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• 計畫英文名稱	Functional Characterization of Chemokines Induced by Activation of Lymphotoxin Beta Receptor (II)
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• 中文關鍵字	乙型淋巴毒素受體; 化學激素
• 英文關鍵字	Lymphotoxin beta receptor; Chemokine
• 中文摘要	乙型淋巴毒素受體屬於腫瘤壞死因子受體家族的成員之一，其 ligand 包括在細胞膜上 trimers LTalpha1/beta2、LTalpha2/beta1、與 LIGHT (homologous to lymphotoxins, showsinducible expression, and competes with herpes simplex virus glycoprotein D forherpesvirus entry mediator, a receptor expressed by T lymphocytes)，除了 T 與 B 淋巴球外，乙型淋巴毒素受體幾乎表現於所有細胞。現在有許多證據顯示，乙型淋巴毒素受體除了對於淋巴系統的發育極爲重要外，其也參與發炎反應的進行，並能調節化學激素的分泌。然而乙型淋巴毒素受體在非免疫細胞調節化學激素的機制，及此種調節作用其功能上的重要性，所知仍十分有限。本實驗選擇肺泡上皮 A549 細胞，分別就 mRNA 和蛋白質兩種層次來分析乙型淋巴毒素受體活化後，所影響的化學激素層面爲何。我們最近的研究發現 RANTES (regulated onactivation, normal T cell expressed, and presumable secreted) 此種化學激素，可在細胞受乙型淋巴毒素受體活化刺激 48 小時後誘發出來，而乙型淋巴毒素受體下游訊息傳導的分子，參與了 RANTES 誘發之調控。之前研究指出許多化學激素的 promoter 區域內，含有許多轉錄因子可結合的 cis-element，尤其 NF-？辣 結合的位置，在很多化學激素的 promoter 區域都被發現，在本實驗將針對乙型淋巴毒素受體所誘發的化學激素，分別由何種訊息傳導途徑引發來做一討論。單一化學激素的功能多年來已被探討，但愈來愈多的證據顯示在多種化學激素的協同作用下，細胞的行爲及功能受到明顯的影響。乙型淋巴毒素受體活化 A549 細胞所釋放的化學激素，其個別在白血球趨化作用的重要性，本實驗也將探討。
• 英文摘要	The lymphotoxin beta receptor (LTbetaR) has been shown to be the receptor for the membrane bound lymphotoxin trimers LTalpha1/beta2, LTalpha2/beta1 and LIGHT (homologous to lymphotoxins, shows inducible expression, and competes with herpes simplex virus glycoprotein D

for herpesvirus entry mediator, a receptor expressed by T lymphocytes), and LTbetaR is expressed on the surface of most cell types, except T and B lymphocytes. There are evidences to demonstrate that LTbetaR plays critical roles not only in the development of the secondary lymphoid system but also in the establishment of ectopic organized lymphoid structures in chronically inflamed sites. LTbetaR has been reported to stimulate chemokine secretion in inflammation. However, the mechanism and the functional significance of chemokines induced by LTbetaR activation on non-immune cells are still limited. In this study, we use LTbetaR-stimulated bronchial epithelial A549 cells as a system to investigate the chemokine profile at the mRNA and protein level. Our current study has shown that RANTES (regulated on activation, normal T cell expressed, and presumable secreted) secretion can be induced 48 hours after LTbetaR ligation, and molecules downstream of LTbetaR can regulate it's production. Since most promoters region of chemokines contain indispensable cis-elements for several trans-activating factors, especially sites for NF-kappaB, and LTbetaR induce sequential activation of distinct NF-kappaB factors (classical p50-RelA, p52-RelB) by different signaling pathways, the identification of different NF-kappaB activation for LTbetaR-induced chemokine is crucial in this study. The functional significance of individual chemokine induced by LTbetaR in leukocyte chemotaxis will also be dissected.