• 系統編號	RC9101-0178		
• 計畫中文名稱	篩選活化 PPAPR 之天然化物及其活化路徑之研究		
• 計畫英文名稱	Screening PPARr Ligands From Natural Products and Study on the Activation Pathways		
• 主管機關	行政院國家科學委員會	• 計畫編號	NSC89-2320-B038-075
• 執行機構	台北醫學院醫學系		
• 本期期間	8909 ~ 9007		
• 報告頁數	14 頁	• 使用語言	中文
• 研究人員	梁有志 Liang, Yu-Chih		
• 中文關鍵字	促進過氧化體增生活化受器；活化機制；環氧酵素；一氧化氮合成脢？；類黃酮		
• 英文關鍵字	Peroxisome proliferator-activated receptor (PPAR)；Activation mechanism；Cyclooxygenase；Nitric oxide synthase；Flavonoid		
• 中文摘要	PPARa (過氧化體增殖活化受體) 的活化與抗發炎作用有關。在本次計畫中，篩選 20 餘種類黃素，發現三種類黃素 apigenin, chrysin 及 kaempferol 能有效地活化 PPARa 。在吞噬細胞中，過度表現 PPARa ，可增強此三種類黃素之抑制 LPS 所活化的 COX-2 及 iNOS 。然而在體外的競爭結合分析，發現此三種類黃素只有微弱的 PPARa agonist 活性。有限度蛋白 分解試驗，顯示此三種類黃素會改變 PPARa 的構形，但不同於結合 BRL49653 之 PPARa 。這些結果顯示，此三種類黃素可作爲 PPARa 之 allosteric effectors ，結合在 PPARa 上，並活化之，但結合的位置似乎不同於 BRL49653		
• 英文摘要	PPARg transcription factor has been implicated in anti-inflammatory response. Of the compounds tested, apigenin, chrysin, and kaempferol significantly stimulated PPARg transcriptional activity in a transient reporter assay. In addition, these three flavonoids strongly enhanced the inhibition of inducible cyclooxygenase (COX-2) and nitric oxide synthase (iNOS) promoter activities in LPS-activated macrophages which containing the PPARg expression plasmids. However, these three flavonoids exhibited weak PPARg agonist activities in vitro competitive binding assay. Limited protease digestion of PPARg suggested these three flavonoids produced a conformational change in PPARg and the conformation differences in the receptorbound to BRL49653 versus these three flavonoids. These results suggested that these three flavonoids might act as allosteric effectors and were able to bind to PPARg and activate it, but it’s binding site might be different from the natural ligand BRL49653. Key words: Peroxisome proliferator-activated receptor-g, Flavonoids, Inflammation, Cyclooxygenase, Nitric oxide synthase.		