Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

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).

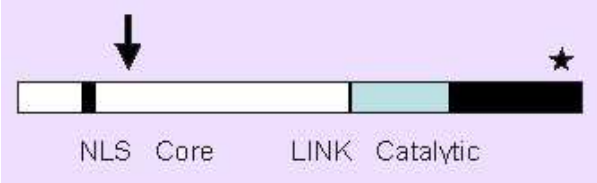
Pseudogene

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

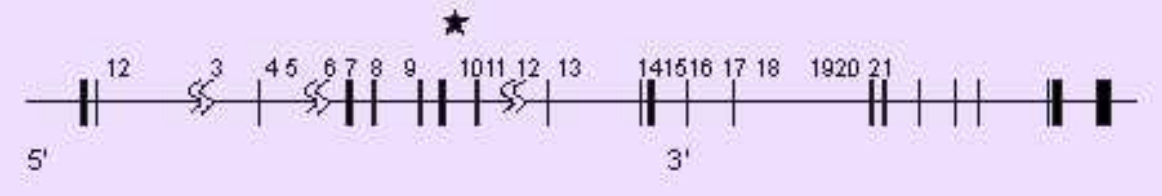
Nucleus.

Function

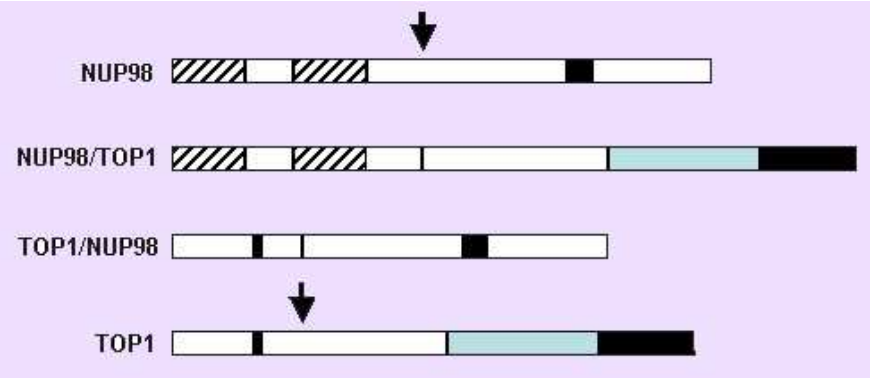
TOP1 catalyzes the breaking and rejoining of single DNA strand.

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.

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