TAT-BH4 exerts a protective effect on damaged neuronal and endothelial cell

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The prevention of neuronal and vascular cell death allows damage reduction and tissue recovery from oxidative stress injury, that plays an important role in many chronic CNS diseases, such as Alzheimer and Parkinson's diseases, traumatic brain injury, as well as spinal cord injury (SCI).
BH4 domain of the anti-apoptotic protein, Bcl-xL, attached to TAT, a membrane transport peptide (TAT-BH4), protects against acute hypoxia/ischemia injury in the brain by preventing endothelial cell apoptosis and inducing neuronal plasticity. Endothelium and neurons are close related and their relationship is fundamental to recover cerebral damaged tissue.
In order to well understand the role of these cell types in the protective effect exerted by TAT-BH4 on damaged cerebral tissue, an in vitro models of co-culture was set up. Experiments on survival and apoptotic cell death were carried out on microvascular endothelial cells and neuronal cells (isolated from mice) and, to mimic a stress condition, cells were subjected to low serum.
TAT-BH4 exerted a protective effect on endothelium in a oxidative stress condition, promoting cell survival and reducing cell death. Despite this protective effect was absent in neurons, in the co-culture model, TAT-BH4 rescues neurons from cell death, and promotes their differentiation. At mechanistic level, we demonstrate that TAT-BH4 promotes the expression and release from endothelium of the neurotrophic growth factor FGF2, responsible of neuron protection and differentiation.
In conclusion these data demonstrate that the protective effect of TAT-BH4 on damage cerebral tissue might be related, at least in part, to the FGF-2 release from endothelial cells.