RTN4 (reticulon 4)
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Identity
Hugo: RTN4
Other names: ASY; NI220/250; NOGO; NOGO-A;
Location: 2p16.3
Local order: Between FLJ42562 and FLJ31438.

Fig 1. Local order.

Fig 2. Genomic structure and transcriptional isoforms.
**DNA/RNA**

**Description**
The RTN4 gene spans about 75kb, and contains 9 major exons and several different cap sites (Fig. 2a).

**Transcription**
Three major, RTN4-A, B1 and C, (Fig. 2b) and several minor transcriptional isoforms result from alternative splicing and/or differential promoter usage. Although RTN4 mRNA is ubiquitously expressed, the expression of isoforms is tissue-specific, for example, RTN4-A and C in brain, RTN4-C in muscle, and RTN4-B1 in many other tissues.

**Protein**

**Description**
Proteins with different sizes are synthesized from different mRNA isoforms: RTN4-A, 129.9 kDa (1192 amino acids); RTN4-B1, 40.3 kDa (373 amino acids); RTN4-B2, 42.3 kDa (392 amino acids); RTN4-C, 22.4 kDa (199 amino acids). All RTN4 protein isoforms retain a common C-terminal domain containing two trans-membrane domains and an endoplasmic reticulum (ER)-retrieval motif.

**Expression**
Ubiquitously expressed (see Transcription).

**Localisation**
RTN4 protein localizes predominantly in the ER and, to a lesser extent, in cytoplasmic membrane.

**Function**
Although definitive functional mechanisms of RTN4 have not yet been clarified, RTN4 protein interacts with several other proteins, including RTN1, RTN3, DP1/Yop1p, BACE1, and Nogo receptor (NogoR). Interaction with DP1/Yop1p, an ER membrane protein, may be necessary for maintenance or stabilization of tubular ER. Binding with BACE1 (beta-amyloid converting enzyme 1) results in reduction in BACE1 activity and production of amyloid-beta. RTN4 also interacts with NogoR, and may lead to activation of RhoA and inhibition of neuronal regeneration in central nervous system. Further, overexpression of RTN4 may cause ER stress and apoptosis in certain cells.

**Homology**
Four reticulon family members (RTN1, RTN2, RTN3 and RTN4) have been identified. They possess a highly conserved C-terminal domain named reticulon homology domain.

**Implicated in**

**Various cancers**
Note: Down-regulation of RTN4 expression was observed in small cell lung carcinomas and adult T-cell leukemia/lymphomas, and RTN3, one of RTN4 interacting proteins, was over-expressed in astrocytomas, suggesting involvement of RTN4 (and RTN3) in certain types of tumorigenesis. However, increased incidence of tumor formation has not been observed in RTN4 knockout mice.
RTN4 is also suspected to involve in schizophrenia and neuronal degenerative diseases.

**References**


This article should be referenced as such: