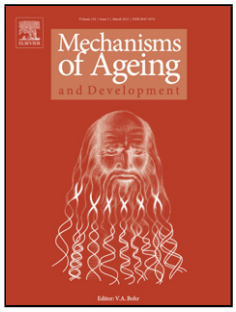

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NFE2L2, PPARGC1α, and pesticides and Parkinson's disease risk and progression

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Running Title: NFE2L2, PPARGC1α, MB/PQ and Parkinson's disease

Highlights:

- Nuclear factor-erythroid 2 related factor 2 (Nrf2) and peroxisome proliferator activator receptor (PPAR) γ coactivator 1α (PGC-1α) are important transcription factors that activate antioxidant defense mechanisms
- In 472 PD patients and 532 population-based controls, we examined three expression-altering *NFE2L2* SNPs and four previously implicated *PPARGC1α* SNPs and their interactions with maneb and paraquat (MB/PQ) pesticide exposure on Parkinson's disease (PD) risk and symptom progression
- *NFE2L2* rs6721961 T allele was associated with a reduced risk of PD and slower cognitive decline
- Statistical interactions were estimated between MB/PQ and two *PPARGC1α* SNPs, such that those with high exposure and the variant allele were at an increased risk of PD
- *PPARGC1α* rs6821591 was associated with faster motor symptom progression as measured with the UPDRS-III
- Our study provides support for the involvement of both *NFE2L2* and *PPARGC1α* in PD susceptibility and progression, marginally and through pathways involving MB/PQ exposure

Abstract