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Gene Section
Review

IGH@ (Immunoglobulin Heavy)

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Identity

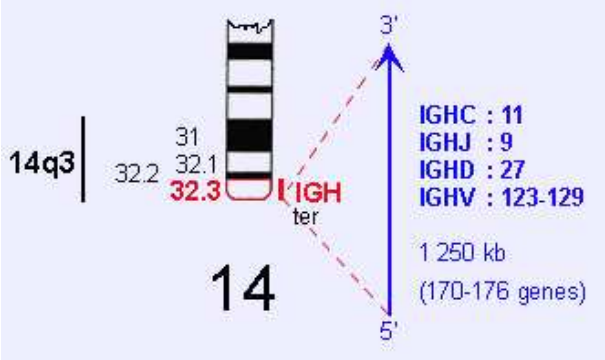
Other names: IGH (Immunoglobulin Heavy)

HGNC (Hugo): IGH@

Location: 14q32.33

Note

The human IGH locus is located on the chromo-some 14 at band 14q32.33, at the telomeric extremity of the long arm; the orientation of the locus has been determined by the analysis of translocations, involving the IGH locus, in leukemia and lymphoma.



For complete Figure, see: chromosome 14, IMGT (The International ImMunoGeneTics information system ®) © Copyright 1995-2003 IMGT, IMGT is a CNRS trademark.

DNA/RNA

Description

The human IGH locus at 14q32.33 spans 1250 kilobases (kb). It consists of 123 to 129 IGHV genes, depending from the haplotypes, 27 IGHD segments belonging to 7 subgroups, 9 IGHJ segments, and 11 IGHC genes.

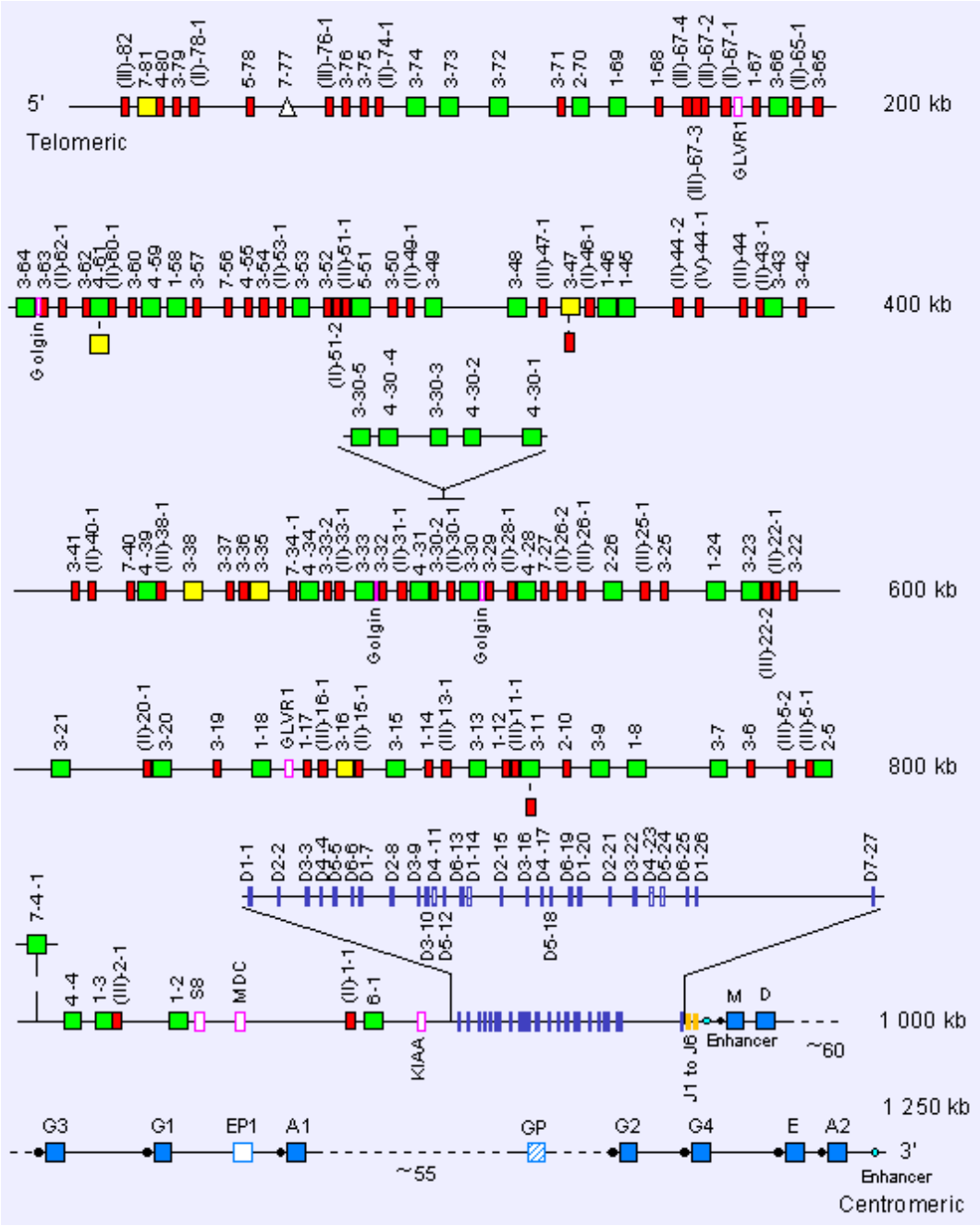
Eighty-two to 88 IGHV genes belong to 7 subgroups, whereas 41 pseudogenes, which are too divergent to be assigned to subgroups, have been assigned to 4 clans. Seven non-mapped IGHV genes have been described as insertion/deletion polymorphism but have not yet been precisely located.

