Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Short Communication

NF1 (neurofibromin 1)

Jean-Loup Huret

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

Published in Atlas Database: September 1997

Online version is available at: http://AtlasGeneticsOncology.org/Genes/NF1ID134.html
DOI: 10.4267/2042/32021

Identity

Location: 17q11.2

DNA/RNA

Description

60 exons; spans 350 kb; presence of 3 cryptic genes: OMGP, EVI2A, and EVI2B ('overlapping genes'), hidden within NF1 intron 27 with an opposite transcription direction.

Transcription

At least 4 alternate splicings; 9.0 mRNA complete cds; coding sequence: CDS 198..8717.

Protein

Description

The protein has been called neurofibromin; 2839 amino acids.

Expression

Is tissue and development stage specific.

Function

GTPase activating protein (GAP) interacting with $p21^{RAS}$ →tumour suppressor.

Homology

Other (GAP); IRA1 and 2, the yeast inhibitors of $p21^{RAS}$.

Mutations

Germinal

Large deletions or insertions in 25% of cases, translocations and point mutations; widely dispersed, with no cluster: yielding difficulties in diagnosis; truncating effect in 2/3 of cases.

Somatic

The second allele remains normal in benign tumours and is often lost in malignant tumours another process in tumourigenesis may involve RNA editing (for the second allele), which gives rise to a truncated neurofibromin having lost its GAP activity.

Implicated in

Neurofibromatosis type 1

Disease

Autosomal dominant cancer prone disease; neurofibromatosis type 1 (NF1: the same symbol is used for the disease neurofibromatosis type 1 and the gene neurofibromin 1) is an hamartoneoplastic syndrome.

Watson syndrome

Disease

Autosomal dominant disease with cardiac malformations, and, as is found in von Recklinghausen neurofibromatosis, low normal intelligence, café-au-lait spots, and neurofibromas but to a lesser extend.

Oncogenesis

In accordance with the two-hit model for neoplasia, as is found in retinoblastoma.

References

Cawthon RM, Weiss R, Xu GF, Viskochil D, Culver M, Stevens J, Robertson M, Dunn D, Gesteland R, O'Connell P, et al. A major segment of the neurofibromatosis type 1 gene: cDNA sequence, genomic structure, and point mutations. Cell 1990 Jul 13; 62(1):193-201. Erratum in Cell 1990 Aug 10; 62(3):608.

Gorlin RJ, Cohen MM, Levin LS. Syndromes of the head and neck. Oxford Monogr Med Genet 1990; 19:392-399.

Viskochil D, Buchberg AM, Xu G, Cawthon RM, Stevens J, Wolff RK, Culver M, Carey JC, Copeland NG, Jenkins NA, et al. Deletions and a translocation interrupt a cloned gene at the neurofibromatosis type 1 locus. Cell 1990 Jul 13; 62(1):187-192.

Wallace MR, Marchuk DA, Andersen LB, Letcher R, Odeh HM, Saulino AM, Fountain JW, Brereton A, Nicholson J, Mitchell AL, et al. Type 1 neurofibromatosis gene: identification of a large transcript disrupted in three NF1 patients. Science 1990 Jul 13; 249(4965):181-186. Erratum in Science 1990 Dec 21; 250(4988):1749.

Allanson JE, Upadhyaya M, Watson GH, Partington M, MacKenzie A, Lahey D, MacLeod H, Sarfarazi M, Broadhead W, Harper PS, et al. Watson syndrome: is it a subtype of type 1 neurofibromatosis? J Med Genet 1991 Nov; 28(11):752-756.

Tassabehji M, Strachan T, Sharland M, Colley A, Donnai D, Harris R, Thakker N. Tandem duplication within a neurofibromatosis type 1 (NF1) gene exon in a family with features of Watson syndrome and Noonan syndrome. Am J Hum Genet 1993 Jul; 53(1):90-95.

Shannon KM, O'Connell P, Martin GA, Paderanga D, Olson K, Dinndorf P, McCormick F. Loss of the normal NF1 allele from the bone marrow of children with type 1 neurofibromatosis and malignant myeloid disorders. N Engl J Med 1994 Mar 3; 330(9):597-601.

Henry I. Médecine-sciences 1995; 11:93. (Review). French.

Li Y, O'Connell P, Breidenbach HH, Cawthon R, Stevens J, Xu G, Neil S, Robertson M, White R, Viskochil D. Genomic organization of the neurofibromatosis 1 gene (NF1). Genomics 1995 Jan 1; 25(1):9-18.

Metheny LJ, Cappione AJ, Skuse GR. Genetic and epigenetic mechanisms in the pathogenesis of neurofibromatosis type I. J Neuropathol Exp Neurol 1995 Nov;54(6):753-760.

Cappione AJ, French BL, Skuse GR. A potential role for NF1 mRNA editing in the pathogenesis of NF1 tumors. Am J Hum Genet 1997 Feb; 60(2):305-312.

Hoffmeyer S, Nürnberg P, Ritter H, Fahsold R, Leistner W, Kaufmann D, Krone W. Nearby stop codons in exons of the neurofibromatosis type 1 gene are disparate splice effectors. Am J Hum Genet 1998 Feb; 62(2):269-77.

This article should be referenced as such:

Huret JL. NF1 (neurofibromin 1). Atlas Genet Cytogenet Oncol Haematol.1997;1(1):5-6.
