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Nucleotides in neuroregeneration and neuroprotection

M.Teresa Miras-Portugal, Rosa Gomez-Villafuertes, Javier Gualix, Juan Ignacio Diaz-Hernandez, Antonio R. Artalejo, Felipe Ortega, Esmerilda G. Delicado, Raquel Perez-Sen



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1 **Nucleotides in neuroregeneration and neuroprotection.**

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3 M. Teresa Miras-Portugal<sup>1</sup>, Rosa Gomez-Villafuertes<sup>1\*</sup>, Javier Gualix<sup>1</sup>, Juan Ignacio Diaz-  
4 Hernandez<sup>1</sup>, Antonio R. Artalejo<sup>2</sup>, Felipe Ortega<sup>1</sup>, Esmerilda G. Delicado<sup>1</sup>, Raquel Perez-Sen<sup>1</sup>.

5 <sup>1</sup>Department of Biochemistry and Molecular Biology IV, Veterinary School, Universidad  
6 Complutense of Madrid. 28040, Madrid. Spain

7 <sup>2</sup>Department of Toxicology and Pharmacology, Veterinary School, Universidad Complutense of  
8 Madrid. 28040, Madrid. Spain

9 \*Corresponding author

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11 **Abstract**

12 Brain injury generates the release of a multitude of factors including extracellular nucleotides,  
13 which exhibit bi-functional properties and contribute to both detrimental actions in the acute  
14 phase and also protective and reparative actions in the later recovery phase to allow  
15 neuroregeneration. A promising strategy toward restoration of neuronal function is based on  
16 activation of endogenous adult neural stem/progenitor cells. The implication of purinergic  
17 signaling in stem cell biology, including regulation of proliferation, differentiation, and cell  
18 death has become evident in the last decade. In this regard, current strategies of acute  
19 transplantation of ependymal stem/progenitor cells after spinal cord injury restore altered  
20 expression of P2X4 and P2X7 receptors and improve functional locomotor recovery. The  
21 expression of both receptors is transcriptionally regulated by Sp1 factor, which plays a key role  
22 in the startup of the transcription machinery to induce regeneration-associated genes  
23 expression. Finally, general signaling pathways triggered by nucleotide receptors in neuronal  
24 populations converge on several intracellular kinases, such as PI3K/Akt, GSK3 and ERK1,2, as  
25 well as the Nrf-2/heme oxygenase-1 axis, which specifically link them to neuroprotection. In  
26 this regard, regulation of dual specificity protein phosphatases can become novel mechanism  
27 of actions for nucleotide receptors that associate them to cell homeostasis regulation.

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