天然保健食品功效研究室

醫學系 張元衍 教授兼教務長

老年性黃斑部病變之動物平台-篩選護眼之保健食品

研究模式

In vitro

ARPE-19 cell line

保健食品萃取物處理 1.5小時

$NaIO_3$處理24 h

- 細胞存活率分析
- 粒線體功能分析
- 抗氧化酵素活性分析
- 探討相關抑制細胞死亡的機轉

In vivo

管餵保健食品3-7天

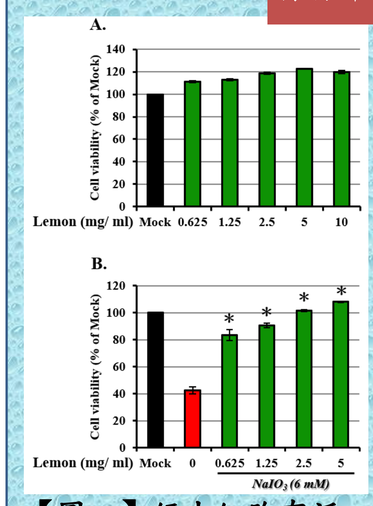
1st d

每日管餵保健食品共7天

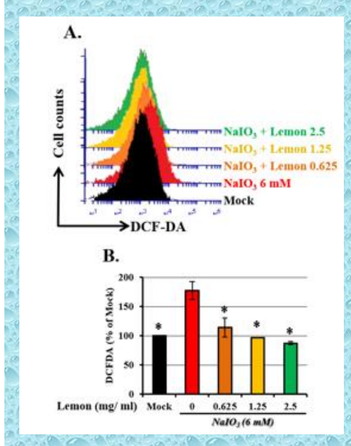
- OCT眼球電腦斷層掃描
- 視網膜電圖(ERG)分析
- 抗氧化酵素活性分析
- 組織學分析
- 預防機制驗證

