PHARMACHOLOGICAL PROPERTIES AND PROLIFERATION-INDUCING EFFECTS OF PURINERGIC RECEPTORS IN P19 EMBRYONAL CELLS AS *IN VITRO* MODEL FOR NEURONAL DIFFERENTIATION

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P19 embryonal carcinoma cells have been excessively been used as an *in vitro* model for early neuronal differentiation. Differentiating P19 cells express neuron-specific proteins and a differential pattern of ionotropic and metabotropic receptors, including ATP-activated P2X ligand-gated ion channels and P2Y G-protein-coupled receptors. We have characterized the participation of purinergic subtypes $P2X_{1-7}$ and $P2Y_{1,2,4,6,11-14}$ receptors families at mRNA transcription and protein expression levels as well as receptor-induced Ca^{2+} transients during neuronal differentiation in the presence of purinergic receptor agonists and antagonists. In embryonic cells $P2Y_{1,2}$, $P2X_4$ receptors, or P2X-heteromultimers with similar $P2X_4$ pharmacology were responsible for ATP and ATP-analog-induced Ca^{2+} transients. After inducing neuronal differentiation by retinoic acid, $P2Y_{2,6}$ receptors and $P2X_2$ subtypes were the major mediators of the $[Ca^{2+}]_i$-response. P2X receptors promoted a short calcium transient, whereas calcium transients induced by P2Y receptors lasted in the presence of purinergic receptor agonists. Besides their participation in triggering neuronal differentiation of P19 cells (Resende et al., submitted), we have collected evidence for the involvement of these receptors in proliferation induction of embryonic cells. Regulation of cell proliferation and differentiation was mostly due to $P2Y_1$ and $P2Y_2$ receptor activation, as these effects were abolished following depletion of intracellular calcium stores.

Keywords: neuronal differentiation; embryonic cell proliferation; purinergic receptors; ATP; calcium signaling.

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