STEM CELLS IN MULTIPLE SCLEROSIS: ACTUALITY VS. POTENTIALITY

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Recent evidence consistently challenges the sole and limited view that neural stem/precursor cells (NPCs) may protect the central nervous system (CNS) from inflammatory damage leading to neurodegeneration exclusively throughout cell replacement. As a matter of fact, NPC transplantation may also promote CNS repair via intrinsic *neuroprotective* bystander capacities, mainly exerted by undifferentiated stem cells releasing, at the site of tissue damage, a milieu of *neuroprotective* molecules whose *in situ* release is temporally and spatially orchestrated by environmental needs. This milieu contains molecules (e.g. immunomodulator substances, neurotrophic growth factors and stem cell regulators), which are *constitutive*ly expressed by NPCs for maintaining tissue homeostasis either both during development and adult life. The intrinsic nature (*pleiotropism and redundancy*) of these molecules as well as their *'constitutive*' characteristics, may also reconcile data showing that other sources of somatic stem cells (e.g. mesenchymal stem cells), with very low capabilities of neural (trans) differentiation, may efficiently promote CNS repair. Thus, cell plasticity can also be viewed as the capacity of somatic stem cells to adapt their fate and function(s) to specific environmental needs occurring as a result of different pathological conditions (*therapeutic plasticity*). The challenging ability of transplanted NPCs to protect the brain from several types of injuries using different and/or articulated *bystander* strategies is of pivotal importance for the future of stem cell based therapeutic approaches.

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