Biosystem analysis of the hypoxia inducible domain family member 2A: Implications in cancer biology

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The expression of HIGD2A is dependent on oxygen levels, glucose concentration, and cell cycle progression. This gene encodes for protein HIG2A, found in mitochondria and the nucleus, promoting cell survival in hypoxic conditions. The genomic location of HIGD2A is in chromosome 5q35.2, where several chromosomal abnormalities are related to numerous cancers. The analysis of high definition expression profiles of HIGD2A suggests a role for HIG2A in cancer biology. Accordingly, the research objective was to perform a molecular biosystem analysis of HIGD2A aiming to discover HIG2A implications in cancer biology. For this purpose, public databases such as SWISS-MODEL protein structure homology-modelling server, Catalogue of Somatic Mutations in Cancer (COSMIC), Gene Expression Omnibus (GEO), MethHC: a database of DNA methylation and gene expression in human cancer, and microRNA-target interactions database (miRTarBase) were accessed. We also evaluated, by using Real-Time Quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR), the expression of Higd2a gene in healthy bone marrow-liver-spleen tissues of mice after quercetin (50 mg/kg) treatment. Thus, among the structural features of HIG2A protein that may participate in HIG2A translocation to the nucleus are an importin ?-dependent nuclear localization signal (NLS), a motif of DNA binding residues and a probable SUMOylating residue. HIGD2A gene is not implicated in cancer via mutation. In addition, DNA methylation and mRNA expression of HIGD2A gene present significant alterations in several cancers; HIGD2A gene

showed significant higher expression in Diffuse Large B-cell Lymphoma (DLBCL). Hypoxic tissues characterize the ?bone marrow-liver-spleen? DLBCL type. The relative quantification, by using RT-qPCR, showed that Higd2a expression is higher in bone marrow than in the liver or spleen. In addition, it was observed that quercetin modulated the expression of Higd2a gene in mice. As an assembly factor of mitochondrial respirasomes, HIG2A might be unexpectedly involved in the change of cellular energetics happening in cancer. As a result, it is worth continuing to explore the role of HIGD2A in cancer biology.

Cancer

DNA methylation

HIGD2A

Hypoxia

MiRNA

MRNA expression

Quercetin

DNA

hypoxia inducible domain family member 2A

hypoxia inducible factor

microRNA

quercetin

unclassified drug

adult

animal experiment

animal model

animal tissue

Article

bone marrow

cell energy

cell nucleus

controlled study

diffuse large B cell lymphoma

DNA binding

DNA methylation

embryo

gene

gene expression

HIGD2A gene

human

human cell

infant

liver

male

malignant neoplasm

mitochondrial respiration

mouse

nonhuman

nuclear localization signal

pathogenesis

protein assembly

protein motif

protein structure

protein transport

somatic mutation

spleen

sumoylation