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• 計畫英文名稱	Studies on the Proinflammatory Mediators Release Induced by Peptidoglycan from Gram-Positive Organis (II)
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• 中文關鍵字	巨噬細胞; 環氧化脢-2,
• 英文關鍵字	Macrophage; Cyclooxygenase-2, Rac 1, Phosphatidylinositiol 3-kinase (PI3K), Akt, NF-kappaB, Peptidoglycan (PGN)
• 中文摘要	先前我們發現金黃色葡萄球菌細胞壁成份 peptidoglycan(PGN)可經由 Ras/Raf/ERK 訊息傳遞途徑，經由 IKKalpha/beta 及 NF-kappaB 的活化來誘導 RAW 264.7 巨噬細胞環氧化脢-2(COX-2)的表現。在本計劃中，我們將探討 Rac 1, phosphatidylinositiol 3-kinase (PI3K)及 Akt 在 PGN 誘導 RAW 264.7 巨噬細胞 NF-kappaB 活化及 COX-2 表現所扮演的角色。PGN 誘導 COX-2 表現可被 Rac1 dominant negative mutant(RacN17)，PI3K 抑制劑(wortamanin 及 LY294002)及 Akt 抑制劑 (1L-6-Hydroxymethyl-chiro-inositol2-[(R)-2-O-methyl-3-O-octadecyl carbonate])所抑制。RAW 264.7 巨噬細胞給予 PGN 可以誘導 Rac1 及 Akt 的活化。PGN 誘導 Akt 的活化可被 RacN17，LY294002 及 Akt inhibitor 所抑制。PGN 增加 IKKalpha/beta？猍瑭 C 酸化會被 RacN17，LY294002 及 Akt inhibitor 所抑制。PGN 增加 NF-kappaB 的活性同樣也會被 RacN17，wortmannin，LY294002，Akt inhibitor 及 AktDN 所抑制。巨噬細胞給予 PGN 可依時間依賴誘導 p85 及 Rac1 與 too-like receptor 2(TLR2)結合在一起。經由以上的結果顯示，在 RAW 264.7 巨噬細胞中，PGN 可由 Rac1/PI3K/Akt 路徑，會使 IKKalpha/beta 之磷酸及 NF-kappaB 活化，最後誘導 COX-2 的表現。
• 英文摘要	Previously, we found that peptidoglycan (PGN), a cell wall component of the gram-positive bacterium Staphylococcus aureus, may activate the as/Raf-1/extracellular signal-regulated kinase (ERK) pathway, which in turn initiates IkappaB kinases/(IKKalpha/beta) and nuclear factor-kappaB (NF-kappaB) activation, and ultimately induces cyclooxygenase-2 (COX-2) expression in RAW 264.7 macrophages. In this study, we further investigated the role of Rac 1, phosphatidylinositiol 3-kinase (PI3K), and Akt in PGN-induced

NF-kappaB activation and COX-2 expression in RAW 264.7 macrophages. PGN-induced COX-2 expression was attenuated by a Rac1 dominant negative mutant (Rac1N17), PI3K inhibitors (wortamanin and LY 294002), and the Akt inhibitor (1L-6-Hydroxymethyl-chiro-inositol2-[(R)-2-O-methyl-3-O-octadecyl carbonate]. Stimulation of RAW 264.7 macrophages with PGN caused the activation of Rac1 and Akt. The PGN-induced Akt activation was inhibited by Rac1N17, LY 294002, and the Akt inhibitor. The PGN-induced increases in IKKalpha/beta？烚 hosphorylation was inhibited by Rac1N17, LY 294002, and the Akt inhibitor. The PGN-induced increases in kappaB-luciferase activity was also inhibited by Rac1N17, wortmannin, LY 294002, the Akt inhibitor, and an Akt dominant negative mutant (AktDN). Treatment of macrophages with PGN induced the recruitment of p85？娗 nd Rac1 to toll-like receptor 2 (TLR2) in a time-dependent manner. These results indicate that PGN may activate the Rac1/PI3K/Akt pathway, which in turn initiates IKKalpha/beta？烚 hosphorylation, and NF-kappaB activation, and ultimately induces COX-2 expression in RAW 264.7 macrophages.