Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Mini Review

FUS (fusion involved in t(12;16) in malignant liposarcoma)

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Identity

Other names: TLS (translocated in liposarcoma)

HGNC (Hugo): FUS

Location: 16p11.2

DNA/RNA

Description

The gene has 15 exons, and the total genomic sequence spanning the FUS gene is approx. 12 Kb.

Transcription

Transcript lenght: 1,9 Kb. There are two isoforms produced by an alternative splicing that involved the exon 4a (145 bp) or the exon 4b (142 bp).

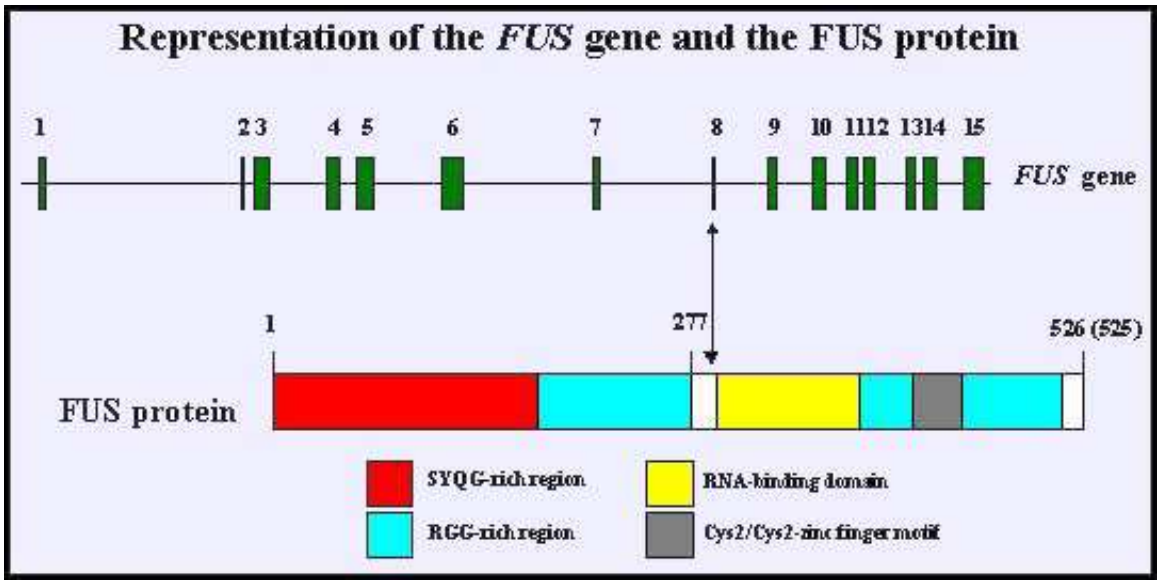
Protein

Description

526 amino acids (isoform with the exon 4a) or 525 aa (isoform with the exon 4b), 68 Kda. The protein contains different domains:
- a N-terminal SYQG-rich region;
- a RGG-rich region;
- a RNA binding domain;
- a RGG-rich region;
- a Cys2/Cys2-zinc finger motif and;
- a C-terminal RGG-rich region.

Expression

FUS is expressed in a housekeeping pattern.



Localisation

Nuclear, although FUS shuttles from the nucleus to the cytoplasm in a large complex that contains mRNA and hnRNPs.

Function

FUS is a RNA-binding protein that is identical to hnRNP P2 and may be implicated in mRNA metabolism. FUS seems to have a function as a heterogeneous ribonuclear protein (hnRNP)-like chaperone of RNA. In addition, it has been suggested that FUS might have a role in the BCR/ABL-mediated leukemogenesis.

Homology

FUS forms a sub-family of RNA binding proteins with EWS and RBP56/hTAFII68. FUS has homologous in mouse (fus), rat (pigpen) and Drosophila (Cabeza/SARFH).

Mutations

Germinal

In the mouse, germline mutation in the fus gene produces male sterility, sensitivity to radiation, defective B-lymphocyte development and active-tion, chromosomal instability and perinatal death.