The most 5' IGHV genes occupy a position very close to the chromosome 14q telomere whereas the IGHC genes are in a more centromeric position.

The potentiel genomic IGH repertoire is more limited since it comprises 38-46 functional IGHV genes belonging to 6 or 7 subgroups depending from the haplotypes 23 IGHD, 6 IGHJ, and 9 IGHC genes.

Thirty-five IGH genes have been found outside the main locus in other chromosomal localizations. These genes designated as orphons cannot contribute to the synthesis of the immunoglobulin chains, even if they have an Open Reading Frame (ORF). 9 IGHV orphons and 10 IGHD orphons have been described on chromosome 15 (15q11.2), and 16 IGHV orphons on chromosome 16 (16p11.2). In addition, one IGHC processed gene, IGHEP2 is localised on chromosome 9 (9p24.2-p24.1).

This is so far the only processed Ig gene described. The total number of human IGH genes per haploid genome is 170 to 176 (206 to 212 genes, if the orphons and the processed gene are included) of which 77 to 84 genes are functional. List of the human IGH genes.



IGH
V-GENE: Green box: Functional; Yellow box: Open reading frame; Red: Pseudogene; Grey triangle: Not sequenced, not found.
D-GENE: Blue: Functional; Blue open box: Open reading frame.
J-GENE: Grey: Functional .
C-GENE: Blue: Functional; Blue dashed box: Open reading frame; Blue open box: Pseudogene.
GENES NOT RELATED: Purple open box: Pseudogene.
For compete Figure, see: locus IGH, IMGT (The International ImMunoGeneTics information system ®)

Protein

Description

Proteins encoded by the IGH locus are the immunoglobulin heavy chains. They result from the recombination (or rearrangement), at the DNA level, of three genes: IGHV, IGHD and IGHJ, with deletion of the intermediary DNA to create a rearranged IGHV-D-J gene.

The rearranged IGHV-D-J gene is transcribed with the IGHM gene and translated into an immuno-globulin mu chain. The gamma, alpha or epsilon heavy chains, result from a new recombination (or switch), again at

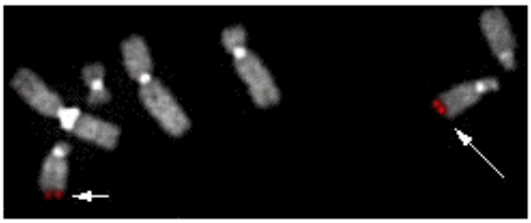
the DNA level, between sequences designated as "Switch" and localized upstream of the IGHM and of each of the functional IGHG, IGHA and IGHE constant genes.
This recombination, accompanied by the deletion of the intermediary DNA, allows the IGHV-D-J initially transcribed with the IGHM, to be now transcribed with a IGHG, IGHA or IGHE gene, and translated into a gamma, alpha or epsilon chain.
Translation of the variable germline genes involved in the IGHV-D-J rearrangements are available at IMGT Repertoire Protein displays. Compared to the germline genes, the rearranged variable genes will acquire somatic mutations during the B cell differentiation in the lymph nodes, which will considerably increase their diversity. These somatic mutations can be analysed using IMGT/V-QUEST tool