研究成果

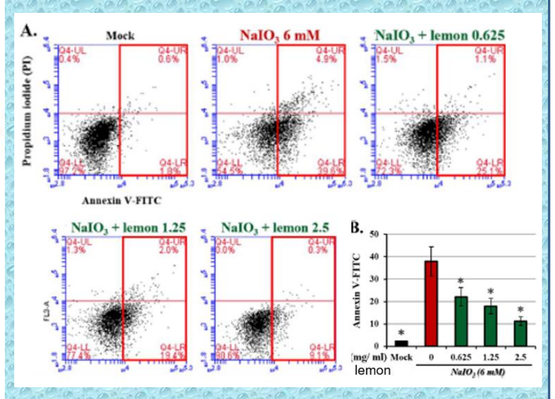
檸檬萃取物:體外細胞實驗初步結果（*in vitro*）



【圖一】經由細胞存活率測試，檸檬萃取物可抑制$NaIO_3$誘發之ARPE-19細胞死亡。

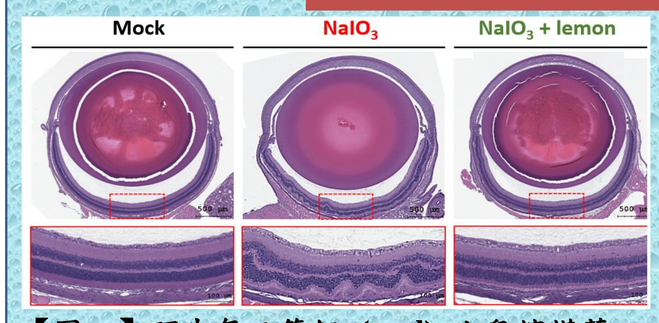


【圖二】檸檬萃取物可減緩 $NaIO_3$ 誘導之ARPE-19細胞ROS上升。

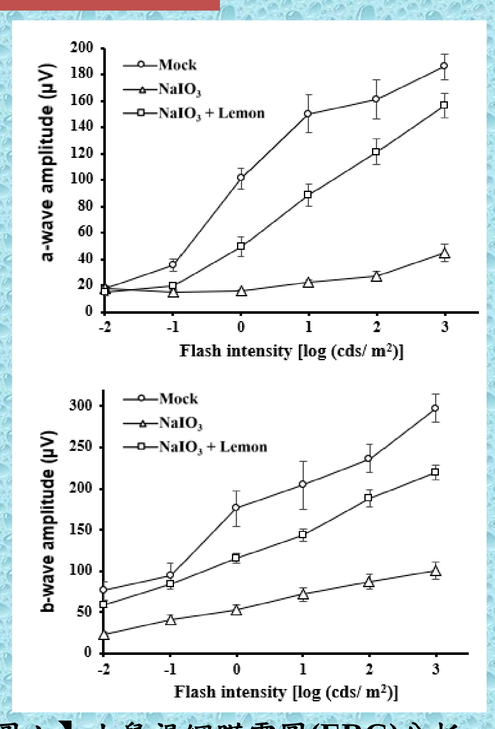


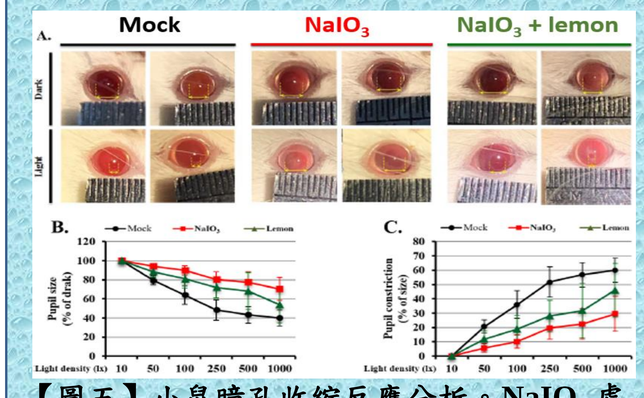
【圖三】 檸檬萃取物可抑制$NaIO_3$誘導ARPE-19細胞凋亡。

檸檬萃取物: 小鼠體內實驗初步結果 (*in vivo*)



