From Neurotoxin Models to Clinical Evidence: Mechanistic Insights into *Lactiplantibacillus plantarum* PS128 (PS128)-Mediated Modulation of Parkinson's Disease (從神經毒素模型到臨床證據：植物乳桿菌 PS128 調控帕金森氏症之機制探討)

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Speaker: Dr. Fu-Sheng Deng

(鄧福勝 博士)

Abstract

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by dopaminergic neuronal loss, α-synuclein aggregation, and a broad spectrum of motor and non-motor symptoms. Emerging evidence highlights the critical role of the microbiota-gut-brain axis (MGBA) in PD pathogenesis, suggesting that microbiota-targeted interventions may provide novel therapeutic opportunities. *Lactiplantibacillus plantarum* PS128 (PS128), a probiotic strain with neuroprotective effect, has gained increasing attention as a potential adjunctive strategy for PD management. This presentation integrates findings from preclinical and clinical studies to evaluate the therapeutic potential and translational relevance of PS128.

Across multiple toxin-induced animal models, including MPTP, 6-hydroxydopamine (6-OHDA), and rotenone paradigms, PS128 consistently demonstrated protective effects against PD-related pathology. In the MPTP mouse model, PS128 attenuated dopaminergic neuronal degeneration, suppressed neuroinflammatory responses, and restored striatal neurotransmitter levels. In the 6-OHDA rat model, PS128 improved motor deficits and reduced abnormal cortical beta oscillations, indicating its potential to modulate disease-associated neural circuit dysfunction. Notably, in the rotenone-induced model, which captures key features of gut-origin PD pathology, PS128 not only improved motor performance but also regulated gut microbiota composition and inflammatory signaling pathways, thereby providing mechanistic insight into its role in microbiota-gut-brain communication.

Importantly, translational evidence is supported by a pilot clinical study in patients with PD, in which 12-week supplementation with PS128 under stable medication regimens resulted in improvements in motor function and quality of life. Although preliminary, these findings suggest that PS128 is a safe and feasible adjunctive intervention in clinical settings.

Collectively, evidence from diverse experimental models supports the notion that PS128 exerts consistent neuroprotective effects through integrated mechanisms

involving neuroinflammation, neurotransmitter regulation, and the MGBA. These cross-model findings reinforce the translational potential of PS128 from preclinical research to clinical application. Nevertheless, further large-scale, randomized controlled trials and in-depth mechanistic studies are required to validate its efficacy and determine its role in disease modification. This work highlights PS128 as a representative probiotic candidate bridging experimental neuroscience and clinical translation in PD.

Keywords: Parkinson's disease (PD), MPTP, 6-OHDA, rotenone, microbiota-gut-brain axis (MGBA)

References

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