Mutations

Note
Mutations which correspond to allelic polymer-phisms of the functional germline IGHV, IGHD, IGHJ and IGHC genes are described in the IMGT database: (IMGT Repertoire>Alignments of alleles)

Implicated in

Translocations which frequently result from errors of the recombinase enzyme complexe (RAG1, RAG2, etc.), responsable of the Immunoglobulin and T cell receptor V-J and V-D-J rearrangements, or from errors of the switch enzyme. IGHV, IGHD or IGHJ recombination signals or isolated heptamer (first case) or switch sequences (second case) are observed at the breakpoints.



c-Immunoglobulin genes IgH at 14q32.33, in normal cells: PAC 998D24 - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

t(1;14)(p21;q32); involve BCL10 in 1p21

Disease
Marginal zone B-cell lymphoma.

t(3;14)(q27;q32); involve BCL6 in 3q27

Disease
B-cell non-Hodgkin lymphomas (NHL), mainly diffuse large cell lymphoma; adult aggressive lymphoma.

Prognosis
Controversial.

t(4;14)(p16;q32); involve FGFR3 in 4p16

Disease
Plasma cell leukaemia and multiple myeloma.

Prognosis
Yet poorly described.

t(5;14)(q31;q32); involve IL3 in 5q31

Disease
B-cell acute lymphoblastic leukemia (ALL) with hypereosinophilia.

Prognosis
Prognosis appears to be poor.

t(8;14)(q11;q32)

Disease
B-cell acute lymphoblastic leukemia (ALL); chronic myelogenous leukemia (CML).

Prognosis
Still unknown.

t(8;14)(q24;q32) ; involve C-MYC in 8q24

Disease
B-cell acute lymphoblastic leukemia (ALL3) and non-Hodgkin lymphomas (NHL), especially in the Burkitt lymphoma.

Prognosis
The prognosis has evolved with new treatments.

t(9;14)(p13;q32); involve PAX5 in 9p13

Disease
Lymphoplasmatic lymphoma.

t(10;14)(q24;q32); involve HOX 11 in 10q24

Disease
B-cell acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma (NHL).

Prognosis
Not unfavourable.

t(11;14)(q13;q32); involve BCL1 in 11q13

Disease
t(11;14) is mainly found in mantle cell lymphoma; B-prolymphocytic leukaemia, chronic lymphocytic leukaemia, splenic lymphoma with villous lymphocytes , and multiple myeloma other B-cell lymphoproliferations.

t(14;18)(q32;q21); involve BCL2 in 18q21

Disease
Follicle centre cell lymphoma mainly, and also diffuse large cell lyphoma; rarely in other B-cell lymphoproliferations.

Prognosis
The t(14;18) may have little or no prognostic significance.

t(14;19)(q32;q13.1); involve BCL3 in 19q13

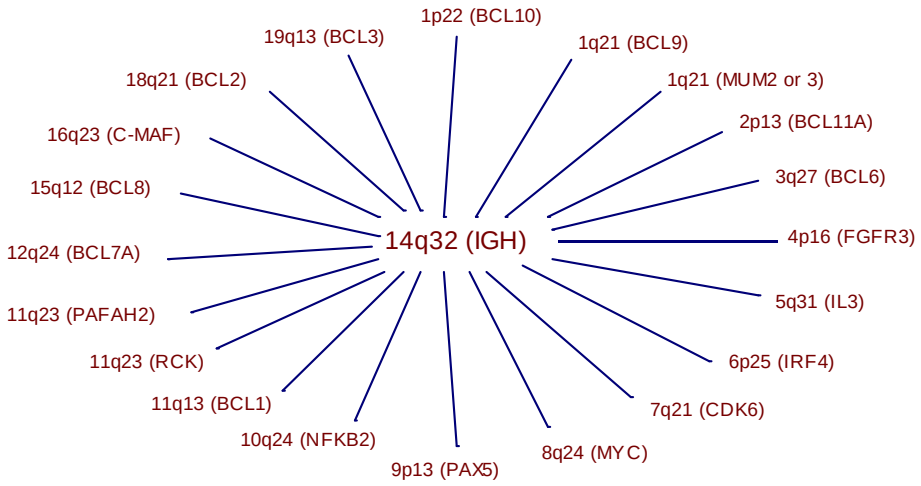
Disease

Chronic lymphocytic leukaemia (CLL) mainly, and other B-cell lymphoproliferations.

Prognosis

t(14;19) is an adverse prognostic factor in CLL, compared to the usual prognosis in CLL.

Breakpoints



IGH and partners. Editor 08/2001

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