【圖四】預先每日管餵 (oral) 小鼠檸檬萃取物，持續一週後，有餵食檸檬萃取物之小鼠組可顯著減緩了視網膜變性的現象。



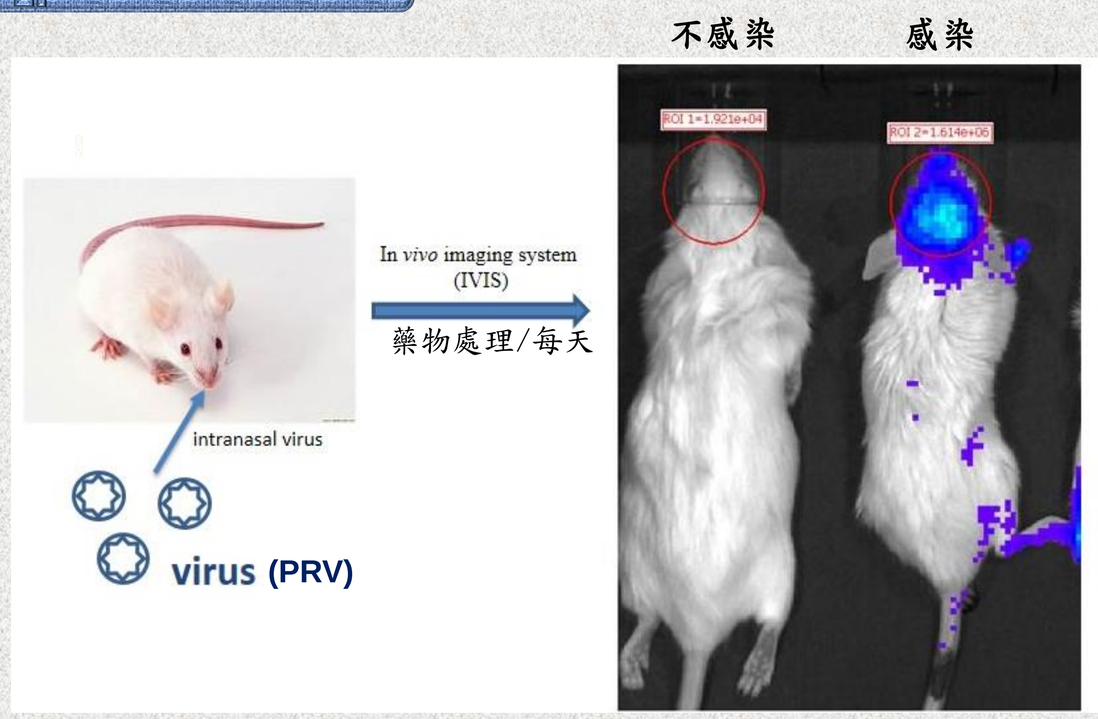


【圖五】小鼠瞳孔收縮反應分析。$NaIO_3$ 處理後會導致感光細胞受損，而影響對光源刺激的的反應，進而導致瞳孔縮放不顯著，檸檬萃取物可抑制$NaIO_3$ 導致感光細胞的受損。

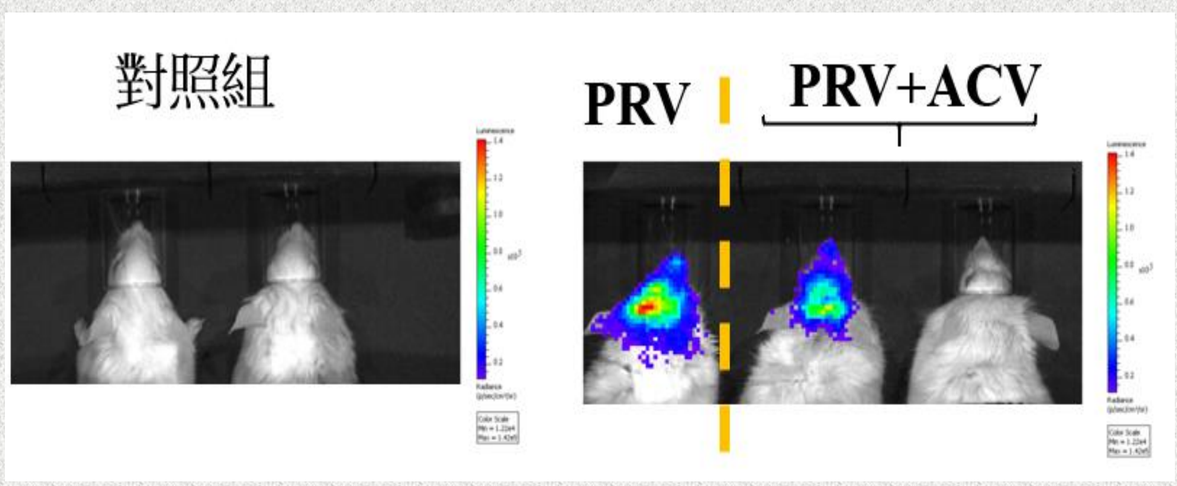
【圖六】小鼠視網膜電圖(ERG)分析。$NaIO_3$ 處理後會導致小鼠ERG中a波與b波振幅顯著下降，而預先餵食檸檬萃取物之小鼠組別 則可顯著回升，這顯示了檸檬萃取物可預防感光細胞(photoreceptor)與雙極細胞(bipolar cells)的損傷。

