HIF-1α-Mediated Neuroprotection on MPP+-Induced Apoptosis in SH-SY5Y Cells

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Considering the facts of neuronal death in PD and survival role of HIF-1α, and the LEGENDS

Figure 3

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Figure 2

The maturation and the role of HIF-1α under the pathogenesis of PD. Mitochondrial complex I inhibitors, such as rotenone and MPP+, and excessive iron, such as FeCl3, may not only cause mitochondrial dysfunction, leading to apoptosis of cells related to PD, but also increase the activity of enzyme PHD, leading to the degradation of HIF-1α and then the reduction of HIF-1α protein level. HIF-1α gene transfection, iron chelation, such as DFO, EGCG, may increase HIF-1α protein level, through which its target genes, such as vascular endothelial growth factor (VEGF) and erythropoietins (EPO), are induced, leading to cell survival. Additionally, iron chelation can also reduce HIF-1α degradation, and PHD, which causes the hydrolysis of 2-aminooxyproline (P400) and P400 as the oxygen-dependent degradation domain (ODD) of HIF-1α, leading to rapid degradation of HIF-1α via ubiquitin-proteasome system (UPS) (Figure 1).

RESULTS

Figure 5

HIF-1α and MPP+-induced neuronal injury. Mitochondrial complex I inhibitor MPP+ caused decrease in cell number (Figure 5A), increase of cleaved PARP and decrease of HIF-1α (Figure 4B), increase of bimetallic-base DNA fragments (Figure 4C), or the increase of dead cells (Figure 4D), all of which were diminished by enhanced expression of HIF-1α in SH-SY5Y cells. The apoptosis was determined by quantitative measurement of cytoskeletal-destroyed bimetallic-base DNA fragments using ELISA kit (Relat Cancer Cell Dev 2007; 15:551-78). The expression of HIF-1α was confirmed by western blot and ELISA assay. (Figure 5A). The mitochondria was disrupted by MPP+ and then the reduction of HIF-1α was increased, whereas, in medium with HIF-1α inhibition, the protein level of VEGF was increased in culture medium under the conditions that HIF-1α was increased, whereas, in medium with HIF-1α inhibition, the protein level of VEGF was decreased (Figure 5C), indicating that increased HIF-1α may target its target gene VEGF, and the function of HIF-1α was largely maintained with the transformation of HIF-1α (-ODD) domain.

Neuroprotection of HIF-1α on MPP+-induced neuronal injury. Mitochondrial complex I inhibitor MPP+ caused decrease in cell number (Figure 5A), increase of cleaved PARP and decrease of HIF-1α (Figure 4B), increase of bimetallic-base DNA fragments (Figure 4C), or the increase of dead cells (Figure 4D), all of which were diminished by enhanced expression of HIF-1α in SH-SY5Y cells. The apoptosis was determined by quantitative measurement of cytoskeletal-destroyed bimetallic-base DNA fragments using ELISA kit (Relat Cancer Cell Dev 2007; 15:551-78). The expression of HIF-1α was confirmed by western blot and ELISA assay. (Figure 5A). The mitochondria was disrupted by MPP+ and then the reduction of HIF-1α was increased, whereas, in medium with HIF-1α inhibition, the protein level of VEGF was increased in culture medium under the conditions that HIF-1α was increased, whereas, in medium with HIF-1α inhibition, the protein level of VEGF was decreased (Figure 5C), indicating that increased HIF-1α may target its target gene VEGF, and the function of HIF-1α was largely maintained with the transformation of HIF-1α (-ODD) domain.

REFERENCES


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