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Therapeutic potential for somatic neural stem cell (NSC) grafts in the restoration of midbrain dopaminergic neuronal function in the aged Parkinsonian brain

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Parkinson's disease (PD) is the most prevalent central nervous system (CNS) movement disorder characterized by the progressive loss of midbrain dopaminergic (mDA) neurons of the substantia nigra pars compacta (SNpc). The causes and mechanisms leading to mDA neuron demise in sporadic PD remain poorly understood, but current evidence indicates that they depend on a complex interaction of genetic susceptibility, environmental factors and, most importantly, aging and inflammation. Particularly, reactive astrocytes (Ras) are key players in the response to PD injury and inflammation, via Wnt/ β -catenin signaling, regulating both helpful and harmful responses. Because aging is the chief risk factor for PD development, we focused on the aged male midbrain microenvironment to address the ability of neural stem progenitor cells (NSCs) to activate intrinsic cues that may instruct midbrain astrocytes to implement mDA neurorepair in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced long-lasting DA neurotoxicity. Here, we discuss our recent data showing that subventricular zone (SVZ)-derived adult NSCs transplanted in the aged MPTP-injured SNpc promote a remarkable time-dependent endogenous nigrostriatal DA neurorestoration. Although multiple modes of reciprocal interactions between exogenous NSCs and the pathological host milieu may underlie the functional improvement observed, our data suggest that NSCs and astrocyte-derived factors, especially Wnt1, might play a major role acting at different levels to rejuvenate the host microenvironment and promote mDA neurorepair/regeneration. In light of the emerging picture implicating deregulated Wnt/ β -catenin signaling in PD, our findings predict a novel perspective on harnessing Wnt/ β -catenin signaling with functionally plastic NSC grafts as a novel therapeutic strategy for PD.

Biography

Bianca Marchetti has completed her PhD from Laval University, Quebec, Canada, and Postdoctoral studies from McGill University. She is Full Professor of Pharmacology at the University of Catania, Medical School and directs the Laboratory of Neuropharmacology at the OASI Scientific Institute for Research and Care (IRCCS) on Mental retardation and Brain Aging of Troina (EN), Italy. She has published more than 100 papers in reputed journals and has been serving as an Editorial Board Member of neuroscientific journals.

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