Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Solid Tumour Section

Mini Review

Kidney: inv(X)(p11.2;q12) in renal cell carcinoma

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Identity

Other names: NONO-TFE3 renal cell carcinoma

Classification

This renal cell carcinoma, of which there is a single reported case, belongs to the family of Xp11 translocation renal carcinomas.

Clinics and pathology

Etiology

Unclear.

Epidemiology

Single case report in a 39-year-old male.

Pathology

The tumor was described as a papillary renal cell carcinoma. The UOK109 cell line was derived from this neoplasm.

Treatment

Surgical excision.

Prognosis

Unknown.

Cytogenetics

Cytogenetics morphological

inv(X)(p11.2;q12)

Genes involved and Proteins

TFE3

Location: Xp11.2

DNA/RNA

The TFE3 gene includes a 5' untranslated region, 8 exons, and a 3' untranslated region.

Protein

TFE3 is a transcription factor with a basic helix-loop-helix DNA binding domain and a leucine zipper dimerization domain. TFE3 contains a nuclear localization signal, encoded at the junction of exons 5 and 6, which is retained within all known TFE3 fusion proteins. TFE3 protein is 575 amino acids, and is ubiquitously expressed. TFE3, TFEB, TFEC and Mitf comprise the members of the microphthalmia transcription factor subfamily, which have homologous DNA binding domains and in fact bind to a common DNA sequence. These four transcription factors may homo- or heterodimerize to bind DNA, and they may have functional overlap.

p54nrb/NONO

Location: Xq12

Protein

p54nrb/NONO is a 471 amino acid protein with several distinctive domains. From N-terminus to C-terminus, it has:
1) an N-terminal basic region composed entirely of Proline, Glutamine, and Histidine,
2) a pair of RNA recognition motifs,
3) a helix-turn helix domain followed by a series of charged amino acids that likely forms a DNA-binding unit,
4) a short C-terminal Proline-rich region.
PSF and p54nrb/NonO are highly homologous and related proteins. p54nrb/NONO has a region of 320 amino acids with a 71% identity and a 7% similarity to a 320 amino acid region within PSF. Both proteins have both DNA and RNA binding domains, which

underlies their multifunctionality. Indeed, these proteins have been implicated in both transcriptional activation and splicing. Both proteins are known to bind to the DNA binding domains of nuclear hormone receptors (such as the thyroid hormone receptor and the retinoid X receptor), and modulate transcriptional activation. These proteins bind to each other, select the same optimal RNA sequence from RNA pools, and have been associated with spliceosomes. Both have been shown to bind to the C-terminal domain of RNA polymerase II, where they may couple pre-mRNA splicing and RNA processing. PSF and NonO enhance Topoisomerase I cleavage of DNA, and induce its jumping to other DNA helices after cleavage. Finally, both have been shown to bind and retain defective and hyperedited mRNAs within the nucleus, preventing translation of mutated proteins.

Result of the chromosomal anomaly

Hybride Gene

Description

5' p54nrb/NONO - 3' TFE3

Fusion protein

Description

The inv (X)(p11.2;q12) results in fusion of virtually the entire sequence of NONO/p54nrb with the C-terminal portion of the TFE transcription factor that contains the basic helix-loop-helix (bHLH) DNA binding domain and Leucine Zipper domain.

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