• 計畫中文名稱	以基因剔除小鼠爲基礎之環境荷爾蒙於肺腺癌致癌效應之研究		
• 計畫英文名稱	A gene-targeting mouse model for effects of environmental hormones on carcinogenesis of lung adenocarcinoma		
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• 計畫編號	DOH96-TD-G-111-018	• 研究方式	委託研究
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• 研究人員	葉劭德		
• 中文關鍵字	雄性素受體；肺腺癌；基因剔除小鼠；Cre-lox 系統；環境荷爾蒙；；；		
• 英文關鍵字	environmental hormone；androgen receptor；adenocarcinoma；lung cancer；cre-lox system；knockout mouse；；		
• 中文摘要	肺癌是台灣癌症死亡率第一位，也是全世界癌症發生率最高的疾病，因此肺癌的成因、預防、與治療是全人類的重要課題。許多環境污染物質如硝基多環芳香族化合物會造成基因突變而進行肺癌發生的起始階段，此類化合物與肺癌的致癌機制較爲了解。另有一些化學物質如多氯聯苯、戴奧辛等，被發現會干擾性腺激素的正常功能，同時也會引起肺腺癌的產生。其次，過去流行病學的研究發現肺癌在兩性之間有許多差異；男性肺癌的罹患率高於女性，但女性罹患肺腺癌的比例卻高於男性。女性罹患肺腺癌與廚房烹煮的油煙有關；且女性肺腺癌對於 Irressa 治療的療效較佳。但是導致這些兩性差異的確實原因卻仍有許多未知之處。爲了進一步了解環境荷爾蒙與肺腺癌之關係，本研究希望建立一種研究環境荷爾蒙與肺腺癌癌化過程的分子機制之小鼠的平台，此平台的建立將對於對於了解肺腺癌的病因、預防、與治療有重要的幫助。過去吾等的研究，已經利用 Cre-lox 系統製造雄性素受體之基因剔除小鼠，並證實此小鼠的表現型，與雄性素受體先天突變之 tfm 小鼠相同。其次，藉由細胞專一表現 Cre 之基因轉殖小鼠與此小鼠交配，產生於睪丸內不同細胞專一之雄性素受體之基因剔除小鼠，並證實雄性素受體於 Sertoli 氏細胞、Leydig 氏細胞、與生殖細胞內有不同功能。在本研究中將運用此雄性素受體基因剔除小鼠之有力工具，建立環境荷爾蒙誘發肺腺癌之平台，並利用此雄性素受體基因剔除肺腺癌小鼠探討環境荷爾蒙對肺腺癌癌化過程之效應，進一步釐清環境荷爾蒙與雄性素受體之交互作用。		
• 英文摘要	Environmental pollutants including cooking oil fumes, cigarette smoke, and automobile emissions are the major causes of lung		

	cancer. Some of chemical carcinogens (environmental hormones) in lung cancer such as dioxins can affect the endocrine system especially the sexual development. It has been suggested that other factors such as sex steroids may act as cocarcinogens, especially in lung adenocarcinoma, the most common histologic type among women. It was proposed that carcinogenesis induced by environmental hormones and the gender differences in lung adenocarcinoma were based on different genetic background induced by sex hormones and their receptors. Although research has clearly shown that environmental hormones can act at multiple sites via multiple mechanisms, receptor-mediated mechanisms have received the most attention. Therefore, it is very important to establish a gene-targeting mouse model to demonstrate the effects of sex steroid hormone receptors during carcinogenesis in lung adenocarcinoma induced by chemical carcinogens. In this proposed study, we will establish a mouse system to demonstrate the interaction between environmental hormones and androgen receptor gene in lung cancer. In previous studies, we have generated androgen receptor and estrogen receptor knockout mice model by using the Cre-lox strategy. In this proposed study, we will apply the same conditional knockout strategy in lung carcinogenesis to generate a gene-targeting mouse model for environmental hormone-induced carcinogensis.