Gα11 Pseudogene在血癌細胞株K562分化之研究 = The Studies of the Gα11 Pseudogene in Leukemia Cell Line K562 Differentiat

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摘 要

異三單元鳥嘌呤核?酸結合蛋白 (heterotrimeric guanine nucleotide-binding proteins, G-protein)，負責傳遞細胞膜上G蛋白耦合受體接收之訊號，將訊號擴大並傳遞至細胞內部啟動訊息路徑。對於細胞生長、分化及發育上極具影響性。慢性骨髓性血癌 (CML) 是一種骨髓多能性造血幹細胞不正常增生性疾病。患者骨髓細胞帶有費城染色體產生致癌基因BCR-ABL融合蛋白，此種細胞失去了正常血球細胞應有的分化能力及老化死亡現象。近幾年來誘導細胞分化療法被提出，利用誘導劑誘導較惡性或轉移性腫瘤使其走向成熟途徑，恢復分化能力成為正常有功能之細胞，而達到治療的目的。本研究選用K562是第一個來自人類慢性骨髓性血癌的永生細胞株，屬於尚未走向終點分化之多能性造血前驅細胞，給予不同的試劑可誘導成紅血球系或巨核細胞系，因此適合做為探討細胞分化和細胞內訊息傳遞研究之模式細胞。本試驗研究策略以中草藥黃耆萃取物、Hemin、HMBA來誘導細胞分化為有功能性之細胞，以合成β血紅球蛋白、γ血紅球蛋白以及巨核細胞之標記蛋白CD41和CD61做為分析指標，並於誘導過程中分析不同異三單元體G蛋白α次單元之表現變化。前人文獻已提出K562細胞之異三單元體G蛋白之Gα11 pseudogene可透過黃耆萃取液誘導而提高表現量。本論文進一步証實其真實性，在Promoter assay中發現添加黃耆萃取液可增加Gα11 pseudogene啟動子之活性。在三種誘導劑影響下，其中HMBA誘導Gα11 pseudogene表現最為明顯，不過K562細胞之其他功能性細胞分化標記未有明顯之變化，探討其原因可能為細胞培養受胎牛血清的影響，使其細胞特性改變，以及轉染效率低以至於使細胞沒有表現該基因。目前已重新電轉高濃度之表現載體於K562細胞，以觀察在Gα11和Gαq等過量表現下對細胞之影響，挑選穩定表現之細胞株 (stable clone) 正進行中，期望可以表現真正應有的功能，以了解異三單元體G蛋白與細胞分化的關聯性，提供未來分化療法及治療血癌之參考。

關鍵詞 : K562細胞、黃耆、Hemin、HMBA、Gαq、Gα11、Gα11 pseudogene

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