The Studies of the Gα11 Pseudogene in Leukemia Cell Line K562 Differentiation

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ABSTRACT

Heterotrimeric guanine nucleotide-binding proteins (G-protein) have been demonstrated to play integral role in the transduction of extracellular signals from cell membrane receptor (G-protein-coupled receptors, GPCR) to intracellular effectors proteins. G proteins regulate critical processes such as cell growth, differentiation and development. Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder of hematopoietic stem cells, that has acquired a Philadelphia (Ph) chromosome encoding the BCR – ABL oncogenic fusion protein, which has lost its differentiation activity. Therefore, in recent years, some scholars proposed differentiation therapy, by treating appropriate inducers to induced advanced or aggressive malignant cells maturation and differentiation into mature cells. K562 is the first human immortalized myelogenous leukaemia cell line and belonging undifferentiated pluripotent hematopoietic progenitor cells. K562 cell can be differentiated into erythrocytic or megakaryocytic lineages upon different inducers treatments and was used as a model cell line to study the relationship between the blood cell differentiation and signal transduction. In this report, three different inducers, huangqi (Astragalus membranaceus) and chemicals Hemin and HMBA were used to induce K562 cell differentiation. Two erythroid markers, β-globin or γ-globin, and two megakaryocyte markers CD41 and CD61 are used to monitor the differentiation process. In former report, the Gα11 pseudogene was induced by the huangqi administration. In this study, in promoter activity assay the pseudogene promoter activity increased by two fold when the presence of 1.5 mg / ml of huangqi extract. However, under the influence of the three-inducing agent, the Gα11 pseudogene were up-regulated in the HMBA-induced K562 cell, but we failed to detect significant changing of cell differentiation markers. It may be the consequence of fetal bovine serum used in cell culture which led to change cell characters and low transfection efficiency of the genes. Currently, re-transfection with higher amount of expression plasmid in K562 cells, and select stable clones are on going. I expect the performance of the proper Gα proteins function will change cell fate. In conclusion, understand the G protein function in cell differentiation, can provide the information need for future differentiation therapy of leukemia.

Keywords : K562 cell、Huangqi、Hemin、HMBA、Gαq、Gα11、Gα11 pseudogene

Table of Contents

目錄

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