Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section

Mini Review

FAIM (Fas apoptotic inhibitory molecule)

Miguel F Segura, Carme Sole, Rana S Moubarak, Victor J Yuste, Joan X Comella

Department of Pathology, New York University School of Medicine, New York, USA (MFS); Department of "Ciencies Experimentals i de la Salut", University Pompeu Fabra, Barcelona, Spain (CS); Cell Signaling and Apoptosis Group, Institut de Neurociencies, Universitat Autonoma de Barcelona and Centro de Investigacion Biomedica en Red Enfermedades Neurodegenerativas (CIBERNED), Spain (RSM, JXC); Cell Death, Senescence and Survival Group, Institut de Neurociencies, Universitat Autonoma de Barcelona and Centro de Investigacion Biomedica en Red Enfermedades Neurodegenerativas (CIBERNED), Spain (VJY)

Published in Atlas Database: December 2009

Online updated version : http://AtlasGeneticsOncology.org/Genes/FAIMID43251ch3q22.html
DOI: 10.4267/2042/44850

Identity

Other names: FAIM1; FLJ10582

HGNC (Hugo): FAIM

Location: 3q22.3

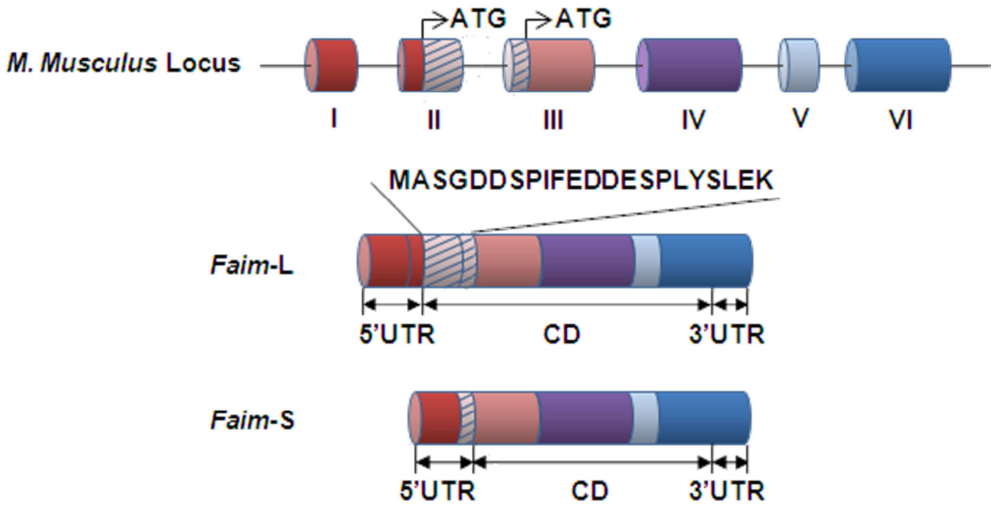
DNA/RNA

Description

The genomic structure of the FAIM locus gives two alternative splicing results, FAIM-S and FAIM-L, that share part of the 5_UTR (exon I). Part of the coding sequence in FAIM-L (diagonal bar of exon III) serves as part of the UTR of FAIM-S. The additional 22 amino acid sequence is indicated above the correlating exons (Zhong et al., 2001).

Transcription

FAIM-S: mRNA size: 1104 nucleotides (nt); coding sequence: 539 nt;
FAIM-L: mRNA size: 1164 nt; coding sequence: 605 nt.

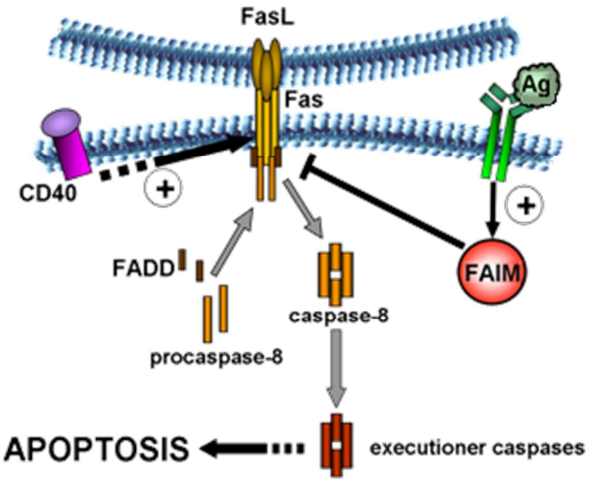


Genomic organization and splice variants of FAIM gene. Schematic representation of the structure of FAIM gene, that contains 4 different transcripts and 6 alternative splice variants but only two resulting proteins have been characterized so far: FAIM-S and FAIM-L (adapted from Zhong et al., 2001).

Protein

Note

Signaling pathways controlling cell death and survival are crucial for the normal development and tissue homeostasis. In contrast to most cell types, differentiated cells such as neurons require a highly controlled mechanism that allows survival for the entire life of the organism and protecting it from multitude of stimuli that can affect cellular integrity. Among those stimuli, cell death induction and more precisely, apoptosis induced by the extrinsic pathway mediated by Death Receptors (DRs), has been widely reported in the pathological loss of neurons. Therefore, those proteins that are able to block the apoptotic pathway will play a key role in the protection from neuronal death. Among all the described anti-apoptotic proteins, FAIM, with no homology with a previously known protein, may constitute a new family of proteins that regulate the DR signaling pathway.



