

Leukaemia Section

Short Communication

t(3;14)(q27;q32) HSP90AA1/BCL6

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Identity

Note

Most of the t(3;14)(q27;q32) where molecular genetics studies were performed showed the involvement of IGH@ and BCL6. It is unknown if the prognoses are different.

Clinics and pathology

Disease

Non Hodgkin lymphoma

Clinics

Four cases available to date: a case of primary gastric lymphoma (Xu et al., 2000); a gastric diffuse large B-cell lymphoma with residual MALT lymphoma (DLCLML) case (Chen et al., 2006), a case of primary central nervous system lymphoma (PCNSL, a diffuse large B cell lymphoma confined to the brain) (Montesinos-Rongen et al., 2003), and another lymphoma case (Akasaka et al., 2000).

Genes involved and proteins

BCL6

Location

3q27.3

Protein

706 amino acids; composed of a NH₂-term BTB/POZ domain (amino acids 1-130 (32-99 according to Swiss-Prot) which mediates homodimerization and protein-protein interactions with other corepressors (including HDAC1 and NCOR2/SMRT to constitute a large repressing complex, another transcription repression domain (191-386), PEST sequences (300-417) with a

KKYK motif (375-379), and six zinc finger at the C-term (518-541, 546-568, 574-596, 602-624, 630-652, 658-681), responsible for sequence specific DNA binding. Transcription repressor; recognizes the consensus sequence: TTCCT(A/C)GAA (Albagli-Curiel, 2003). Role in germinal centers of lymphoid follicles. BCL6 prevents ATM and TP53 to induce apoptosis in response to DNA rearrangements such as somatic hypermutation and class switch recombination. Therefore essential for normal B cell development.

HSP90AA1

Location

14q32.31

Protein

HSP90AA1 is also known as HSP90. Molecular chaperone. Possesses an ATP binding site with intrinsic ATPase activity that regulates its conformation. Promotes the maturation, structural maintenance and regulation of specific target proteins called 'client' proteins. Maintains protein homeostasis. HSP90AA1/HSP90 interacts with regions of client proteins where protein folding clefts merge. Folding clefts are a general topological feature of proteins in native conformation, and many of these hydrophobic clefts, must open to permit access of ligands. HSP90AA1/HSP90 stabilizes the open cleft, impeding further unfolding and Hsp70-dependent ubiquitination (Pratt et al., 2010). HSP90AA1/HSP90 and its associated co-chaperones facilitate a precise and efficient working environment beneficial for telomere function (DeZwaan and Freeman, 2010). HSP90AA1/HSP90 is exploited by cancer cells to support the activated and/or metastable forms of oncoproteins, and to buffer cellular stresses induced by the malignancy. Hsp90 is often overexpressed in cancer cells (Neckers and Workman, 2012).

Result of the chromosomal anomaly

Hybrid gene

Description

The break occurs in HSP90AA1 intron 1, resulting in the exchange of the first non-coding exons of HSP90AA1 and BCL6.

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