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ANRIL potentially regulates NTF3 expression level in hypoxia

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Background: Multiple sclerosis is an autoimmune disorder mediated by activated lymphocytes leads to myelin sheet degradation and physical disabilities. Hypoxia is related to Multiple sclerosis pathogenesis. In Hypoxia HIF-1a activation leads to triggering inflammatory pathways by induction of TNF expression. This hypoxia-inflammatory condition leads to disease aggregation and further damages. Accumulating data suggest regulatory roles for lncRNAs. For instance, by binding to the YY1 transcription factor, ANRIL lncRNA could regulate gene expression. In the promoter region of Neurotrophin 3 (NTF3), there are two conserved transcription factor binding sites for YY1. NTF3 controls the survival and differentiation of neurons. Hence, a correlation could be considered between these two genes. Here, the role of hypoxia on the regulation of ANRIL and NTF3 was surveyed. Methods: U-87 cell line, which is derived from microglioma tumor, were treated by 150 µM CoCl2 for 24 hours to induce hypoxia. Then, RNA was extracted and the first strand of cDNA was synthesized using M-MLV Reverse Transcriptase. The gene expression level was analyzed by qRT-PCR. Results: In microglia, ANRIL lncRNA was upregulated significantly under the hypoxia condition (4.7 fold, p= 0.0008). Consistently, hypoxia induction leads to upregulation of NTF3 mRNA level (10.2 fold, p= 0.001). Discussion: In hypoxic milieu, upregulation of ANRIL is simultaneous with a rise in NTF3 level. Considering the regulatory role of ANRIL in gene expression through binding to YY1 transcription factor and the existence of YY1 binding site on NTF3 promoter region, probably ANRIL could regulate the NTF3 expression in hypoxia condition.
Keywords: ANRIL; NTF3; YY1; Hypoxia

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The effect of nobiletin on behavioral and histological alterations in a model of Parkinson's disease induced by intranigral injection of lipopolysaccharide in the rat

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Background and Objective: Anti-inflammatory property of nobiletin, a compound in citrus fruit's peel, has been shown. Besides, neuroinflammation is involved in triggering and progression of neurodegenerative disorders such as Parkinson's Disease (PD). The purpose of this study was to determine the effect of nobiletin on behavioral and histological changes in an experimental model of PD induced by intranigral injection of lipopolysaccharide (LPS) in rats.

Materials and Methods: In this study, to generate PD model, 5µg of LPS was injected into right midbrain of rats through stereotaxic surgery. Nobiletin was administrated daily for one week after the surgery at a dose of 10 mg/kg p.o. via gavage. Behavioral changes were evaluated by Y maze, Elevated plus maze, Passive avoidance, Novel object recognition, Forced swimming, and Rotational tests. For histological assessments, number of dopaminergic neurons was counted.

Results: Findings of this study demonstrated that administration of nobiletin to parkinsonian rats induced by LPS resulted in a significant decrease in the number of rotations and immobility time, and an insignificant decrease in percentage of alternation and significant increase of novel object discrimination and insignificant increase in the percentage of open arm spending time. Also, nobiletin treatment prevented loss of dopaminergic neurons.

Conclusion: Nobiletin treatment alleviated motor asymmetry and caused improvement of learning and memory and depressive like disorder in PD model induced by LPS and part of its beneficial effect is mediated via its neuroprotective effect.
Keywords: Parkinson Disease, Nobiletin, Behavioral changes, Lipopolysaccharide, Dopaminergic