Solid Tumour Section
Short Communication

Soft tissue tumors: t(2;2)(p23;q35) in alveolar rhabdomyosarcoma

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Clinics and pathology

Phenotype / cell stem origin
Alveolar rhabdomyosarcoma (ARMS).

Epidemiology
Occurs in a small subset of ARMS cases (<5%). There are five reported cases.

Pathology
No information available.

Cytogenetics

Cytogenetics Morphological
Of the five reported cases, cytogenetics was only performed on one case and demonstrated a normal karyotype.

Cytogenetics Molecular
Several of these cases were detected using fluorescence in situ hybridization analysis by the finding of PAX3 rearrangement without evidence of a PAX3-FOXO1 fusion or FOXO1 rearrangement. Other cases were detected by directly assaying cases with a PAX3-NCOA1 fusion-specific RT-PCR assay.

Genes involved and proteins

Note
A variant t(2;8)(q35;q13) translocation has been identified, both in ARMS and in cases of embryonal rhabdomyosarcoma.

NCOA1
Location
2p23
Protein
Nuclear receptor transcriptional coactivator - p160 family.

PAX3
Location
2q35
Note
The NCOA2 gene (encoding another member of the p160 family of transcriptional coactivators) is located at 8q13 and involved in the variant t(2;8).
Protein
Transcription factor - paired box (PAX) family.

Result of the chromosomal anomaly

Hybrid Gene
Description
Based on the cloned cDNA, there appears to be two possible scenarios for formation of fusion genes. In some cases, the translocation apparently breaks within PAX3 intron 6 and NCOA1 intron 12 (type 1), and in other cases the translocation breaks within PAX3 intron 7 and NCOA1 intron 11 (type 2).

Transcript
The type 1 fusion transcript consists of the first six PAX3 exons fused to the last nine NCOA1 exons.
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Generation of chimeric genes by the 2;2 translocation in ARMS. The exons of the wild-type and fusion genes are shown as boxes above each map and the translocation breakpoint distributions are shown as line segments below the map of the wild-type genes.

The type 1 fusion gene encodes a 894 amino acid fusion protein and the type 2 fusion gene encodes a 1026 amino acid fusion protein. The fusion proteins encode novel transcription factors with the PAX3 DNA binding domain and the NCOA1 transcriptional activation domains.

Oncogenesis

Transcription dysregulation. At the cellular level there is evidence of alterations in control of growth, resulting in transformation of recipient cells (NIH3T3) in culture.

References

Barr FG. Gene fusions involving PAX and FOX family members in alveolar rhabdomyosarcoma. Oncogene. 2001 Sep 10;20(40):5736-46


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