

# Solid Tumour Section

## Short Communication

### Bone and Soft Tissue: Ewing-like sarcoma

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#### Abstract

Ewing-like sarcoma is a recently defined subset of bone or soft tissue sarcomas. It is one of the pediatric small, round, blue cell tumors and is fusion gene-driven cancer. However, the driving fusions are distinct from that of the FET-ETS family rearrangements that define Ewing sarcoma (see separate entry for Ewing sarcoma).

#### Keywords

Ewing-like sarcoma

#### Identity

Previously classified as Ewing tumors.

#### Classification

Ewing-like sarcoma can arise in the bone or soft tissue.

#### Clinics and pathology

##### Disease

Ewing-like sarcoma

##### Etiology

Ewing-like sarcomas are characterized by EWSR1/NFATC2 fusions, CIC fusions, or BCOR rearrangements.

##### Clinics

Ewing-like sarcoma is a very rare subtype of bone, soft tissue or visceral sarcoma.

##### Pathology

Small, round blue cells, with variable CD99

staining.

##### Treatment

Patients with Ewing-like sarcoma are currently treated following Ewing sarcoma therapy protocols. This may change over time as more is understood about the individual fusions driving Ewing-like sarcomas.

##### Prognosis

Survival is generally poorer for Ewing-like sarcomas compared to that of Ewing sarcoma.

The exact prognoses for individual Ewing-like fusions types is still under investigation.

In general, CIC-fused Ewing-like sarcomas have a very poor prognosis (<50%).

#### Cytogenetics

Ewing-like sarcomas harbor distinct fusions from that of Ewing sarcoma:

t(X;4)(p11.4; q31.1) BCOR/MALM3  
t(X;22)(p11.4; q13.2) ZC3H7B/BCOR  
t(X;4)(q13.1; q35.2) CIC/FOXO4  
t(4;15)(q35.2; q14)CIC/NUTM1  
t(4;19)(q35.2; q13.2)CIC/DUX4  
t(20;22)(q13.2; q12.2) EWSR1/NFATC2  
and fusion BCOR/CCNB3 (Xp11.4-Xp11.22)

#### Genes involved and proteins

The following genes have been identified in Ewing-like sarcomas: EWSR1, NFATC2, BCOR, CCNB3, MAML3, CIC, DUX4, ZC3H7B, FOXO4, NUTM1.

**EWSR1 (Ewing sarcoma breakpoint region 1)****Location** 22q12.2**Protein** Contains both a transcriptional activation domain and an RNA-binding domain.**NFATC2 (Nuclear factor of activated T cells 2)****Location** 20q13.2**Protein** DNA binding protein, responsive to T-cell receptor signaling.**BCOR (BCL6 corepressor)****Location** Xp11.4**Protein** Suppresses some genes by interacting with proteins comprising DNA binding complexes.**MAML3 (Mastermind like transcriptional coactivator 3)****Location** 4q31.1**Protein** Involved in the NOTCH pathway.**CCNB3 (Cyclin B3)****Location** Xp11.22**Protein** Cyclin family member; involved in cell cycle regulation.**CIC (Capicua transcriptional repressor)****Location** 19q13.2**Protein** HMG-box family member.**DUX4 (Double homeobox 4)****Location** 4q35.2**Protein** Associated with various forms of muscular dystrophy.**ZC3H7B (Zinc Finger CCCH-type containing 7B)****Location** 22q13.2**Protein** Nuclear protein; Contains domains involved in protein-protein and protein-nucleic acid interactions.**FOXO4 (Forkhead Box O4)****Location** Xq13.1**Protein** Involved in cell growth and differentiation.**NUTM1 (NUT midline carcinoma family member 1)****Location** 15q14**Protein** TERT expression regulation.**Result of the chromosomal anomaly****Fusion Protein**

EWSR1/NFATC2

BCOR/MALM3

BCOR/CCNB3

ZC3H7B/BCOR

CIC/DUX4

CIC/NUTM1

CIC/FOXO4

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