Implicated in

Note

The FUS gene is implicated in several chromo-somal translocations associated to both solid tumors and leukemias. The results of these chromosomal translocations are gene fusions. FUS contributes to these fusions with its N-terminal part, just before the RNA-binding domain. This domain confers to the fusion protein a transcriptional activation domain. These fusion genes generated as a result of chromosomal rearragements are used to monitor diagnosis and treatment.

t(12;16)(q13;p11) chromosomal translocation. It produces the fusion protein FUS/ATF-1.

Disease

Angiomatoid fibrous histiocytoma (AFH).

Hybrid/Mutated gene

FUS was interrupted at codon 175 (exon 5) and fused to codon 110 (exon 5) of ATF-1, resulting in an in-frame junction with a glycine to valine (GGT to GTT) transition.

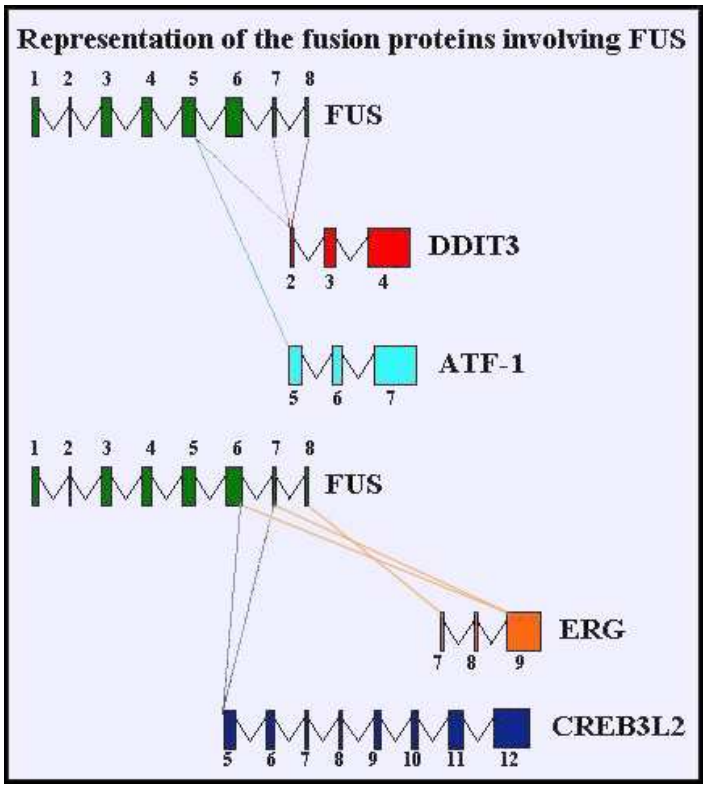
t(7;16)(q33;p11) chromosomal translocation. It produces the fusion protein FUS/CREB3L2 (also known as BBF2H7).

Disease

Low grade fibromyxoid sarcoma (LGFMS).

Hybrid/Mutated gene

The breakpoints in the fusion transcripts are produced between the exons 6 or 7 of FUS and the exon 5 of CREB3L2.



t(12;16)(q13;p11) chromosomal translocation. It produces the fusion protein FUS/DDIT3 (also known as CHOP).

Disease

Myxoid liposarcoma (MLS).

Hybrid/Mutated gene

9 different types of fusions between the genes FUS and DDIT3 have been reported. The most frequent rearragements join the exons 5, 7 or 8 of FUS with the exon 2 of DDIT3.

Oncogenesis

The unequivocally relation between FUS/DDIT3 and the MLS was shown by the generation of a transgenic mouse model expressing FUS/DDIT3 from a housekeeping promoter.

t(16;21)(p11;q22) chromosomal translocation. It produces the fusion protein FUS/ERG.

Disease

Acute myeloid leukemia (AML).

Hybrid/Mutated gene

The junction of both genes is produced between the exons 6 or 7 of FUS and the exon 9 of ERG,or between the exon 8 of FUS and the exon 7 of ERG.

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