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• 中文關鍵字	發炎;轉錄因子;細胞激素巨;脂質媒介物質;單核球/噬細胞	
• 英文關鍵字	Inflammation, Transcription Factors, Cytokines, Lipid Mediators, Monocytes/Macrophage	
• 中文摘要	<p>在本研究中，我們將探討革蘭氏陽性菌細胞壁成分 peptidoglycan (PGN)誘導 RAW264.7 巨噬細胞 IL-6 產生之訊息傳遞路徑。PGN 依劑量及時間相關曲線增加 IL-6、PGE2 及 cAMP 的產生。PGN 媒介 IL-6 產生可被非選擇性 COX 抑制劑(indomethacin)、選擇性 COX 抑制劑(NS398)、PGE2 (EP2)拮抗劑(AH6809)、EP4 拮抗劑(AH23848)及 protein kinase A 抑制劑(KT5720) 所抑制，但不受非選擇性 NO synthase 抑制劑(NG-nitro-arginine methyl ester)所抑制。更進一步 PGE2、EP2 作用劑(butaprost)、EP2/PGE3 (EP3)/EP4 作用劑(mioprostol)及具有 AH6809 與 mioprostol 共同存在下皆可誘導 IL-6 產生，然而 EP1/EP3 作用劑(sulprostone) 則不會。PGN 可以依照時間曲線活化 IκB kinase α/β (IKKα/β)及 p65 之 Ser276 之磷酸化，這些作用可被 NS398 及 KT5720 所抑制。PGE2 及 8-bromo-cAMP 二者也可以誘導 IKKα/β 之磷酸化。PGN 可以依二項增加 NF-κB-特異 DNA-蛋白複合物的形成，第一項 NF-κB 的活化發生在 10-60 分，而第二項則發生在 2-12 小時。PGN 增加 κB-luciferase 的活性可被 NS398、AH6809、AH23848、KT5720、protein kinase C 抑制劑(Ro31-8220)及 p38 MAPK 抑制劑(SB203580)所抑制。經由以上的結果發現 PGN 誘導 IL-6 的產生其中包含 COX-2 產生 PGE2、活化 EP2/EP4 受體、cAMP 形成、活化 PKA、PKC、p38 MAPK、IKKα/β、p65 磷酸化及 NF-κB。然而 PGN 誘導 NO 釋放並不參與在 PGN 誘導 IL-6 的產生。</p>	
• 英文摘要	<p>Inflammation, Transcription factor, Cytokines, Lipid mediators, Monocytes/Macrophage In this study, we investigated the signaling pathway involved in interleukin-6 (IL-6) production caused by peptidoglycan (PGN), a cell wall component of the gram-positive bacterium, Staphylococcus aureus, in RAW 264.7 macrophages. PGN caused concentration- and time-dependent</p>	

increases in IL-6, PGE2 and cAMP production. PGN-mediated IL-6 production was inhibited by a non-selective cyclooxygenase (COX) inhibitor (indomethacin), a selective COX-2 inhibitor (NS398), an EP2 antagonist (AH6809), an EP4 antagonist (AH23848), and a protein kinase A (PKA) inhibitor (KT5720), but not by a non-selective nitric oxide synthase inhibitor (NG-nitro-arginine methyl ester). Furthermore, PGE2, an EP2 agonist (butaprost), an EP2/EP3/EP4 agonist (misoprostol), and misoprostol in the presence of AH6809 all induced IL-6 production, whereas an EP1/EP3 agonist (sulprostone) did not. PGN caused time-dependent activations of IKK $\alpha$ /IKK $\beta$  and p65 phosphorylation at Ser276, and these effects were inhibited by NS398 and KT5720. Both PGE2 and 8-bromo-cAMP, also caused IKK $\alpha$ /IKK $\beta$  phosphorylation. PGN resulted in two waves of the formation of NF- $\kappa$ B-specific DNA-protein complexes. The first wave of NF- $\kappa$ B activation occurred at 10~60 min of treatment, while the later wave occurred at 2~12 h of treatment. The PGN-induced increase in  $\kappa$ B-luciferase activity was inhibited by NS398, AH6809, AH23848, KT5720, a PKC inhibitor (Ro31-8220), and a p38 MAPK inhibitor (SB203580). These results suggest that PGN-induced IL-6 production involves COX-2-generated PGE2, activation of the EP2 and EP4 receptors, cAMP formation, and the activation of PKA, PKC, p38 MAPK, IKK $\alpha$ /IKK $\beta$ , p65 phosphorylation, and NF- $\kappa$ B. However, PGN-induced nitric oxide release is not involved in the signaling pathway of PGN-induced IL-6 production.