Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

NFKB2 (nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100))

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Identity

Other names: NF-kB p100; NF-kB p52; Lyt10

HGNC (Hugo): NFKB2

Location: 10q24

Note
See also, in the Deep Insight section: Upstream Signal Transduction of NF-kB Activation.

DNA/RNA

Description

The gene encoding human nfkb2 has 24 exons spanning 8 kb. The expression of nfkb2 can be regulated by two distinct promoters, P1 and P2, in which a number of consensus binding sites for transcription factors, including SP1, AP1 and putative NF-kappa B (kappa B sites), were identified.

Protein

Description

The human nfkb2 gene encodes a protein composed 900 amino acids with an approximately molecular weight of 100 kDa, which was considered as a precursor of p52 subunit of NF-kB complexes. The structural characteristics of NF-kB2 are much similar with that of NF-kB1: A N-terminal RHD; two nuclear localization sequences within the C-terminus of RHD, a putative GRR region that possibly contributes to the generation of NF-kB p52 from the precursor, NF-kB2. The C-terminal region of NF-kB2 also contains multiple copies of the so-called ankyrin repeats and one proline, glutamic acid, serine, and threonine (PEST) domain. Studies demonstrated that NF-kB2 was posttranslationally cleaved to produce the p52 molecule through the ubiquitin-proteasome dependent degradation of the C-terminal 406-900 portion of NF-kB2. However, other studies revealed that the mechanism for the generation of NF-kB p52 is through cotranslational processing. Recent studies demonstrated that the processing of NF-kB p52 required IKKa- and/or NIK-dependent C-terminal phosphorylation of NF-kB2.

Expression

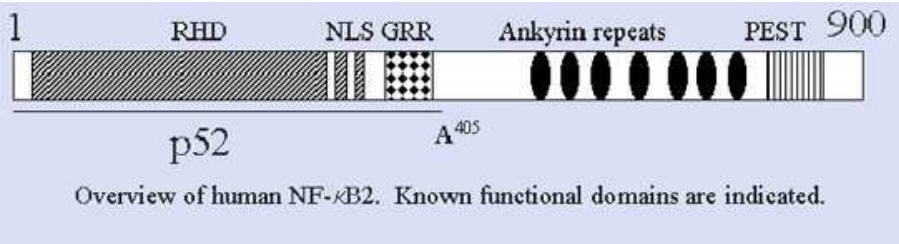
Nfkb2 is expressed mainly in lymphoid cells and mononuclear cells.

Localisation

Cytosol, nuclei after activation.

Function

Regulation of the genes involved in cell-to-cell interaction, intercellular communication, cell recruitment or transmigration, amplification or spreading of primary pathogenic signals, and initiation or acceleration of tumorigenesis.



Overview of human NF-κB2. Known functional domains are indicated.

Similar with NF-kB1, the full length of NF-kB2 can serve as an endogenous inhibitor for the NF-kB p50/ p65(RelA) or NF-kB p52/p65 heterodimer. The homodimer of NF-kB p52 was transcriptionally inactive in the absence of Bcl3. Furthermore, the NF-kB p52 homodimer may function to competitively inhibit B binding by transactivating NF- B dimers. The Bcl3 protein can form a complex with this homodimer at B sites and act as a transactivator of NF-kB p52 homodimer. Interaction with: members of IkB family and Rel family, Bcl3.

Implicated in

Hematological malignancies (see below) and other diseases: autoimmune arthritis, glomerulonephritis, asthma, inflammatory bowel disease, septic shock, lung fibrosis, cancer, HTLV-1 infection, and AIDS

Disease

t(10;14)(q24;q11) or t(10;14)(q24;q32) in haematological malignancies.

Cytogenetics

Poor.

Oncogenesis

Unlike its relative nfkb1, rearrangement of nfkb2 gene locus has been found in many forms of lymophomas. The chromosomal translocations by t(10;14)(q24;q11) and t(10;14)(q24;q32) cause deletions of sequences encoding the ankyrin repeat motif of NF-kB2. Consequently, this carboxyl terminal truncated NF-kB2 is constitutively located in the nucleus of cells, which was found in small percentage of B-cell non-Hodgkin's lymphoma, cutaneous lymphomas, T-cell acute lymphoblastic leukemia, chronic lymphocytic leukemias, and multiple myelomas. Chromosomal translocation generated a fusion NF-kB2- IGHA1 or NF-kB2- TCRa or TCRd transcriptional unit.

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