

Gene Section

Mini Review

NBS1 (Nijmegen breakage syndrome 1)

Nancy Uhrhammer, Jacques-Olivier Bay, Richard A Gatti

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

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Identity

Location : 8q21.3

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.

Expression

Wide; shorter transcript expressed at higher level in the testis (may have a role 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.

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 bases deletion at codon 218, called 657del5, and are due to a founder effect.

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 superfamily genes, in particular inv(7)(p13q35).

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