國立臺灣海洋大學食品科學系碩士班
專題討論書面報告

利用秀麗隱桿線蟲探討益生菌與後生元對健康老化與 β-澱粉樣蛋白誘導神經毒性的影響

授課老師：龔瑞林 老師

林家媛 老師

指導教授：陳詠宗 老師

學　　號：11332049

學　　生：周立翔 (5115)

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指導教授簽名:_____

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周立翔 (5115)

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大綱

I. 前言
II. 益生菌與後生元對健康老化的影響
III. 益生菌與後生元透過不同途徑改善 Aβ 誘導神經毒性
IV. 結論

摘要

本研究使用秀麗隱桿線蟲 (*Caenorhabditis elegans*) 動物模型探討益生菌與後生元對健康老化及 Aβ 誘導神經毒性的影響，因應用廣泛且適合研究益生菌特性和分子機制，且因週期短以及可轉殖表達人類 Aβ，所以常用於老化及阿茲海默症的研究。在健康老化方面，熱滅活的 *Levilactobacillus brevis* MKAK9 (HK MKAK9) 及其胞外多醣 (Exopolysaccharides) 能顯著延長線蟲壽命並改善老化指標，透過下調 IIS、上調 p38 MAPK 途徑、增強蛋白穩態（蛋白質泛素化、自噬溶酶體途徑，涉及 *sqst-3, lmp-1*，部分受 *mir-243* 調控）以及提升抗氧化及免疫反應， 而 *Lacticaseibacillus rhamnosus* HA-114 和 *Bacillus subtilis* R0179 也表現出在野生型以及阿茲海默症線蟲株皆可顯著延長壽命。在 Aβ 誘導神經毒性方面，*Lactococcus laudensis* (LL) 和 *Pediococcus parvulus* (PP) 可顯著改善 Aβ 誘導的趨化性降低與癱瘓。其機制是抑制 Aβ 寡聚化及與如卵黃生成素結合從而減少 Aβ 累積，而非影響 Aβ mRNA 表現量；HA-114 和 R0179 也能顯著降低 Aβ 誘導的癱瘓，HA-114 其作用依賴脂肪酸去飽和化途徑（*fat-5* 基因）；而 R0179 的對癱瘓的保護作用則與粒線體自噬（*pink-1* 基因）相關，且熱滅活形式仍具保護作用。以上結果表示益生菌及後生元透過同表型且不同機制影響健康老化及 Aβ 誘導神經毒性，且展現出菌株特異性，具發展年齡相關與阿茲海默症臨床用藥之潛力。

Exploring Probiotic and Postbiotic Effects on Healthy Aging and β-Amyloid –Induced Neurotoxicity in *Caenorhabditis elegans*

周立翔 (5115)

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Outline

I. Introduction
II. Effects of Probiotics and Postbiotics on Healthy Aging
III. Probiotics and Postbiotics Mitigate Aβ-Induced Neurotoxicity through Distinct Pathways
IV. Conclusions

Abstract

Using the nematode *Caenorhabditis elegans* as an animal model, this study investigates how probiotics and postbiotics affect healthy aging and Aβ-induced neurotoxicity. *C. elegans* is widely used to study probiotic properties and molecular mechanisms and owing to its short life cycle and feasibility of transgenic human Aβ expression is commonly used as a model for aging and Alzheimer's disease (AD) research. For healthy aging, heat-killed *Levilactobacillus brevis* MKAK9 (HK MKAK9) and its extracellular polysaccharides (EPS) significantly extend lifespan and improve aging markers by down-regulating IIS and up-regulating the p38 MAPK pathway, enhancing proteostasis (ubiquitination and the autophagy–lysosome pathway involving *sqst-3* and *lmp-1*, partly regulated by *mir-243*), and boosting antioxidant and immune responses. *Lacticaseibacillus rhamnosus* HA-114 and *Bacillus subtilis* R0179 also significantly prolong lifespan in both wild-type and AD worm strains. Regarding Aβ-induced neurotoxicity, *Lactococcus laudensis* (LL) and *Pediococcus parvulus* (PP) significantly alleviate Aβ-induced chemotaxis deficits and paralysis. Mechanistically, they inhibit Aβ oligomerization and its association with host proteins such as vitellogenin, thereby reducing Aβ accumulation rather than altering Aβ mRNA levels. HA-114 and R0179 likewise significantly reduce Aβ-induced paralysis; HA-114 acts via the fatty-acid desaturation pathway (the *fat-5* gene), whereas R0179's protection is linked to mitophagy (the *pink-1* gene) and is retained in the heat-killed form. These results indicate that probiotics and postbiotics influence healthy aging and Aβ-induced neurotoxicity through the same phenotypes but different mechanisms, exhibit strain specificity, and have the potential to be developed into clinical therapeutic strategies for age-related conditions and Alzheimer's disease.

Reference

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