Atlas of Genetics and Cytogenetics
in Oncology and Haematology

OPEN ACCESS JOURNAL

INIST-CNRS

Gene Section
Short Communication

ERGIC3 (ERGIC and golgi 3)

Mingsong Wu, Yi Cao

Department of Cell Biology and Genetics, Zunyi Medical University, Guizhou Zunyi 563000, China (MW), Laboratory of Molecular and Experimental Pathology, Kunming Institute of Zoology, Chinese Academy of Sciences, Kunming, 650223, China (YC)

Published in Atlas Database: September 2014
Online updated version : http://AtlasGeneticsOncology.org/Genes/ERGIC3ID42222ch20q11.html
Printable original version : http://documents.irevues.inist.fr/bitstream/handle/2042/62258/09-2014-ERGIC3ID42222ch20q11.pdf
DOI: 10.4267/2042/62258

Abstract

Review on ERGIC3, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Keywords
ERGIC3; Erv46.

Identity

Other names: C20orf47, CGI-54, Erv46, NY-BR-84, PRO0989, SDBCAG84, dJ477O4.2

HGNC (Hugo): ERGIC3

Location: 20q11.22

Local order: ERGIC3 is located on the forward strand of chromosome 20 at 20q11.22 (figure 1.A). It is between base pairs 35542029-35557634 (figure 1.B) and is composed of 15606 nucleotides encoding 13 or 14 exons (figure 2). NCBI gene ID is 51614.

Note

According to hg38/GRCh38-Dec_2013: (GRCh38)
- ERGIC3 at chr20: 35542029-35557634 (NM_198398) endoplasmic reticulum-Golgi intermediate compartment protein 3 isoform 1
- ERGIC3 at chr20: 35542029-35557634 (NM_015966) endoplasmic reticulum-Golgi intermediate compartment protein 3 isoform 2

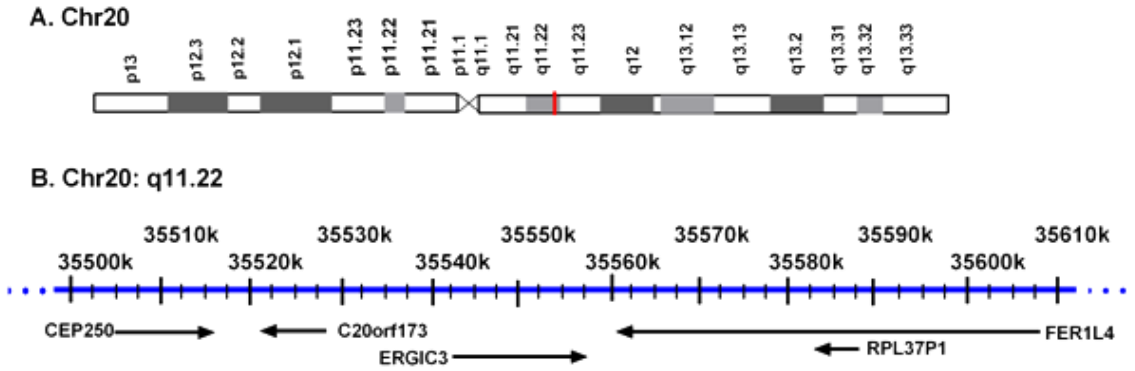

Figure 1. ERGIC3 chromosomal localization (A) (adapted from GeneCards) and the ERGIC3 gene maps on chromosome 20q11.22 (B). The red line is the location of ERGIC3 on chromosome 20 (chr20).

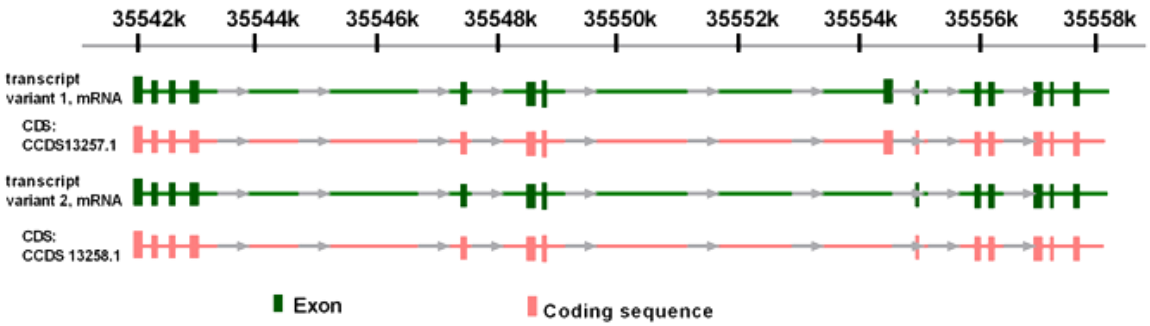

Figure 2. The transcript variants and coding sequence (CDS) of ERGIC3.