Proposed mechanism of FAIM action in B-cells.

Description

Fas apoptosis inhibitory molecule (FAIM) is a Fas antagonist that was initially characterized by differential display as a gene that is up-regulated in B cells resistant to Fas-mediated cell death and functions as an inhibitor of Fas-induced cell death (Schneider et al., 1999). Shortly after, a new alternative splice variant was described and named FAIM-L. FAIM-S is composed of 179 aminoacids (aa), with stable structure and rich in beta-sheets, and FAIM-L contains 22 additional aa in the N-terminus part of the protein. This extra sequence does not have any particular defined structure.

Expression

FAIM-S mRNA has been detected in all tissues analyzed so far, whereas FAIM-L has a more restricted pattern of expression, being predominantly expressed in the nervous system and testis. Protein immunostaining confirmed restricted expression in different areas of the brain.

Localisation

Both isoforms, FAIM-S and FAIM-L are cytosolic.

Function

Fas apoptosis inhibitory molecule (FAIM) was first identified as a Fas antagonist in B-cells. The overexpression of FAIM-S, but not FAIM-L, enhances NGF-induced neurite outgrowth in different neuronal populations through activation of the NF-kB pathway. No anti-apoptotic function of FAIM-S has been described in the nervous system (Sole et al., 2004). However, FAIM-L is specifically expressed in neurons and its expression is regulated during development. FAIM-L does not affect neurite outgrowth, nor does it modulate NF-kB activation. However, cells overexpressing FAIM-L are resistant to apoptotic cell death induced by DRs such as Fas or TNFR1. Reduction of endogenous expression shows that endogenous FAIM-L protects primary neurons against DR-induced cell death. FAIM-L normally binds the Fas receptor and prevents its activation. Fas-L binding to Fas induces the release of FAIM-L from Fas, allows the binding of FADD and caspase-8, and leads to apoptosis activation (Segura et al., 2007).

Homology

FAIM is highly conserved in evolution from Caenorhabditis elegans to humans (Rothstein et al., 2000). However, FAIM-L is only conserved in superior vertebrates (Zhong et al., 2001; Segura et al., 2007). There is no homology with previously characterized families of proteins.

References

Schneider TJ, Fischer GM, Donohoe TJ, Colarusso TP, Rothstein TL. A novel gene coding for a Fas apoptosis inhibitory molecule (FAIM) isolated from inducibly Fas-resistant B lymphocytes. J Exp Med. 1999 Mar 15;189(6):949-56

Rothstein TL. Inducible resistance to Fas-mediated apoptosis in B cells. Cell Res. 2000 Dec;10(4):245-66

Rothstein TL, Zhong X, Schram BR, Negm RS, Donohoe TJ, Cabral DS, Foote LC, Schneider TJ. Receptor-specific regulation of B-cell susceptibility to Fas-mediated apoptosis and a novel Fas apoptosis inhibitory molecule. Immunol Rev. 2000 Aug;176:116-33

Zhong X, Schneider TJ, Cabral DS, Donohoe TJ, Rothstein TL. An alternatively spliced long form of Fas apoptosis inhibitory molecule (FAIM) with tissue-specific expression in the brain. Mol Immunol. 2001 Jan;38(1):65-72

Sole C, Dolcet X, Segura MF, Gutierrez H, Diaz-Meco MT, Gozzelino R, Sanchis D, Bayascas JR, Gallego C, Moscat J, Davies AM, Comella JX. The death receptor antagonist FAIM promotes neurite outgrowth by a mechanism that depends on ERK and NF-kapp B signaling. J Cell Biol. 2004 Nov 8;167(3):479-92

Segura MF, Sole C, Pascual M, Moubarak RS, Perez-Garcia MJ, Gozzelino R, Iglesias V, Badiola N, Bayascas JR, Llecha

N, Rodriguez-Alvarez J, Soriano E, Yuste VJ, Comella JX. The long form of Fas apoptotic inhibitory molecule is expressed specifically in neurons and protects them against death receptor-triggered apoptosis. J Neurosci. 2007 Oct 17;27(42):11228-41

Yu LY, Saarma M, Arumäe U. Death receptors and caspases but not mitochondria are activated in the GDNF- or BDNF-deprived dopaminergic neurons. J Neurosci. 2008 Jul 23;28(30):7467-75

Hemond M, Rothstein TL, Wagner G. Fas apoptosis inhibitory molecule contains a novel beta-sandwich in contact with a partially ordered domain. J Mol Biol. 2009 Mar 6;386(4):1024-37

Huo J, Xu S, Guo K, Zeng Q, Lam KP. Genetic deletion of faim reveals its role in modulating c-FLIP expression during CD95-mediated apoptosis of lymphocytes and hepatocytes. Cell Death Differ. 2009 Jul;16(7):1062-70

Kaku H, Rothstein TL. Fas apoptosis inhibitory molecule enhances CD40 signaling in B cells and augments the plasma cell compartment. J Immunol. 2009 Aug 1;183(3):1667-74

Kaku H, Rothstein TL. Fas apoptosis inhibitory molecule expression in B cells is regulated through IRF4 in a feed-forward mechanism. J Immunol. 2009 Nov 1;183(9):5575-81

This article should be referenced as such:

Segura MF, Sole C, Moubarak RS, Yuste VJ, Comella JX. FAIM (Fas apoptotic inhibitory molecule). Atlas Genet Cytogenet Oncol Haematol. 2010; 14(9):878-880.