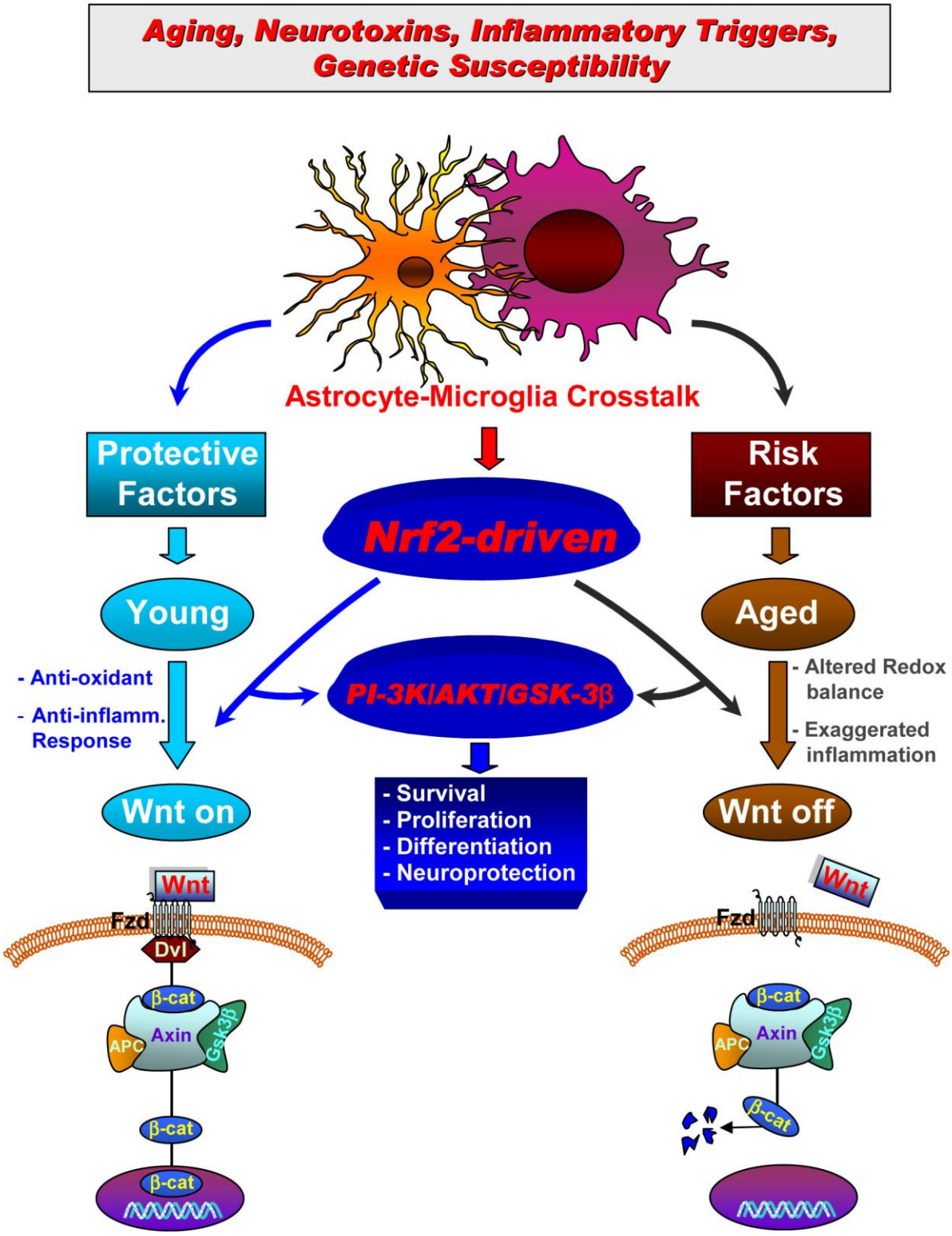

Supplementary Figure S1 Aging-induced Nrf2-ARE pathway disruption in the subventricular zone (SVZ) drives neurogenic impairment in parkinsonian mice via PI3K-Wnt/β-catenin dysregulation. In young mice a regulatory circuit linking microglial activation and pro-inflammatory cytokine to NF-E2-related factor 2 (Nrf2)-Anti-oxidant-responsive elements (ARE) protective pathway

in SVZ, provides an efficient self-adaptive mechanism against inflammatory/neurotoxin-induced oxidative stress. In addition to govern the redox balance within the SVZ niche, *Nrf2*-induced heme-oxygenase, *Hmox,* target gene may simultaneously protect astrocytes, thereby up-regulating the expression of vital Wnt signaling elements switching-on key components required for maintaining SVZ cells in a proliferative state, promote differentiation and/or for exerting neuroprotective effects. Crosstalk between two pivotal pathways, the phosphatydil-inositol3-kinase, PI3-K/Akt/GSK-3β and Wnt/β-catenin signaling cascades appear to cooperate to finely control the transcriptional activator, β-catenin, in turn representing a point of convergence to direct proliferation/differentiation/survival in SVZ stem niche. Importantly, SVZ "rejuvenation" may have beneficial consequences for DAergic neuroprotection, and viceversa (L'Episcopo et al., 2013). Astrocytes (blue), neuroblasts (red), transit-aplifying cells (yellow) and ependymal (purple) cells in SVZ niche are schematically illustrated (from L'Episcopo et al. 2013, with permission).

Reference

L'Episcopo, F., Tirolo, C., Testa, N., et al. (2013). Aging-induced Nrf2-ARE pathway disruption in the subventricular zone (SVZ) drives neurogenic impairment in parkinsonian mice via PI3K-Wnt/β-catenin dysregulation. J. Neurosci. 33, 1462-1485.