treatment with octreotide and pasireotide (10 nM to 10 μM) had no significant effect on mRNA levels of tyrosine hydroxylase (*Th*), DOPA decarboxylase and dopamine-β-hydroxylase in PC12 cells. Regarding the interaction with steroids, treatments with SSAs also had no effect on dexamethasone- or aldosterone-induced *Th* mRNA expression, while pasireotide reduced mRNA expression of the glucocorticoid receptor (*Gr*). As for the interaction with BMP-4, which can suppress *Th* mRNA expression by PC12 cells, SSAs did not affect *Th* expression reduced by BMP-4 and *Id1* or Smad1/5/9 activation induced by BMP-4. However, BMP-4 treatment upregulated mineralocorticoid receptor (*Mr*) expression, while treatment with noggin, which neutralizes endogenous BMPs, downregulated *Mr* expression, and the presence of noggin also attenuated aldosterone-induced *Th* expression, suggesting that endogenous BMPs act to enhance MR activity. Moreover, BMP-4 treatment suppressed the expression of somatostatin receptors including *Sstr2* and *Sstr5* in PC12 cells, while treatment with noggin upregulated the expression of *Sstr2* and *Sstr5*, suggesting that BMPs play a desensitizing role in SSA actions. Collectively, the results revealed that SSAs have no direct effect on catecholamine synthesis; however, adrenomedullar BMPs could be modulators for the responsiveness to MR and SSTRs.