花蓮慈濟醫院研究部

分 子 病 理 及 藥 理 研 究 室

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研究簡介

以ATF3基因轉殖小鼠的動物轉譯模式，觀察氧化壓力及發炎反應，對腦部及身體其他器官如肺部、膀胱及腸道所造成的影響。進而以抗氧化、抗發炎藥物如中藥黃芩素(Baicalein)治療，觀察藥物治療前後，組織之分子病理變化。由此了解氧化壓力所造成的疾病機轉及抗氧化藥物的療效。

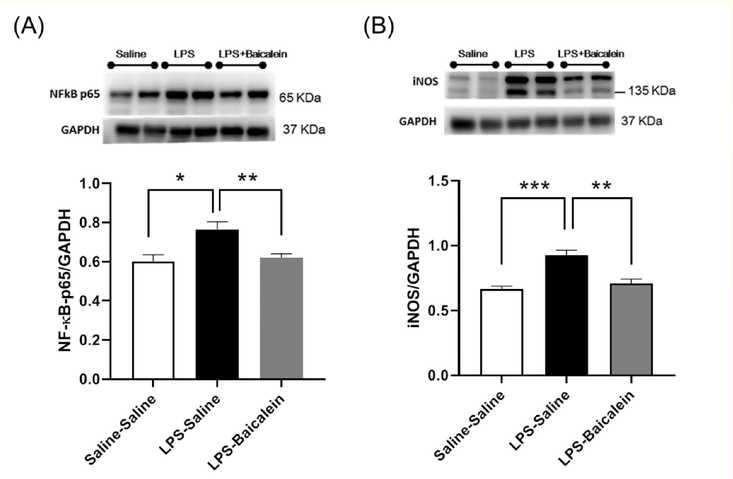

Figure 6. Effect of Baicalein on the protein levels of NF-κB-p65 and iNOS in the hippocampi of mice. Levels of NF-κB-p65 (**A**) and iNOS (**B**) in the hippocampus increased after administration of LPS (5 mg/kg, i.p.). Treatment with baicalein (3 mg/kg, i.p.) 1 h after LPS administration could significantly reduce the levels of both proteins. Data are presented as means ± SEM. ($n = 8$) * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

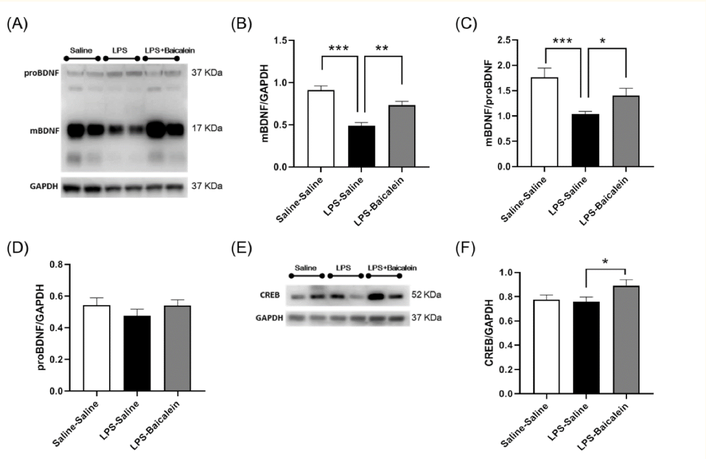

Figure 7. Effect of baicalein on the protein levels of BDNF and CREB in the hippocampi of mice. (**A**) Western blots showing levels of mBDNF and proBDNF. The levels of mBDNF (**B**) and the ratio of mBDNF/proBDNF (**C**) in the hippocampus decreased significantly after the administration of LPS (5 mg/kg, i.p.). Treatment with baicalein (3 mg/kg, i.p.) 1 h following LPS administration could inhibit the reduction. The levels of proBDNF (**D**) did not differ among the groups. (**E**) Western blots showing levels of CREB. Baicalein promoted a significant increase in the expression of CREB protein (**F**), as observed in LPS-Baicalein-treated mice. Data are presented as means ± SEM. ($n = 8$) * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

