t(4;22)(q35;q12) in embryonal rhabdomyo-sarcoma (ERMS)

Jean-Loup Huret

Genetics, Dept Medical Information, University of Poitiers, CHU Poitiers Hospital, F-86021 Poitiers, France (JLH)

Disease

Rhabdomyosarcomas, the most common pediatric soft tissue sarcomas, are tumours related to the skeletal muscle lineage. The 2 major subtypes are alveolar rhabdomyosarcoma (ARMS) and embryonal rhabdomyosarcoma (ERMS). Other subtypes are botryoid, spindle cell, anaplastic, pleomorphic, and undifferentiated RMS. Most ERMS are characterized by chromosome gains and a loss of heterozygocity in 11p15.

Epidemiology

Only one case to date, a 19-year-old female patient with an embryonal RMS, who was alive and well 6 years after diagnosis (Sirvent et al., 2009).

Cytogenetics

Cytogenetics Morphological
The t(4;22)(q35;q12) was the sole anomaly.

Genes involved and proteins

DUX4

Location
4q35

Protein
DUX4 (double homeobox, chromosome 4) contains two homeodomains (about 60 amino acids, involved in DNA-binding), each similar in sequence to PAX3 and PAX7 homeodomains. It is a transcription factor DUX4 is involved in myogenic differentiation and cell-cycle control (Dixit et al., 2007).

EWSR1

Location
22q12

Protein
From N-term to C-term: a transactivation domain (TAD) containing multiple degenerate hexapeptide repeats, 3 arginine/glycine rich domains (RGG regions), a RNA recognition motif, and a RanBP2 type Zinc finger. Role in transcriptional regulation for specific genes and in mRNA splicing.

Result of the chromosomal anomaly

Hybrid Gene

Description
Breakpoints were located in the EWSR1 gene at 22q12 and the region of the DUX4 at 4q35. A 5’ EWSR1 - 3’ DUX4 hybrid gene is likely.

Fusion Protein

Description
One may speculate that the N terminal transactivation domain of EWSR1 was fused to one of the DNA binding domains of DUX4 (either the domain amino acids 19-78, or the domain aa 94-153).

References


This article should be referenced as such: