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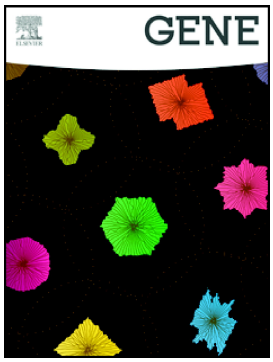

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C-RAF function at the genome-wide transcriptome level: A systematic view

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Abstract

C-RAF was the first member of the RAF kinase family to be discovered. Since its discovery, C-RAF has been found to regulate many fundamental cell processes, such as cell proliferation, cell death, and metabolism. However, the majority of these functions are achieved through interactions with different proteins; the genes regulated by C-RAF in its active or inactive state remain unclear. In the work, we used RNA-seq analysis to study the global transcriptomes of C-RAF bearing or C-RAF knockout cells in quiescent or EGF activated states. We identified 3353 genes that are promoted or suppressed by C-RAF. Gene ontology and Kyoto Encyclopedia of Genes and Genomes analyses revealed that these genes are involved in drug addiction, cardiomyopathy, autoimmunity, and regulation of cell metabolism. Our results provide a panoramic view of C-RAF function, including known and novel functions, and have revealed potential targets for elucidating the role of C-RAF.

Keywords: C-RAF; transcriptome; gene expression control

1. Introduction

RAF kinase family proteins are involved in many fundamental cellular processes, including cell proliferation, differentiation, cell death and survival, metabolism, and motility (Matallanas et al., 2011; Desideri et al., 2015). The mammalian RAF kinase family includes A-RAF, B-RAF, and C-RAF (RAF1). These proteins all have auto-inhibitory, regulatory, and catalytic domains, and contain multiple phosphorylation sites (Dhillon et al., 2009; An et al., 2015). Among the three members, C-RAF has drawn the most attention since it was identified 30 years ago (Kozak et al., 1984; Fukui et al., 1987).

C- and B-RAF are positioned at the hub level of the mitogen-activated protein kinase (MAPK) signaling cascade (Zanucco et al., 2014). C-RAF is stimulated by extracellular stress