不同型G蛋白在藥劑誘導K562細胞分化下所扮演調合者角色 = G-Proteins play concerted roles in chemical induced K562 cell ...

來國鈞、李泰林

E-mail: 9708017@mail.dyu.edu.tw

摘 要

人類慢性骨髓性白血病細胞株 (chronic myeloid leukemia cell line, CML) K562，於不同之誘導劑，如Hemin、HMBA、sodium butyrate及DMSO等刺激下，可使K562血癌細胞分化成具有功能性之紅血球細胞。而異三元體鳥糞嘌呤核酸結合蛋白 (heterotrimeric guanine nucleotide binding proteins)，簡稱G 蛋白 (G-protein)，其位於細胞內雙層膜內部，為膜上之周邊蛋白 (peripheral protein) 的一種，是負責接受細胞膜上受體 (G protein coupled receptor, GPCR) 所耦合 (couple) 之訊號後，以放大 (amplification) 訊號並活化作用體 (effector)，切換 (switch) 之傳遞路徑。G蛋白於訊息傳遞中扮演著最重要之一環，於荷爾蒙 (hormones) 的調控、細胞之生長、分化 (differentiation) 及發育 (development) 上，為極具重要之角色。而G蛋白是由?恁B β 和 γ 三種次單元 (subunit) 所組合而成，而其中G蛋白?悁董璊落膃蛄TPase之活性，能夠水解 (hydrolysis) GTP成GDP。而依據蛋白質功能性與同源性的不同，可分為四大家族：Gs、Gi / o、Gq / 11和G12 / 13。本研究使用K562人類血癌細胞株作為模式細胞，利用Hemin、HMBA以及黃耆 (Huangqi) 來誘導細胞進行分化，以合成 β -球蛋白 (globin) 或 γ -球蛋白作為分析指標，並以半定量反轉錄? – 聚合?連鎖反應 (semi-quantitative RT-PCR) 分析不同誘導劑誘導後不同家族之G蛋白?悁董璊葵穮{變化。從試驗中觀察到四種基因為GNAS isoform (GNAS和GNASS)、G α i2、G α 11以及G α 11 pseudo gene，其中： (1) G α i2於HMBA誘導後表現量顯著高於控制組，其表現量高出一倍之多 (P＜0.05)；(2) 經黃耆誘導後，GNAS表現量與控制組相較明顯之增加許多，而另一方面添加黃耆後之GNAS的short form表現量則較控制組的少 (P＜0.05)；而將GNAS isoform基因片段分別轉染至K562細胞中並以黃耆加以誘導，發現經GNAS form轉染後，細胞中 β -球蛋白表現量顯著高於GNAS short form之 β -球蛋白表現量 (P＜0.05)。因此本實驗室提出一種假說，在經由黃耆誘導K562細胞中，G蛋白?悁董璊矮NAS form會將訊號傳遞給作用體腺核酸環化? (adenylyl cyclase, AC)，增加cAMP含量，因而活化PKA；再經由PKA路徑活化下游因子以產生 β -球蛋白；(3) 此外由於本研究所選殖之G α 11，也選殖到G α 11 pseudogene，經由酵素Xho I剪切確認發現，經誘導劑誘導後均會表現G α 11 pseudogene，而G α 11在誘導劑誘導下，表現量均顯著高於控制組 (P＜0.05)，此意味G α 11與G α 11 pseudogene是否會互相競爭而抑制了G α 11之功能，此發現值得更進一步研究探討其原因及調控機制。以上不同之G蛋白?悁董璊落鋮T息傳遞調控機制尚未完全明瞭，仍需更進一步之研究，尤其是中藥黃耆對於血液疾病之治療極具幫助，若能完全了解其分化機制，或許能讓紅血球相關疾病患者，可藉此得到治癒或減緩病情的機會。 關鍵字：G蛋白，黃耆，GNAS form， β -球蛋白

關鍵詞 : G蛋白 ; 黃耆 ; GNAS form ; β -球蛋白

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