TOP1 (topoisomerase (DNA) 1)

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Identity

HGNC (Hugo): TOP1
Location: 20q12-q13.1
Location (base pair): 39090K-39190K on chromosome 20
Local order: centromer to telomer.

DNA/RNA

Note
The sequence is split into 21 exons over 85kbp. Introns are 0.2-30 kbp in size.

Description
21 exons with 20 introns.

Transcription
3.8 kb (single band).

Pseudogene
2 pseudogenes: TOP1P1 on chromosome 1q23-q24, and TOP1P2 on chromosome 22q12-q13.1.

Protein

Note
Type I DNA topoisomerase, EC (5.99.1.2).

The arrow indicates the breaking point of translocation, and the star denotes the sites of point mutation.

Description
765 amino acids, about 100kDa; contains NLS in the N-term, a core domain which recognizes its binding sequences, a link domain which connects the core and catalytic domains, and the catalytic domain in the C-term.

Expression
Ubiquitous. The expression level is up-regulated along with cell proliferation signals.

Localisation
Nucleus.

Function
TOP1 catalyzes the breaking and rejoining of single DNA strand.

Homology
The core and catalytic domains are conserved between the human and S.cerevisiae enzyme.

The star denotes intron 7 where chromosome translocation occurs.
Mutations

Somatic
Translocation of chromosome t(11;20)(p15;q12) has been reported in hematological malignancies (see below).
Point mutations with amino acid substitution in the catalytic domain have been implicated in irinotecan-resistance.

Implicated in

t(11;20)(p15;q12)

Disease
de novo acute myeloid leukemia, acute monocytic leukemia, therapy-related myelodysplastic syndrome/leukemia(t-MDS/AML).

Prognosis
Poor (?)

Hybrid/Mutated gene
NUP98/TOP1.

Oncogenesis
NUP98-TOP1 fusion protein has been proved to have leukemogenic activities independent of topoisomerase activity.

Breakpoints

The breakpoints locate in intron 7, causing the fusion protein to lack the N-terminal 169 amino acids. The breakpoints locate in the repetitive elements or close to them which exist in intron 7 of TOP1 gene.

To be noted

Note
Point mutations W736stop and G737S were detected in lung non-small cell carcinoma. The significance of mutations in catalytic domain has been suspected to be relevant to susceptibility to irinotecan.

References


Ahuja HG, Felix CA, Aplan PD. The t(11;20)(p15;q11) chromosomal translocation associated with therapy-related myelodysplastic syndrome results in an NUP98-TOP1 fusion. Blood. 1999 Nov 1;94(9):3298-61


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