研究 c-Jun 的調控與細胞命運的關係

The relationship between c-Jun regulation and cell fates

中文摘要

轉錄因子 c-Jun 在細胞增生，存活和分化上皆扮演重要的角色。據最近的文獻指出，在人類造血前驅細胞中，c-Jun 會抑制 EPO 及 SCF 所誘導的紅血球系分化。而 c-Jun 在其它細胞激素及化學試劑誘導的紅血球系分化過程中所扮演的角色未明。因此，在本篇論文中，我們發現細胞激素(activinA 及 TGF-)及 hemin，Bcr/Abl 抑制劑 STI571 會抑制 human erythroid leukemia cell line K562 細胞的 c-Jun 表現量。但 HDACIs (apicidine，sodium butyrate，MS275)並不抑制 c-Jun 的表現。經由 c-Jun 大量表現的分析，發現 c-Jun 不影響細胞增生，但抑制 STI571，TGF- ，Hemin，HDACIs 所誘導的分化。此外，c-Jun 可回復 activinA 所抑制的細胞增生，且抑制 activinA 所誘導的血紅素合成。Activin A 活化的 p38 pathway 受到抑制時，則 c-Jun 蛋白表現會增加。這些結果顯示，activin A 可透過 p38 pathway 負調控 c-Jun 使紅血球系分化。

英文摘要

The transcription factor c-Jun plays important roles in cell proliferation, survival, and differentiation. It has been demonstrated recently that c-Jun inhibits EPO and SCF-mediated erythroid differentiation in primary human hematopoietic progenitors. However, the role of c-Jun in other cytokines and chemical agents-mediated erythroid differentiation is unknown. In this study, we found that cytokines (activinA and TGF-), hemin, and Bcr/Abl inhibitator STI571 down-regulated c-Jun expression in hematopoietic progenitor cell line K562, but histone deacetylase inhibitators (HDACIs : apicidine, sodium butyrate, MS271) did not . We examined the effect of c-Jun overexpression in K562 cells. Stable clones overexpressing c-Jun showed no alterations in proliferation but blocked TGF- hemin and HDACIs -mediated hemoglobin synthesis. In addition, c-Jun restored activin A-inhibited proliferation and blocked activinA-induced hemoglobin synthesis. The blocking of activin A -mediated p38 MAPK activation that up-regulated c-Jun expression. These data suggest that activin A down-regulated c-Jun via p38 MAPK pathway to mediate erythroid differentiation.