

CO-mediated cytoprotection is dependent on cell metabolism modulation – implication on neuronal differentiation, anti-inflammation role and prevention of cell death

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Carbon monoxide (CO) is a gasotransmitter endogenously produced by the activity of heme oxygenase, which is a stress-response enzyme and is under the control of Nrf2. Endogenous CO or low concentrations of exogenous CO have been described to present several cytoprotective functions: anti-apoptosis, anti-inflammatory, vasomodulation, maintenance of homeostasis, stimulation of preconditioning and modulation of cell differentiation. Herein it is demonstrated and discussed how CO regulates cell metabolism and how it is involved in the distinct cytoprotective roles of CO. Using different brain cell models (neurons, astrocytes and microglia) we have demonstrated that CO promotes mitochondrial ROS generation, stimulation of mitochondrial biogenesis and increased oxidative phosphorylation. Likewise, CO negatively regulates glycolysis and improves pentose phosphate pathway. These alterations in cell metabolism are implicated in: (i) prevention of astrocytic cell death; (ii) improvement of neuronal differentiation and (iii) anti-neuroinflammatory effect in microglia.

Publications related to the talk

- Dias-Pedroso D., Ramalho J.S., Sardão V.A., Jones J.G., Romão C.C., Oliveira P.L. and Vieira H.L.A, Carbon monoxide-Neuroglobin axis targeting metabolism against inflammation in BV-2 microglial cells, *Molecular Neurobiology*, **2021**, doi: 10.1007/s12035-021-02630-4
- Almeida A.S., Soares N.L., Sequeira CO, Pereira S.A., Sonnewald U., Vieira H.L.A. Improvement of neuronal differentiation by carbon monoxide: role of pentose phosphate pathway. *Redox Biol.* **2018** Jul 17:338-347. doi: 10.1016/j.redox.2018.05.004
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- Almeida A.S., Queiroga C.S.F., Sousa M.F., Alves P.M. and Vieira H.L.A., Carbon monoxide modulates apoptosis by reinforcing oxidative metabolism in astrocytes: role of Bcl-2, *Journal of Biological Chemistry* **2012**, 287: 10761-70