Hindawi Publishing Corporation
Journal of Signal Transduction
Volume 2013, Article ID 497383, 5 pages
http://dx.doi.org/10.1155/2013/497383

Research Article

AP-1 Gene Expression Levels May Be Correlated with Changes in Gene Expression of Some Stemness Factors in Colon Carcinomas

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Received 13 August 2013; Accepted 30 October 2013

Academic Editor: Leonidas C. Platanias

The AP-1 transcription factor is a heterodimer protein that regulates gene expression in response to a variety of extrinsic stimuli through signal transduction. It is involved in processes including differentiation, proliferation, and apoptosis. Among the genes it regulates are transcription factors that contribute to the stemness phenotype. Cancer stem cells have the ability to self-renew and initiate differentiation into heterogenic cancer cells, which may cause metastasis and relapses. In the present study, we evaluated the effect of AP-1 complexes, as well as the *C-FOS* and *C-JUN* genes, in relation to NANOG, OCT3/4, and SOX2 transcription factors. All assays were undertaken with colon cancer stem cells. Knockdown experiments with siRNA were performed for each individual gene as well as their combination. Changes in gene expression were calculated with quantitative polymerase chain reaction experiments, while the effect on cell cycle distribution and apoptosis was studied by flow cytometry. The results differed depending on the percentage of repression, as well as the gene that was suppressed. In all cases, the number of apoptotic cells was increased. These findings indicate that AP-1 may have a crucial role in the maintenance of cancer stem cells.

1. Introduction

The AP-1 transcription factor consists of various proteins including C-FOS and C-JUN. Its function is to regulate gene expression in response to many stimuli, and it is involved in multiple cellular processes, such as differentiation, proliferation, and apoptosis [1, 2]. The monomers of the AP-1 complex are encoded by different genes. These transcription factors are located downstream many transduction pathways, thus making their role critical [3, 4]. Cancer stem cells (CSCs) are cells that are defined by their ability to self-renew and undergo asymmetric cell division, proliferation, and differentiation. With respect to their origin, these cells may be caused by disturbance of the self-renewal and differentiation programs occurring in multipotential stem cells, tissue-specific stem cells, progenitor cells, mature cells, and cancer cells [5]. The hallmarks of the CSC phenotype are defined by many genes; however, NANOG, *POU5F1* (OCT3/4), and SOX2 have crucial roles [6, 7].

Recent experimental data indicated that C-JUN is important for the maintenance of the self-renewal and tumorigenicity of glioma stem-like cells [8]. According to another study in colon cancer, C-JUN and TCF4 promoted a subpopulation of colorectal cancer tumor cells to adopt a stem-like phenotype via the *NANOG* promoter [9]. Moreover, C-FOS maintains hematopoietic stem cells in quiescence [10]. The present study aimed to identify the relationship between the AP-1 complex and stemness transcription factors. We attempted to address whether the AP-1 transcription factor is necessary to activate or suppress NANOG, OCT3/4, and SOX2 transcription factors as well as if it has an effect on apoptosis and the cell cycle.

2. Materials and Methods

2.1. Cell Culture. Human colon cancer stem cells (36112-39P; Celprogen) were cultured in appropriate growth medium