# Naturally-occurring secreted membrane nanovesicles and therapeutic neural stem cell plasticity

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Compelling evidence exists that somatic stem cell-based therapies protect the central nervous system (CNS) from chronic inflammation-driven degeneration, such as that occurring in experimental autoimmune encephalomyelitis (EAE), multiple sclerosis (MS) and cerebral ischemic/hemorrhagic stroke. However, while it was first assumed that stem cells may act trough direct replacement of lost/damaged cells, it has now become clear that they are able to protect the damaged nervous system through a number of '*bystander'* mechanisms other than cell replacement. In immune-mediated experimental demyelination and stroke – both in rodents and non-human primates - others and we have shown that transplanted neural stem/precursor cells (NPCs) possess a constitutive and inducible ability to mediate efficient '*bystander'* myelin repair and axonal rescue. Yet, a comprehensive understanding of the multiple mechanisms by which NPCs exert their therapeutic impact is lacking. We envisage that the remarkable therapeutic plasticity of NPCs results from their capacity to engage highly sophisticated programmes of horizontal cell-to-cell communication at the level of the (micro)environment and we attribute a key role to the transfer of secreted membrane vesicles (MVs) from (*donor*) NPCs to (*recipient*) neighbouring cells. We are starting to define whether this form of communication is biologically relevant for NPCs, and look forward to establishing whether it is associated to cell-to-cell trafficking of non-coding RNAs (ncRNAs), and indeed on elucidating its molecular signature and therapeutic significance for MS. We believe that the true innovation of this approach relies in its unique peculiarity to *look into an innate cellular mechanism* with the visionary focus of *translating the knowledge of basal stem cell functions into innovative high-impact clinical therapeutics for MS*.