

JOINT EVENT

14th International Conference on **Generic Drugs and Biosimilars**
&
9th Global Experts Meeting on **Neuropharmacology**

November 15-16, 2018 | Berlin, Germany

Novel methodology for the development of early diagnosis of Parkinson's disease based on translational medicine**M V Ugrumov**

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Numerous attempts to develop a preclinical diagnosis of neurodegenerative diseases (NDD) - Parkinson's and Alzheimer's disease, by searching peripheral biomarkers as changes in biological fluids and non-motor functions were not successful. A drawback of this methodology is the search for markers in patients at the clinical stage without guarantees that they are characteristic for preclinical stage. Indeed, all markers detected so far are nonspecific. We propose to upgrade this methodology, using only markers found both in patients and animals at modeling clinical and preclinical stages of NDD. Detection of the same marker in patients and symptomatic animals is believed to indicate adequate reproduction of pathogenesis along this metabolic pathway, and detection of this marker in pre-symptomatic animals proves its specificity for preclinical stage. We showed that 50% and 20% of the markers found in blood of patients were characteristic of MPTP-treated symptomatic and pre-symptomatic mice, respectively. Besides, we propose a different approach to early diagnosis of NDD - a provocative test that has long been successfully used in internal medicine. We showed that the systemic administration of α -methyl-p-tyrosine, a reversible inhibitor of dopamine synthesis (provocative agent), to MPTP-treated mice at pre-symptomatic stage results in a reversible decrease in dopamine level in the striatum up to the threshold (30%) and short-term motor disorders. In controls, although the dopamine level decreases under α -methyl-p-tyrosine administration, it does not reach the threshold level and is not accompanied by motor disorders. Thus, we propose a new complex methodology for the development of preclinical diagnosis of NDD.

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