Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

BUB1B (BUB1 budding uninhibited by benzimidazoles 1 homolog beta (yeast))

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Identity

Other names: BUBR1: Bub1A; MAD3L

HGNC (Hugo): BUB1B

Location: 15q15

DNA/RNA

Description

The gene spans 60 kb and is composed of 23 exons.

Protein

Note

Protein name: BUBR1

Description

1050 amino acids, 120 kDa.

Expression

Ubiquituously expressed.

Localisation

Cytoplasmic in interphase cells. Bound to BUB3 or CENPE, it can be localized to nuclear kinetochores.

Function

A central component of the mitotic spindle checkpoint that directly inhibits the anaphase-promoting complex/cyclosome until sister chromatids are correctly attached to the spindle, thus ensuring proper chromosome segregation during cell division. Also binds the motor protein CENPE, an interaction required for regulation of kinetochore-microtubule interactions and checkpoint signalling.

Homology

BUBR1 is the mammalian homolog of yeast Mad3, a significant difference being that BUBR1 possesses a kinase domain which is absent in Mad3.

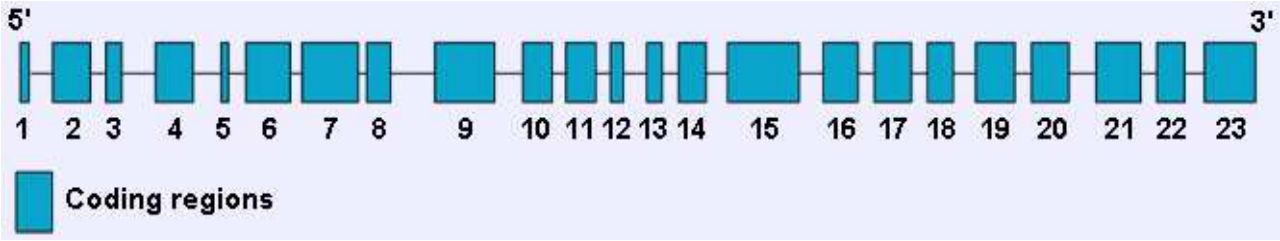

Figure 1: Schematic representation of BUB1B demonstrating the relative exon sizes (introns are not drawn to scale)

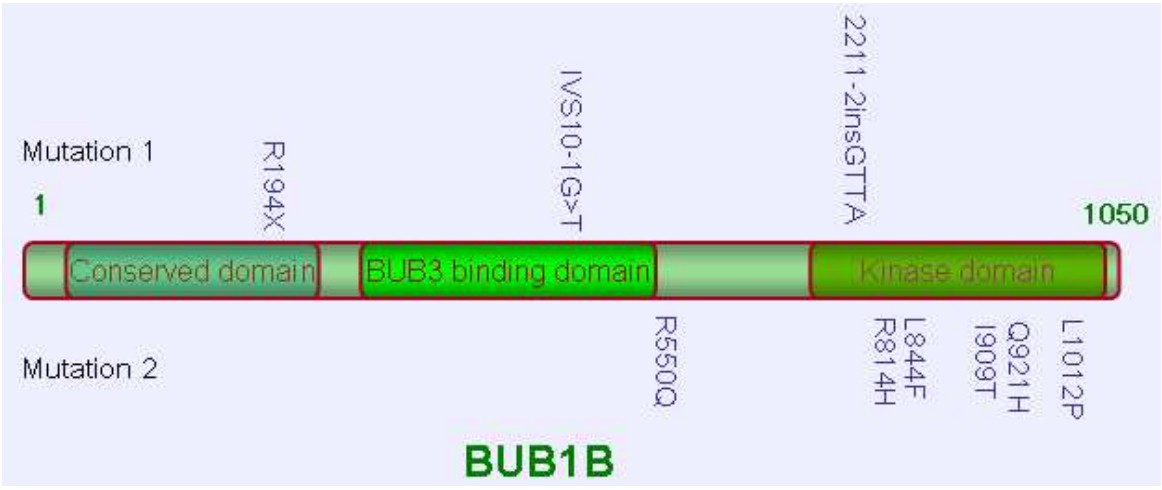

Figure 2 : Schematic representation of BUBR1 showing position of mutations, with truncating mutations depicted above the protein and missense mutations below.

Mutations

Note

See figure 2 above.

Germinal

Biallelic germline mutations found in five Mosaic Variegated Aneuploidy (MVA) cases. Each family carries one missense mutation and one mutation that results in premature protein truncation or an absent transcript.

Somatic

Deletion of T at codon 1023 predicted to remove part of the kinase domain.

Implicated in

Mosaic variegated aneuploidy (MVA)

Note

Is a rare recessive condition characterised by mosaic aneuploidies, predominantly trisomies and monosomies, involving multiple different chromosomes and tissues. Affected individuals typically present with severe intrauterine growth retardation and microcephaly. Eye anomalies, mild dysmorphism, variable developmental delay and a broad spectrum of additional congenital abnormalities and medical conditions may also occur.

Prognosis

There is early mortality in a significant proportion of cases due to failure to thrive and/or complications of congenital abnormalities, epilepsy, infections or malignancy.

Cytogenetics

The proportion of aneuploid cells varies but is usually >25% and is substantially greater than in normal individuals.

Oncogenesis

The risk of malignancy in MVA is high, with rhabdomyosarcoma, Wilms tumour and leukaemia reported in several cases. Two of the five cases with BUB1B mutations developed an embryonal rhabdomyosarcoma.

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