IMGT Colliers de Perles for antibody engineering

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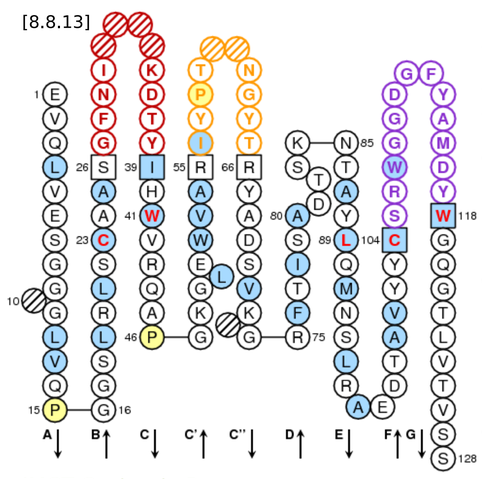
IMGT®, the international ImMunoGeneTics information system®, created in 1989 at Montpellier, France (CNRS and Université Montpellier II)

- is the international reference in immunogenetics and immunoinformatics
- contains:
  - immunoglobulin superfamily (IgSF) proteins [immunoglobulins (IG), T cell receptors (TR), and proteins other than IG and TR with at least one domain of V type or C type]
  - MHC superfamily (MhcSF) proteins [major histocompatibility complex (MHC) and proteins other than MHC with domains of G type]
- provides standardized data based on the IMGT-ONTOLOGY concepts
- uses IMGT unique numbering for domains of V type (V, V-LIKE), C type (C, C-LIKE) and G type (G, G-LIKE)

On one layer

VH (V-DOMAIN)



IMGT Collier de Perles on one layer.
VH from trastuzumab FAB-GAMMA-1_KAPPA (IMGT/3Dstructure-DB: **1n8z**).

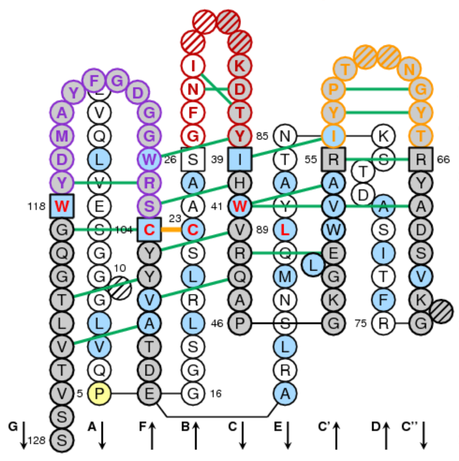
IMGT Colliers de Perles are standardized graphical 2D representations of domain amino acid sequences:

1. They bridge the gap between sequences and 3D structures
2. They are **highly valuable in the absence of 3D structures**
3. The V-DOMAIN IMGT-Collier de Perles is based on the **IMGT unique numbering for V- and V-LIKE-DOMAIN** [1]

[1] *Lefranc, M.-P. et al. Dev. Comp. Immunol. 27:55-77 (2003)*

On two layers

VH (V-DOMAIN)



IMGT Collier de Perles on two layers.
VH from **1n8z**, with hydrogen bonds between the strands in the GFCC'C".

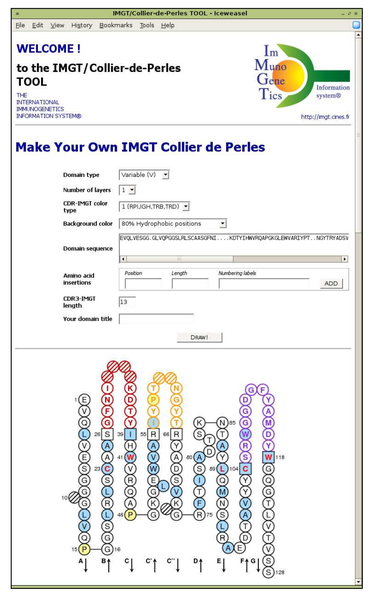
IMGT Colliers de Perles are particularly useful for antibody engineering:

1. to map a sequence on the **domain conserved topology**
2. to compare with **germline sequences**
3. to provide standardized **FR-IMGT and CDR-IMGT delimitations** [4]

[4] *Ruiz, M. and Lefranc, M.-P. Immunogenetics 53:857-883 (2002)*

IMGT tools

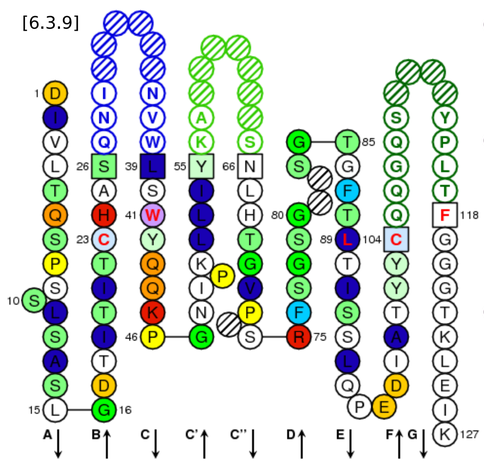
IMGT/Collier-de-Perles



The IMGT/Collier-de-Perles tool allows to draw an IMGT Collier de Perles, **from a user amino acid sequence with IMGT gaps**:

- for V-DOMAIN or C-DOMAIN
- on one or two layers
- with different color menus
- with user special insertions.

