Research on factors that control the activation of spinal cord endogenous stem cells

ANA DEKANIĆ, MIRANDA MLADINIĆ
UNIVERSITY OF RIJEKA, DEPARTMENT OF BIOTECHNOLOGY, RIJEKA, CROATIA
INTERNATIONAL SCHOOL FOR ADVANCED STUDIES, TRIESTE, ITALY

dekanic@sissa.it

The stem/progenitor cells in the central nervous system are the subject of the intense research since they open new possibilities for the treatment of the brain and spinal cord injuries and neurodegenerative diseases, but the molecular and cellular pathways that control their activity are largely unknown.
In the present study the factors that regulate spinal cord endogenous stem/progenitor cells were explored using Activating Transcription Factor 3 (ATF3) as their novel dynamic marker in the neonatal rat spinal cord in vitro preparation. We have previously shown that ATF3 is expressed in the cytoplasm of the quiescent ependymal spinal stem/progenitor cells (nestin, vimentin and Sox2 positive), but that the expression changes into nuclear after activation and mobilization of ependymal cells in vitro.
We hypothesized that the activation of the spinal stem/progenitor cells in vitro may be influenced by neonatal neuronal network activity, by excitotoxic or ischemic damage and by the lack of molecules in the culture medium. The results have shown that the pharmacological inhibition of glutamate, GABAA or glycine receptors has no influence on spinal stem cell activation in vitro. Thus, we conclude that the in vitro activation of spinal stem cells is not neuronal network dependent. Similarly, we have shown that neither excitotoxic nor ischemia-like experimental spinal cord injury have further enhanced the activation of spinal ependymal stem cells in vitro. On contrary, our results have shown that the addition of the molecules such as Nerve Growth Factor (NGF), goat serum and insulin into culture medium, could change the number of activated ATF3-nuclearly positive ependymal spinal cord stem cells, suggesting that the molecules contained in blood or cerebrospinal fluid could regulate the spinal stem cell quiescence or activity. Additionally, we have shown that the short time window of 3 days in vitro is not enough to allow the stem cell differentiation into neuronal or glial cells.
This study contributes to our knowledge of the factors controlling the activity and quiescence of the spinal cord stem cells and opens the directions for further studies that would enable their controlled activation after injury.

Keywords: ATF3, endogeneous stem cells, in vitro spinal cord preparation

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