Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

TRAF3 (TNF Receptor Associated Factor 3)

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Published in Atlas Database: August 2002

Online updated version : http://AtlasGeneticsOncology.org/Genes/TRAF3ID271.html
DOI: 10.4267/2042/37920

Identity

Other names: CAP-1; CD40bp; CRAF1; LAP1

HGNC (Hugo): TRAF3

Location: 14q32.33

Local order: Between a potential gene LOC254285 and the gene encoding for amnionless protein.

DNA/RNA

Description

13 exons spanning approximately 130 kb.

Transcription

Three alternatively spliced transcript variants encoding two distinct isoforms have been reported.

Protein

Description

Isoform 1: 568 amino acids.
Isoform 2: 543 amino acids.

Expression

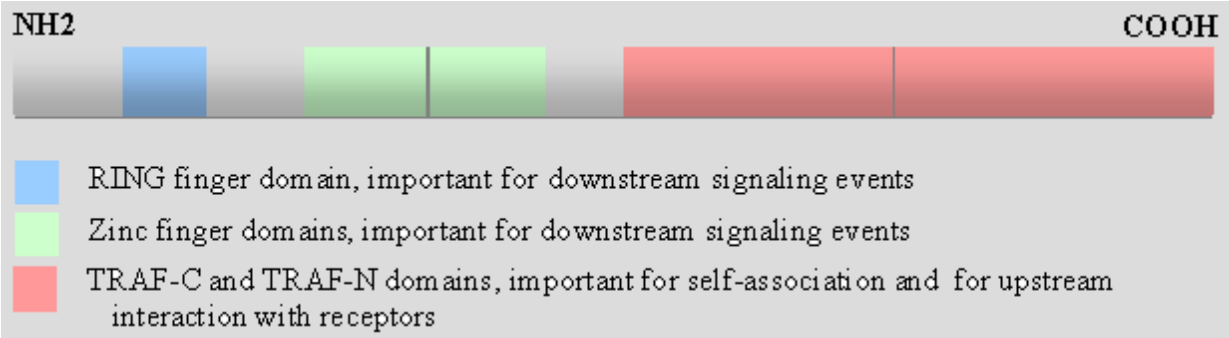
TRAF3 protein is detected in the skin, with a stronger intensity in more differentiated cells in the upper layers of the complex epithelium. TRAF3 is also expressed in the cartilage, in the cardiovascular system, in the trachea, in the salivary gland, in the liver, in the pancreas, in the prostate gland, in the pituitary gland. A gradient of TRAF3 expression appears to exist along the nephron, with progressively higher expression from proximal tubule to collecting duct. In the central nervous system, many but not most neurons in the cerebral cortex, basal ganglia, and brain stem contain at least low levels of TRAF3 protein. In contrast, almost no expression of TRAF3 is detected in the immune system.

Localisation

Mainly cytoplasmic.

Function

The TRAF family proteins act at least in part as adapter proteins that recruit other signaling molecules to ligand-bound TNF family receptors.
TRAF3 was first described as a molecule that binds the cytoplasmic tail of CD40. Signaling through CD40 in B cells induces rescue from apoptosis, proliferation, differentiation, Ig production, class switching and expression of co-stimulatory molecules.
Insights into the in vivo functions of TRAF3 have come from generation of mice deficient for TRAF3. These mice are depleted in all lineages of peripheral leucocytes, and die shortly after birth. However, B cells from TRAF3-/- upregulate CD23 and proliferate normally in response to CD40 ligand stimulation. Moreover, fetal liver cells from TRAF3 deficient mice can reconstitute the immune system of irradiated wild type mice, although isotype switching in response to T-dependent antigens is defective. Thus, TRAF3 is not required for CD40 signaling, but appears important in T cell-dependent immune responses.
These effects of TRAF3 may be mediated through other TNF receptor family members: TRAF3 can bind directly to the cytosolic domains of CD27, CD30, LTbR, LMP-1, and also binds indirectly TNF-R2.



Homology

TRAF3 belongs to a family of six proteins (TRAF1 to 6), sharing a common structural organization. TRAF3 counterparts are found in mouse, fly and worm.

Implicated in

Disease

Hodgkin disease, lymphomas.

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This article should be referenced as such:

Kedinger V. TRAF3 (TNF Receptor Associated Factor 3). Atlas Genet Cytogenet Oncol Haematol. 2003; 7(1):4-5.