病毒性腦炎動物模式平台-篩選抗病毒藥物

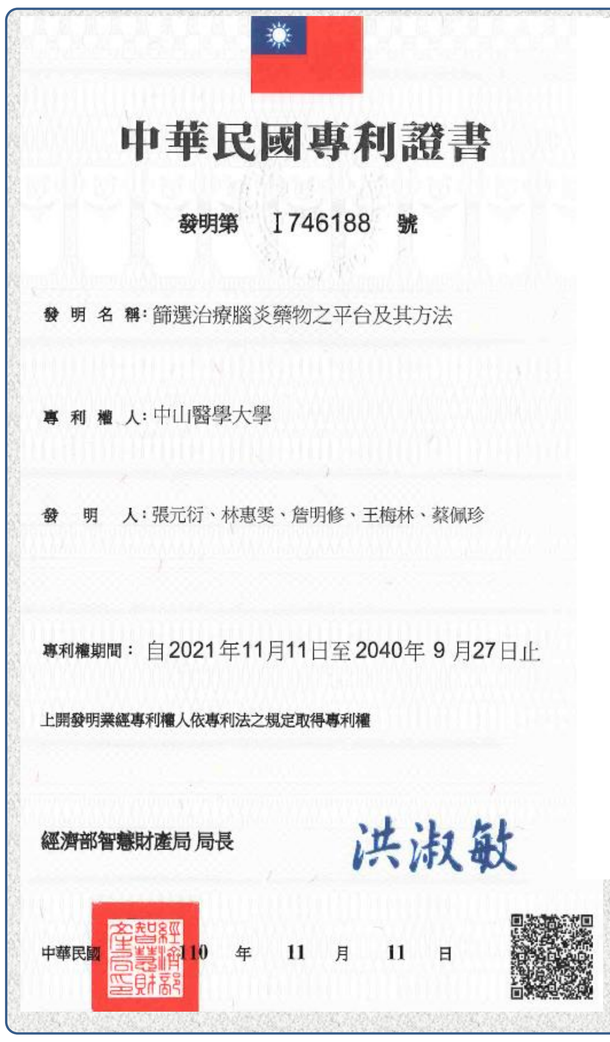
研究模式



研究成果



感染病毒3天後:
(1) PRV組死掉剩1隻，狀況亦不佳，並於第4天死亡；
(2) PRV+ACV(抗病毒藥)剩2隻，有1隻已無腦部炎症反應，另一隻炎症反應相較PRV組顯著下降，最後小鼠並無死亡，存活率提升至67%。



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發明第 I746188 號

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專利權人：中山醫學大學

發明人：張元衍、林惠雯、詹明修、王梅林、蔡佩珍

專利權期間：自2021年11月11日至2040年 9 月27日止

上開發明業經專利權人依專利法之規定取得專利權

經濟部智慧財產局 局長

洪淑敏

中華民國 110 年 11 月 11 日

veterinary sciences

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Article

The Establishment of a Noninvasive Bioluminescence-Specific Viral Encephalitis Model by Pseudorabies Virus-Infected NF-κBp-Luciferase Mice

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Abstract: Encephalitis is a rare brain inflammation that is most commonly caused by a viral infection. In this study, we first use an in vivo imaging system (IVIS) to determine whether NF-κBp-luciferase expression could be detected in the brain of pseudorabies virus (PRV)-infected NF-κBp-luciferase mice and to evaluate proinflammatory mediators in a well-described mouse model of PRV encephalitis. In in vitro studies, we used murine microglia (BV-2) cells to demonstrate the PRV-induced encephalitis model entailing the activation of microglia cells. The results indicate that PRV-induced neuroinflammation responses through the induction of IL-6, TNF-α, COX-2, and iNOS expression occurred via the regulation of NF-κB expression in BV-2 cells. In in vivo studies, compared with MOCK controls, the mice infected with neurovirulent PRV exhibited significantly elevated NF-κB transcription factor activity and luciferase protein expression only in the brain by IVIS. Mild focal necrosis was also observed in the brain. Further examination revealed biomarkers of inflammation, including inducible cyclooxygenase (COX)-2, inducible nitric oxide synthase (iNOS), and tumor necrosis factor (TNF)-α and interleukin (IL)-6, both of which constituted proinflammatory cytokines. PRV infection stimulated inflammation and COX-2 and iNOS expression of IL-6 and TNF-α. The presented results herein suggest that PRV induces iNOS and COX-2 expression in the brain of NF-κBp-luciferase mice via NF-κB activation. In conclusion, we used NF-κBp-luciferase mice to establish a specific virus-induced encephalitis model via PRV intranasal infection. In the future, this in vivo model will provide potential targets for the development of new therapeutic strategies focusing on NF-κB inflammatory biomarkers and the development of drugs for viral inflammatory diseases.