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LETTER

Atractylenolide-I Ameliorates Motor Deficits and Reduces Inflammation of the Spinal Cord by SIRT1/PGC-1α Pathway in MPTP Subacute Mouse Model of Parkinson's Disease [Letter]

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Dear editor

We read with great interest the recent study by Gao et al exploring the therapeutic potential of Atractylenolide-I (ATR-I) in a Parkinson's disease (PD) mouse model. The authors provide valuable insights into ATR-I's role in alleviating motor deficits and reducing inflammation in the MPTP-induced PD mouse model.[1] We particularly appreciate the authors' focus on the SIRT1/PGC-1α pathway and their thorough investigation into the neuroprotective effects of ATR-I.

Gao et al demonstrate that ATR-I not only mitigates motor deficits in the MPTP-induced subacute PD model but also prevents dopaminergic (DA) neuron loss in the substantia nigra pars compacta (SNpc). Additionally, the study shows that ATR-I suppresses microglial activation in both the SNpc and spinal cord. The upregulation of SIRT1/PGC-1α-related proteins in the spinal cord is particularly noteworthy, and the authors suggest that ATR-I has broad neuroprotective properties, positioning it as a promising candidate for PD treatment. While this study is both comprehensive and impressive, we believe several aspects warrant further discussion to strengthen the conclusions and clarify the mechanisms involved.

Firstly, ATR-I is known to exert anti-inflammatory effects through multiple pathways, including ERK1/2, p38, and NF-κB signaling.[2] While the authors focus on the SIRT1/PGC-1α pathway, the study did not directly confirm whether ATR-I's beneficial effects are dependent on this specific pathway. A more definitive demonstration would involve using specific inhibitors of SIRT1 or PGC-1α to validate whether ATR-I's action is indeed mediated through this pathway. Furthermore, the role of upstream regulators, such as NAD+ levels,[3] and downstream effectors, such as genes involved in mitochondrial biogenesis,[4] remains unexplored. Investigating these factors would provide a more comprehensive understanding of how ATR-I modulates the SIRT1/PGC-1α pathway and exerts its neuroprotective effects. Moreover, the study employed only a single dose of ATR-I (30 mg/kg), which limits the ability to assess dose-response relationships. It is well established that varying doses of therapeutic agents can lead to differential activation of cellular pathways, including the SIRT1/PGC-1α axis, and thus may result in distinct therapeutic outcomes. Future studies would benefit from a dose-response analysis to determine the optimal therapeutic window for ATR-I, ensuring both efficacy and safety.

In conclusion, while Gao et al study provides important insights into the therapeutic potential of ATR-I in PD,[1] addressing the aforementioned points would further enhance the rigor and depth of their findings. We believe these considerations will contribute to the translational potential of ATR-I as a viable therapeutic strategy for PD.

Disclosure

The authors report no conflicts of interest in this communication.

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