Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

FCGR2B (Fc fragment of IgG, low affinity IIb, receptor (CD32))

Mary Callanan, Dominique Leroux

Lymphoma Research Group - Groupe de Recherche sur les Lymphomes, Institut Albert Bonniot, La Tronche 38706, France (DL)

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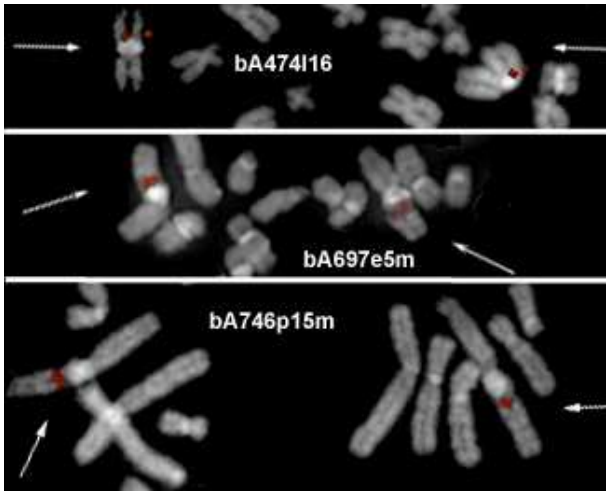
Identity

Other names: CD32; FCG2; FCGR2; IGFR2

HGNC (Hugo): FCGR2B

Location: 1q22

Local order: location, by FISH/genome sequencing; FCGR2B is contained within a locus that spans approximately 200kb and that encodes 5 low affinity IgG Fc receptor genes.The published gene orientation is as follows; Cen 1q -- 3' FCGR2A 5' -- 5'- FCGR3A - 3' -- 3' FCGR2B 5' -- 5' -FCGR3B- 3' -- 5' FCGR2C 3'.



Probe(s) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Description

The FCGR2B gene spans a 15kb genomic region; Gene orientation: centromere - 3' FCGR2B 5' - telomere; 8 exons (denoted S1, S2, EC1, EC2, TM, IC1, IC2, IC3). S1 and S2 encode the signal peptide domain, EC1 and EC2 encode the extracellular domain, TM encodes the transmembrane domain and IC1, IC2, IC3 encode the intracytoplasmic region.

Transcription

1.7kb mRNA. Two alternately spliced mRNA exist in humans; FcgRIIb1 and FcgRIIb2 (a 19 aa insertion encoded by IC1 is present in b1 but not in b2).

Protein

Note
Called Fc gamma RIIB.

Description

40kD transmembrane glycoprotein that possesses an intracytoplasmic Immunoreceptor Tyrosine-based Inhibition Motif (ITIM) (encoded by IC3).

Expression

B, myeloid and mast cells.

Localisation

Transmembrane.

Function

Low affinity IgG Fc receptor. Founding member ITIM family of immune inhibitory receptors. Fc gamma RIIB functions to down-regulate activatory responses mediated by Immunoreceptor Tyrosine-based Inhibition Motif (ITAM) bearing receptors such as the B-cell receptor on B cells. For example, on B-cells, negative regulation of B-cell receptor activatory signalling is initiated through co-recruitment of BCR and Fc gamma RIIB to IgG/ immune complexes. This leads to tyrosyl phosphorylation of the Fc gamma RIIB ITIM motif / recruitment of the inositol phosphatase SHIP and activation of the adaptor protein Dok - these events ultimately lead to the inhibition of ITAM-dependant Ca++ mobilisation and cellular proliferation (reduced MAPK signalling), respectively.
A proapoptotic signal through the Fc gamma RIIB transmembrane sequence has been described in conditions of homo-aggregation of Fc gamma RII on murine B cells.

Homology

Contains two immunoglobulin-like C2 domains.

Implicated in

1q21-23 rearrangements in NHL (Nnon-Hodgkins Lymphoma)

Disease

NHL (< 5% of cases with 1q21-23 breaks).

Prognosis

It is now known that cytogenetically determined 1q21-23 breaks can target a diversity of 1q21-23 genes. Early data has suggested a poor prognosis for 1q21 rearrangements in diffuse large cell lymphoma.

Cytogenetics

Deregulation of the FCGR2B gene by chromosomal translocation was first demonstrated in 3 NHL patients that showed a t(1;22)(q22;q22) in association with a t(14;18)(q32;q21). Two further cases of NHL with rearrangements affecting the FCGR2B region have since been identified. Both cases also showed t(14;18) (see below for description). This suggests a role for this deregulation in lymphoma progression.

Hybrid/Mutated gene

Dysregulation of the FCGR2B gene has been identified as a consequence of a t(1;22)(q22;q11) (3 patients) and t(1;14)(q21;q32) (1 patient). The FCGR2B coding sequence and promoter region appear to remain intact in these translocations. The principal consequence is overexpression of the Fc gamma RIIb2 isoform of Fc gamma RIIB. Deregulation of FCGR2B most likely occurs as a consequence of Ig gene transcriptional enhancer activity. Other mechanisms may exist; an NHL patient with dup(1)(q21q25) and rearrangement in the FCGR2B region has also been identified.

Abnormal protein

None.

Oncogenesis

Contribution of FCGR2B deregulation to lymphoma development or progression is currently not known.

References

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