六號腺?酸環化?在藥物誘導K562細胞分化巨核細胞過程之分析

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摘 要

慢性骨髓性血癌（CML）為一種造血幹細胞失控之疾病，造血幹細胞係補充體內氣體交換之紅血球、凝血功能之血小板、免疫相關之白血球、漿細胞、淋巴細胞，巨噬細胞等。慢性骨髓性血癌患者一旦發病後這些功能性細胞會逐漸減少，反之未分化且不正常增生之前驅細胞比例逐漸增加。因此，誘導細胞分化的結果，可應用於改善患者因功能性細胞降低的不適。K562細胞乃分離自處於急性期之慢性骨髓性血癌患者之胸肋膜滲液。在體外培養仍具有費城染色體特性之細胞株。而K562細胞處於尚未分化之細胞，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為誘導劑試圖誘導K562分化為特定細胞株系，結果顯示HMBA可誘導出血小板前驅巨核細胞之標記CD61，黃耆萃取物可誘導出較早期之巨核細胞標記CD41。前人文獻已提出K562細胞之異三單元體G蛋白之Gi2次單元和Gs次單元可透過HMBA誘導而提高表現量，因此探討兩個次單元之下游作用體腺?酸環化?（ADCY）。以RT-PCR分析經三種誘導劑誘導之K562細胞中九種ADCY異構物基因表現量，試圖找出和細胞分化相關之ADCY異構物。其中ADCY1和ADCY6受到HMBA誘導。由於ADCY1主要表現於腦，ADCY6全面性存在於細胞。因此以ADCY6為研究對象。本試驗以電破法轉染質體DNA進入K562細胞使之大量表現ADCY6，接著以三種誘導劑分別誘導已轉染之K562細胞株。以RT-PCR分析其細胞分化標記之基因表現量。K562細胞經轉染後，ADCY6確實有大量表現，於此情形下，只有ADCY6大量表現亦提高K562細胞之CD61 mRNA表現量。三種誘導劑皆可促使K562細胞大量提高CD61 mRNA之表現，顯示ADCY6參與巨核細胞分化，而誘導劑訊號可能經過ADCY6使K562細胞走向巨核細胞分化途徑。在三種誘導劑影響下，K562細胞之其它功能性細胞分化標記未有如巨核細胞標記般之變化。本試驗發現K562細胞可經由ADCY異構物改變信號路徑，以改變細胞分化路徑，可做為基因治療血癌之參考。

關鍵詞 : K562細胞、巨核細胞、HMBA、異三單元體G蛋白、腺?酸環化?

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