DNA/RNA

Note

According to hg38/GRCh38-Dec_2013:(GRCh38)
- Start: chr20: 35542029 bp from pter
- End: chr20:35557634 bp from pter
- Size: 15606 bases
- Orientation: forward strand.

Transcription

Two alternatively spliced transcript variants encoding different isoforms have been demonstrated for this gene.

Isoform 1 transcript is 1383 bases (RefSeq: NM_198398.1), which is comprised of 14 exons and coding the longer isoform (Figure 2).

Isoform 2 represents the shorter 1368 bases, RefSeq: NM_015966.2, which is comprised of 13 exons and coding the shorter isoform (Figure 2). The open reading frame (ORF) is shifted because the variant is not spliced. Therefore, compared to isoform 1 the protein is shorter.

Pseudogene

No observed pseudogenes.

Protein

Note

Human ERGIC3 protein is a type II transmembrane protein containing two external membrane areas (1~19, 368~383), two transmembrane areas (20~42, 341~362), as well as a endoplasmic reticulum lumen area (43~344) from amino acid residues (figure 3). Human ERGIC3 consists of 383 amino acid with the molecular mass 43.2 kD and the value of theoretical isoelectric point 5.68, (Geng et al., 2014).

ERGIC3 protein contains two conserved domains, ERGIC_N and COPIIcoated_ERV (figure 3) which are localized to the early secretory pathway and are involved in protein maturation and processing in the endoplasmic reticulum and/or sorting into COPII vesicles for transport to the Golgi (Otte et al., 2001). There are 2 glycosylation sites in the N241, N266 (figure 3).

Description

388 aa (Accession: NM_198398.1, NP_938408) isoform 1; 383 aa (Accession: NM_015966.2, NP_057050.1). isoform 2. ERGIC3 belongs to the family of the ER vesicle (Erv) proteins (Otte et al., 2001). ERGIC3 interacts with ERGIC2 (Welsh et al., 2006) and ERGIC1 (Breuza et al., 2004) and forms a heterotrimeric protein complex. Both isoforms contain ERGIC_N domain and COPIIcoated_ERV domain (figure 3) which is conserved from fungi to humans.

ERGIC3 works in close on junction with ERGIC2 and together they form a complex which cycles between the endoplasmic reticulum and cis-Golgi network. Both are integral membrane proteins with two membrane spanning segments each, short N- and C-terminal tails expose to the cytosol, and large central luminal domains (figure 3) (Welsh et al., 2006).

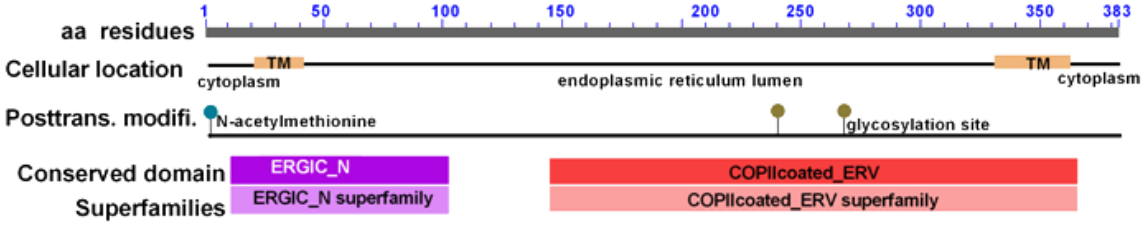

Figure 3. The domains of ERGIC3 protein (adapted from NCBI). aa: amino acid; posttrans. modifi.: posttranslational modification. TM: transmembrane domain.

Expression

In normal human tissues, ERGIC3 is found in some epitheial cells such as liver, pancreas, stomach, intestine, and so on, but is undetected in lung, cerebral cortex, cerebellum, heart, spleen, thymus, muscle (Lin, 2014).
In human tumor tissues, ERGIC3 is highly expressed in lung cancer, hepatocellular carcinoma, pancreatic carcinoma, gastric carcinoma, colon cancer, esophagus cancer, but is negative in osteosarcoma, chondrosarcoma, and fibrosarcoma by immunohistochemical (IHC) staining (Lin, 2014).
In addtion, ERGIC3 is highly expressed in the spinal cord and kidney of mouse (Nishikawa et al., 2007).

Localisation

ERGIC3 mainly localizes to endoplasmic reticulum, endoplasmic reticulum-golgi intermediate compartment (ERGIC) and cis-Golgi network, (Breuza et al., 2004; Orci et al., 2003; Wu et al., 2013).

