

Gene Section

Mini Review

EWSR1 (Ewing sarcoma region 1)

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Identity

Location: 22q12



Probe(s) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Description

Spans over 40 kb; open reading frame: 2.0 kb (from 44 to 2014); 17 exons.

Transcription

2.4 kb mRNA; centromere to telomere direction; differential splicing.

Protein

Description

656 amino acids; serine-tyrosine tandem repeats (N-term to amino acid 285 in a region rich in glutamine, threonine and proline; 3 glycine, arginine, proline rich regions in C-term, with a RNA-binding signal in 410-417.

Expression

Wide.

Function

RNA binding.

Homology

With FUS.

Implicated in

**Ewing tumours with: $t(11;22)(q24;q12)$
→ *FLI1/EWSR1***

Disease

Ewing tumours: including Ewing's Sarcoma and peripheral primitive neuroectodermal tumour.

Cytogenetics

$t(11;22)(q24;q12)$ is found in 85% of cases of Ewing tumours.

Hybrid/Mutated Gene

5' EWS - 3' FLI1; breakpoints clustered over a 2-3 kb genomic region and over a 30-40 kb genomic region.

Abnormal Protein

Oncogenic protein on the der(22) chromosome generated by fusion of the N terminal domain of EWS protein with DNA binding domain of human FLI1 protein.

Oncogenesis

EWS -FLI1 is a dominant oncogene transformed cells by subverting normal transcriptional controls/FLI1 member of ETS family.

**Ewing tumours with $t(21;22)(q21;q12)$
→ *ERG/EWSR1***

Disease

Ewing tumours (Ewing's Sarcoma and peripheral primitive neuroectodermal tumour).

Hybrid/Mutated Gene

5' EWS - 3' ERG; the orientation of the ERG gene might be from telomere to centromere, opposite to that demonstrated for EWS.

Abnormal Protein

Oncogenic protein on the der(22) chromosome generated by fusion of the N terminal domain of EWS protein with DNA binding domain of human ERG protein.

Ewing tumours with t(7;22)(p22;q12) → ETV1/ EWSR1**Disease**

Ewing tumours (Ewing's Sarcoma and peripheral primitive neuroectodermal tumour).

Hybrid/Mutated Gene

5' EWS - 3' ETV1

Ewing tumours with t(17;22)(q12;q12)**→ E1AF/ EWSR1****Disease**

Ewing tumours (Ewing's Sarcoma and peripheral primitive neuroectodermal tumour).

Hybrid/Mutated Gene

5' EWS - 3' E1AF

t(11;22)(p13;q12)/Intra abdominal desmoplastic small round cell sarcoma (IADSRCT) → WT1/EWSR1**Hybrid/Mutated Gene**

5' EWS - 3' WT1; breakpoints: between EWS exons 7 and 8 and between WT1 exons 7 and 8.

Abnormal Protein

Transcription activator.

t(12;22)(q13;q12)/Malignant melanoma of soft parts → ATF1/EWSR1**Hybrid/Mutated Gene**

5' EWS - 3' ATF-1

Abnormal Protein

N terminal domain of EWS fused to the bZIP domain of ATF1.

t(9;22)(q22;q12)/Myxoid chondrosarcoma → TEC/EWSR1**Hybrid/Mutated Gene**

5' EWS - 3' TEC (or CHN); the EWS/CHN gene fusion was not detected in any of the remaining cases suggesting genetic heterogeneity within extraskeletal myxoid chondrosarcomas with t(9;17)(q22;q11).

Breakpoints

Note: clustered over a 2.3 kb genomic region.

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