Calmodulin-dependent protein kinase kinase B plays a role in MEL cell differentiation.

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ABSTRACT

蛋白質激?（protein kinase）參與許多細胞內反應，其功能包含訊息傳遞、細胞週期調控、細胞分裂及細胞分化，如果因發生突變或是調控失當，而影響蛋白質激?活性，便有機會造成癌症的生成。癌症細胞是一群脫離正常循環控制的細胞，其失去了進行終點分化以及正常細胞調控分裂增生之能力，這些細胞有一些不正常的基因表現存在，而這些基因表現會控制著抑制細胞進行分化過程或促進細胞分裂的途徑。本研究選用小鼠白血癌細胞（murine erythroleukemia cell, MEL cell）作為細胞模式，利用誘導劑HMBA及hemin誘導細胞進行分化，兩種誘導劑均可提高B-血紅素之產量。本論文利用保守區域PCR擴增法，探討細胞分化的過程中蛋白質激?之變化。本研究發現未經誘導分化之MEL細胞中，具有蛋白質激?C theta（protein kinase C theta, PKC theta）及活化有絲分裂蛋白質激?3（mitogen activated protein kinase 3, Mapk3）參與調控，而在MEL細胞誘導分化的過程中有鈣依賴蛋白質激?之上游激?B（Ca2+/CaM-dependent protein kinase kinase beta, CaMKK B）參與調控（CaMKK B可活化鈣依賴蛋白質激? Ⅰ或Ⅳ）；此外，重組鈣依賴蛋白質激?之上游激?B（CaMKK B）序列與基因庫CaMKK B序列比對後發現其具有差異性，基因庫序列定名為CaMKK B-a（NM_145358），其含有1626 base氨基酸轉譯區，而新發現之序列為CaMKK B-b，其含有1496 base氨基酸轉譯區（1324~1452 base消失）。CaMK Ⅰ在誘導分化細胞中有較高表現量，而CaMKIV則在未誘導及hemin誘導細胞較多，因此推論CaMKK B可能經由活化CaMK Ⅰ達到誘導血紅素表現。

Keywords : differentiation ; protein kinase

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