miR-9-5p as a potential biomarker of intestinal inflammatory statusin an animal model of Parkinson's disease

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Parkinson's disease (PD) is a neurodegenerative disorder characterized by selective loss of dopaminergic neurons in the substantia nigra pars compacta (SNc) projecting to the striatum, which triggers the motor symptoms of the disease (tremor, rigidity and bradykinesia). Although this disease is considered the prototypical movement disorder, non motor manifestations, such as autonomic dysfunctions, in particular those involving the gastrointestinal (GI) tract, are increasingly recognized as being part of a wider clinical picture. PD patients experience non-motor symptoms especially at GI level, that often appear several years before the onset of motor symptoms. The link among PD, enteric nervous system (ENS) and central nervous system (CNS) is wellknown and led to the formulation of the 'Braak's hypothesis', implying that the GI tract represents the 'gate' through which environmental noxae enter the human body and spread to the CNS via intrinsic and extrinsic neural circuitries. A modification of intestinal epithelial barrier (IEB) as a consequence of inflammatory signals that epigenetically regulate gene expression maybe responsible for the GI symptoms.
In the last few years microRNAs (miRNAs) have emerged as regulators of gene expression acting at post transcriptional level. These sequences are endogenous non-coding single-stranded RNAs of about 22 nucleotides in length that can bind to RNA messenger (mRNA) containing complementary sequences, the consequence is a downregulation or the suppression of gene expression depending on the complementarity degree.
The aim of our study was to investigate the expression of miR9-5p, a isomir which targets the same messengers in human and rat, in colonic preparation of longitudinal muscle of the mienteric plexus (LMMP) in a rat model of PD induced by neurotoxin 6-hydroxydopamine (6-OHDA). miR-9 directly regulates NF-kB signaling pathway (mirtarbase). Some previous published data (Weilin et al., 2016) reported miR-9 has a role in regulating proliferation and migration of neuronal precursors. In particular a lack of miR-9 results in the upregulation of proinflammatory cytokines/chemokines (i.e. IL-1b, TNF-alpha, IL-6 and MCP-1). In the present study miR-9 expression was evaluated in proximal and distal colon fragments by quantitative real-time PCR (qRT-PCR). The results showed a significant decrease of miR-9-5p expression in both proximal and distal fragments of 6-OHDA rats compared to sham-operated (-99,97 % and -98,54 %, respectively, ($p<0.001$).This is an intriguing result since the inflammatory processes observed in neurodegenerative diseases, like PD, occurs likewise in peripheral regions showing a close brain-gut connection. For this reason miR9-5p might be useful as a potential biomarker of intestinal inflammatory status in PD.

Weilin et al. (2016) Int J Mol Med. 37 (2): 309-318.