Function

The precise function of ERGIC3 is presently unclear, especially in mammal cells. There is a strong interaction between ERGIC3 and ERGIC2 so as to form a heteromer complex which exerting its biological function. The complex may be involved in : 1) the sorting of some secretory molecules during vesiclar transport (Belden and Barlowe, 2001; Otte and Barlowe, 2004) due to the hydrophobic signals present on both C-terminal tails of the ERGIC3-ERGIC2 complex control sorting into COPII vesicles for anterograde transport, and retrieval from the Golgi is mediated by a COPI binding KKxx motif on ERGIC3 (Otte and Barlowe, 2002) ; 2) protein folding and glycoprotein processing in the endoplasmic reticulum and cis- Golgi network (Nishikawa et al., 2007; Welsh et al., 2006). Glucosidase II is not transported into COPII vesicles in vitro as well as cells lacking a cycling ERGIC3-ERGIC2 complex have a mild glycoprotein processing defect and a partial loss of glucosidase (Leah, 2006) inhibiting endoplasmic reticulum stress (ERS)-induced cell death by tunicamycin in HEK-293 cells (Nishikawa et al., 2007).

Homology

ERGIC3 is highly conserved in species. The amino acid sequence is at least 98% among 8 vertebrates, human, pongo, macaca, ailuropoda, myotis, bovini, mus, heterocephalus. There is only one change in amino acid (T164) between human and pongo, 2 changes in amino acid (T112, W170) between human and macaca (Geng et al., 2014).

Mutations

Note

No observed mutation sites.

Implicated in

Non-small cell lung cancer (NSCLC)

Note

ERGIC3 is highly up-regulated in NSCLC. A study (Wu et al., 2013) demonstrated that ERGIC3 was positive in 89% of NSCLCs while ERGIC3 was not detected in normal bronchial epithelial cells and alveolar cells.
Moreover, the positive rate of lung adenocarcinoma was higher than that of lung squamous cell carcinoma, and the positive rate of poorly differentiated NSCLCs was higher than that of the well and moderately differentiated NSCLCs.
The study suggested that ERGIC3 may be a potential biomarker for lung cancer.
Additionally, the over-expression of ERGIC3 promotes the cell proliferation, migration, and invasion in NSLCs (Wu et al., 2013).

Hepatocellular carcinoma (HCC)

Note

ERGIC3 was up-regulated in HCC.
The over-expression of ERGIC3 modulates the epithelial to mesenchymal transition (EMT), and increases the cell proliferation, migration, and invasion in HCCs (Zhang et al., 2013). Furthermore, ERGIC3 expression is regulated by MiR-490-3p (Zhang et al., 2013).

References

Otte S, Belden WJ, Heidtman M, Liu J, Jensen ON, Barlowe C. Erv41p and Erv46p: new components of COPII vesicles involved in transport between the ER and Golgi complex. J Cell Biol. 2001 Feb 5;152(3):503-18

Otte S, Barlowe C. The Erv41p-Erv46p complex: multiple export signals are required in trans for COPII-dependent transport from the ER. EMBO J. 2002 Nov 15;21(22):6095-104

Orci L, Ravazzola M, Mack GJ, Barlowe C, Otte S. Mammalian Erv46 localizes to the endoplasmic reticulum-Golgi intermediate compartment and to cis-Golgi cisternae. Proc Natl Acad Sci U S A. 2003 Apr 15;100(8):4586-91

Breuza L, Halbeisen R, Jenö P, Otte S, Barlowe C, Hong W, Hauri HP. Proteomics of endoplasmic reticulum-Golgi intermediate compartment (ERGIC) membranes from brefeldin A-treated HepG2 cells identifies ERGIC-32, a new cycling protein that interacts with human Erv46. J Biol Chem. 2004 Nov 5;279(45):47242-53

Welsh LM, Tong AH, Boone C, Jensen ON, Otte S. Genetic and molecular interactions of the Erv41p-Erv46p complex involved in transport between the endoplasmic reticulum and Golgi complex. J Cell Sci. 2006 Nov 15;119(Pt 22):4730-40

Nishikawa M, Kira Y, Yabunaka Y, Inoue M. Identification and characterization of endoplasmic reticulum-associated protein, ERp43. Gene. 2007 Jan 15;386(1-2):42-51

Wu M, Tu T, Huang Y, Cao Y. Suppression subtractive hybridization identified differentially expressed genes in lung adenocarcinoma: ERGIC3 as a novel lung cancer-related gene. BMC Cancer. 2013 Feb 1;13:44

Zhang LY, Liu M, Li X, Tang H. miR-490-3p modulates cell growth and epithelial to mesenchymal transition of hepatocellular carcinoma cells by targeting endoplasmic reticulum-Golgi intermediate compartment protein 3 (ERGIC3). J Biol Chem. 2013 Feb 8;288(6):4035-47

Geng N, Wu M, Zheng X, Liu X, Li X.. Construction of prokaryotic expression vector with hERGIC3 gene and the bioinformatics analysists of hERGIC3 protein. J mod med health.2014;30:2404-2406.

Lin Q.. Preparation and identification of ERGIC3 monoclonal antibody and preliminary application research. Beijing: Graduate University of Chinese Academy of Sciences. 2014.

This article should be referenced as such:

Wu M, Cao Y. ERGIC3 (ERGIC and golgi 3). Atlas Genet Cytogenet Oncol Haematol. 2015; 19(8):499-502.