Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section

Mini Review

NBN (Nijmegen breakage syndrome 1)

Nancy Uhrhammer, Jacques-Olivier Bay, Richard A Gatti

Centre Jean-Perrin, BP 392, 63000 Clermont-Ferrand, France (NU, JOB, RAG)

Published in Atlas Database: October 2002

Online updated version : http://AtlasGeneticsOncology.org/Genes/NBS1ID160.html
DOI: 10.4267/2042/37922

This article is an update of:
Uhrhammer N, Bay JO, Gatti RA. NBS1 (Nijmegen breakage syndrome 1). Atlas Genet Cytogenet Oncol Haematol.1999;3(4):175-176.
Huret JL. NBS1 (Nijmegen breakage syndrome 1). Atlas Genet Cytogenet Oncol Haematol.1999;3(1):13-14.

Identity

Other names: NBS1 (Nijmegen breakage syndrome 1)

HGNC (Hugo): NBN

Location: 8q21.3

Note: See also, in Deep Insight section: Ataxia-Telangiectasia and variants.

DNA/RNA

Description

Spans over 51 kb; 16 exons.

Transcription

4.4 and 2.6 kb (alternative polyadenylation); open reading frame of 2265 nucleotides.

Protein

Description

The 754 amino acid protein is called nibrin; predicted MW 85 kDa, 95 kDa by SDS-PAGE; contains in N-term a forkhead associated domain (amino acids 24-100) and a breast cancer domain (BRCT; amino acids 105-190), both domains being found in the various DNA damage responsive cell cycle checkpoint proteins; 4 possible nuclear localization domains in the C-term half. Identified as the p95 subunit of the Rad50/Mre11/p95 double-strand DNA break repair complex. Nibrin is an essential component of this complex, and is responsible for its nuclear localization.

Expression

Wide; shorter transcript expressed at higher level in the testis (plays a role in DNA damage repair, though not in meiotic recombination, as ATM does).

Function

Member of the MRE/RAD50/nibrin double-strand break repair complex of 1600 kDa; necessary for localization of Rad50/Mre11 at DSB sites, and for the nucleolytic activities of this complex. Mice homozygous for null alleles of Nbs1 are inviable, while those with mutations corresponding to the common human mutation recapitulate the NBS phenotype. A 70 kDa protein containing the C-terminal portion of NBS1 produced from an alternative initiation site is associates with Rad50 and Mre11 and is apparently partially functional.

Homology

No known homology.

Mutations

Germinal

Missense mutations in the BRCT domain or truncating mutations downstream the BRCT are found in Nijmegen breakage syndrome (see below); most mutations are a 5 base deletion at codon 218, called 657del5, and are due to a founder effect.

Somatic

Missense mutations in NBS1 have been associated with childhood acute lymphoblastic leukemia.

Implicated in

Nijmegen breakage syndrome

Disease

Nijmegen breakage syndrome is a chromosome instability syndrome/cancer prone disease at risk of non Hodgkin lymphomas.

Cytogenetics

Chromosome rearrangements involving immunoglobulin superfamilly genes, in particular inv(7)(p13q35).

References

Jongmans W, Vuillaume M, Chrzanowska K, Smeets D, Sperling K, Hall J. Nijmegen breakage syndrome cells fail to induce the p53-mediated DNA damage response following exposure to ionizing radiation. Mol Cell Biol. 1997 Sep;17(9):5016-22

Maser RS, Monsen KJ, Nelms BE, Petrini JH. hMre11 and hRad50 nuclear foci are induced during the normal cellular response to DNA double-strand breaks. Mol Cell Biol. 1997 Oct;17(10):6087-96

Carney JP, Maser RS, Olivares H, Davis EM, Le Beau M, Yates JR 3rd, Hays L, Morgan WF, Petrini JH. The hMre11/hRad50 protein complex and Nijmegen breakage syndrome: linkage of double-strand break repair to the cellular DNA damage response. Cell. 1998 May 1;93(3):477-86

Matsuura S, Tauchi H, Nakamura A, Kondo N, Sakamoto S, Endo S, Smeets D, Solder B, Belohradsky BH, Der Kaloustian VM, Oshimura M, Isomura M, Nakamura Y, Komatsu K. Positional cloning of the gene for Nijmegen breakage syndrome. Nat Genet. 1998 Jun;19(2):179-81

Varon R, Vissinga C, Platzer M, Cerosaletti KM, Chrzanowska KH, Saar K, Beckmann G, Seemanová E, Cooper PR, Nowak NJ, Stumm M, Weemaes CM, Gatti RA, Wilson RK, Digweed M, Rosenthal A, Sperling K, Concannon P, Reis A. Nibrin, a novel DNA double-strand break repair protein, is mutated in Nijmegen breakage syndrome. Cell. 1998 May 1;93(3):467-76

Dong Z, Zhong Q, Chen PL. The Nijmegen breakage syndrome protein is essential for Mre11 phosphorylation upon DNA damage. J Biol Chem. 1999 Jul 9;274(28):19513-6

Zhong Q, Chen CF, Li S, Chen Y, Wang CC, Xiao J, Chen PL, Sharp ZD, Lee WH. Association of BRCA1 with the hRad50-hMre11-p95 complex and the DNA damage response. Science. 1999 Jul 30;285(5428):747-50

Buscemi G, Savio C, Zannini L, Micciché F, Masnada D, Nakanishi M, Tauchi H, Komatsu K, Mizutani S, Khanna K, Chen P, Concannon P, Chessa L, Delia D. Chk2 activation dependence on Nbs1 after DNA damage. Mol Cell Biol. 2001 Aug;21(15):5214-22

Maser RS, Zinkel R, Petrini JH. An alternative mode of translation permits production of a variant NBS1 protein from the common Nijmegen breakage syndrome allele. Nat Genet. 2001 Apr;27(4):417-21

van Engelen BG, Hiel JA, Gabreëls FJ, van den Heuvel LP, van Gent DC, Weemaes CM. Decreased immunoglobulin class switching in Nijmegen Breakage syndrome due to the DNA repair defect. Hum Immunol. 2001 Dec;62(12):1324-7

Varon R, Reis A, Henze G, von Einsiedel HG, Sperling K, Seeger K. Mutations in the Nijmegen Breakage Syndrome gene (NBS1) in childhood acute lymphoblastic leukemia (ALL). Cancer Res. 2001 May 1;61(9):3570-2

Williams BR, Mirzoeva OK, Morgan WF, Lin J, Dunnick W, Petrini JH. A murine model of Nijmegen breakage syndrome. Curr Biol. 2002 Apr 16;12(8):648-53

This article should be referenced as such:

Uhrhammer N, Bay JO, Gatti RA. NBN (Nijmegen breakage syndrome 1). Atlas Genet Cytogenet Oncol Haematol. 2003; 7(1):6-7.