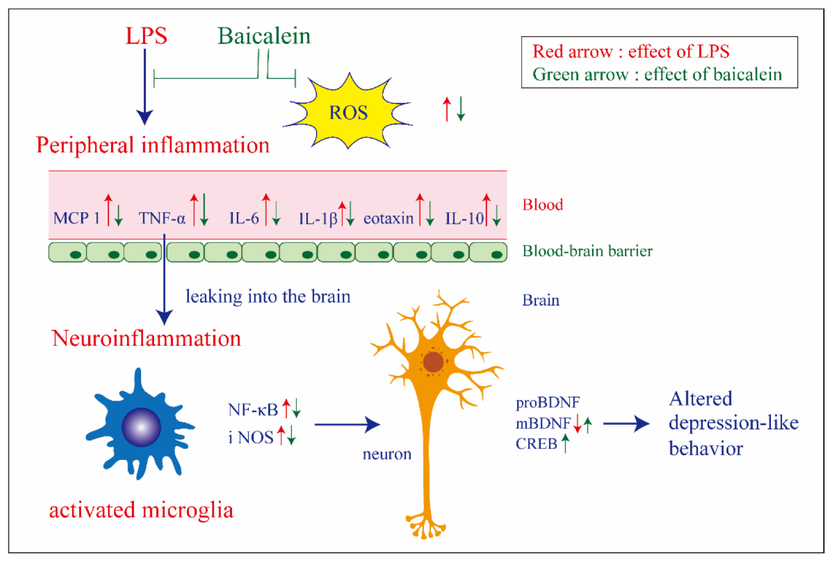

Figure 8. Graphic summary of the antidepressant effect of baicalein on LPS-induced depression-like behavior in mice and the possible mechanism involved. By decreasing the overproduction of reactive oxidative species (ROS) and pro-inflammatory cytokines (IL-6, TNF-α, MCP-1, and eotaxin), baicalein could attenuate neuroinflammation and restore the protein level of the mature brain-derived neurotrophic factor (mBDNF) in the hippocampus, thus contributing to the diminishing of depression-like behavior.

計畫與經費來源

計 畫 名 稱	計畫內擔任之工作	起迄年月
探討活化轉錄因子3於氧化壓力造成膀胱損傷之角色TCRD107-43; TCRD108-42	主持人	107/01/01~108/12/31
中藥黃芩應用於治療情緒疾病功效之評估TCRD108-62	共同主持人	108/01/01~108/12/31
中藥黃芩素於小鼠慢性結腸發炎所誘發情緒疾病之療效評估TCRD109-84	共同主持人	109/01/01~109/12/31
血液疾病病患的端粒動態變化(1/3):利用流式細胞儀 - 螢光原位雜交技術測量端粒長度TCRD109-92RB	共同主持人	109/01/01~109/12/31
小分子核糖核酸-155-5p 及活化轉錄因子 3 於敗血症引發肺損傷之分子機轉TCRD110-31	主持人	110/01/01~110/12/31
血液疾病病患的端粒動態變化(2/3)：週邊血造血幹細胞驅動過程中的端粒動態變化。TCRD111-053	共同主持人	111/01/01~111/12/31
探討黃芩素對腸道發炎疾病的療效及機轉--檢測端粒長度及發炎細胞因子變化。TCRD113-061	主持人	113/01/01~113/12/31

研究成果

1. **Wen, Z. H.; Kuo, H. M.; Shih, P. C.; Hsu, L. C.; Chuang, J. M.; Chen, N. F.; Sun, H. W.; Liu, H. T.; Sung, C. S.; Chen, W. F., Isoaaptamine increases ROS levels causing autophagy and mitochondria-mediated apoptosis in glioblastoma multiforme cells. Biomed Pharmacother 2023, 160, 114359. (IF:7.76)**

2. **Liu, H. T.*; Lin, Y. N*.; Tsai, M. C.; Wu, Y. C.; Lee, M. C., Baicalein Exerts Therapeutic Effects against Endotoxin-Induced Depression-like Behavior in Mice by Decreasing Inflammatory Cytokines and Increasing Brain-Derived Neurotrophic Factor Levels. Antioxidants (Basel) 2022, 11, (5). (IF:7.07) (*: first author)**

3. **Li, H. F*.; Liu, H. T*.; Chen, P. Y.; Lin, H.; Tseng, T. L., Role of PVAT in obesity-related cardiovascular disease through the buffering activity of ATF3. iScience 2022, 25, (12), 105631. (IF:6.01) (*: equivalent to first author)**

4. **Hsu, S. Y.; Wen, Z. H.; Shih, P. C.; Kuo, H. M.; Lin, S. C.; Liu, H. T.; Lee, Y. H.; Wang, Y. J.; Chen, W. F.; Chen, N. F., Sinularin Induces Oxidative Stress-Mediated Apoptosis and Mitochondrial Dysfunction, and Inhibits Angiogenesis in Glioblastoma Cells. Antioxidants (Basel) 2022, 11, (8). (IF:7.07)**

5. **Chen, Y. J.; Lu, J. T.; Huang, C. W.; Wu, W. H.; Lee, K. F.; Liu, H. T.*; Shih-Hsin Wu, L*., Pharmacogenetic study of methadone treatment for heroin addiction: associations between drug-metabolizing gene polymorphisms and treatment efficacy. Pharmacogenet Genomics 2022, 32, (1), 31-38. (IF:2.6) (*: equivalent to corresponding author)**

6. **Wen, Z. H.; Huang, J. S.; Lin, Y. Y.; Yao, Z. K.; Lai, Y. C.; Chen, W. F.; Liu, H. T.; Lin, S. C.; Tsai, Y. C.; Tsai, T. C.; Jean, Y. H., Chondroprotective Effects of a Histone Deacetylase Inhibitor, Panobinostat, on Pain Behavior and Cartilage Degradation in Anterior Cruciate Ligament Transection-Induced Experimental Osteoarthritic Rats. Int J Mol Sci 2021, 22, (14). (IF:5.60)**

2024.06.2更新