V-KAPPA (V-DOMAIN)

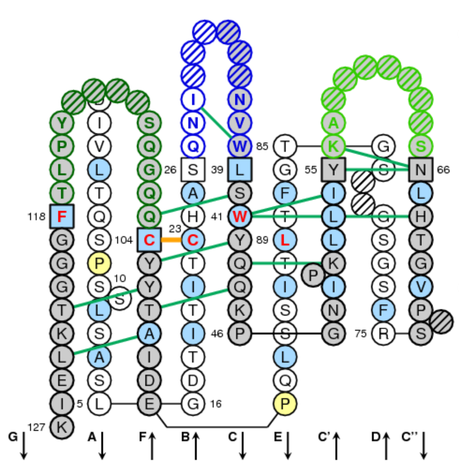


V-KAPPA from **1n8z**. Color menu for the eleven IMGT amino acid classes.

4. **CDR-IMGT** identified by their color menu
5. **Conserved positions** *C23, W41, hydrophobic 89, C104, and F/W118*
6. IMGT Colliers de Perles profiles for **hydropathy, volume and physico-chemical properties** [2] *For IGHV, IGHKV or IGLV*

[2] *Pommié, C. et al. J Mol Recognit 17:17-32 (2004)*

V-KAPPA (V-DOMAIN)

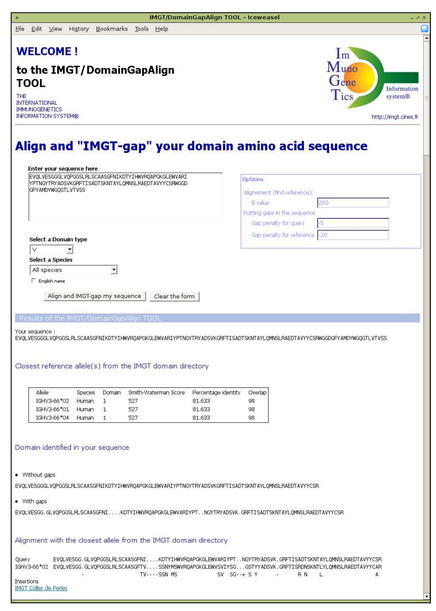


V-KAPPA from **1n8z**, with hydrogen bonds between the strands in the GFCC'C" sheet.

4. to visualize **hydrogen bonds in known 3D structures** from IMGT/3Dstructure-DB [5]
5. to identify amino acids with **hydrogen bonds to the antigen** in known 3D structures from IMGT/3Dstructure-DB [5]

[5] *Kaas, Q. et al. Nucleic Acids Res. 32:208-210 (2004)*

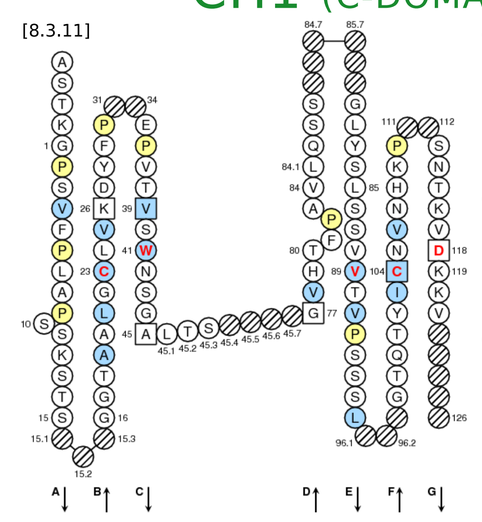
IMGT/DomainGapAlign



The IMGT/Domain GapAlign tool:

- aligns the user sequence with the **IMGT domain reference directory**
- identifies the closest sequence with **IMGT gene and allele name**
- provides IMGT gaps for V-REGION and C-DOMAIN and the associated **IMGT Colliers de Perles**.

CH1 (C-DOMAIN)

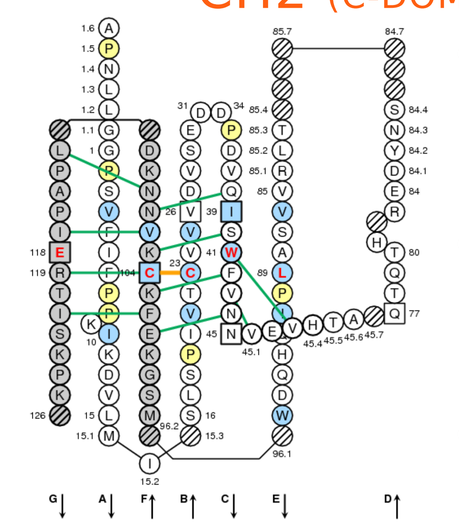


CH1 from **1n8z**. Hydrophobic core positions in blue.

7. The C-DOMAIN IMGT Collier de Perles is based on the **IMGT unique numbering for C- and C-LIKE-DOMAIN** [3]
8. **Hydrophobic core** positions are in blue *Found in more than 50% of analysed sequences*
9. The IMGT Colliers de Perles allow to compare domains **whatever the species, the domain type** (V or C), **the chain type and the receptor type** (IG or TR).

[3] *Lefranc, M.-P. et al. Dev. Comp. Immunol. 29:185-203 (2005)*

CH2 (C-DOMAIN)

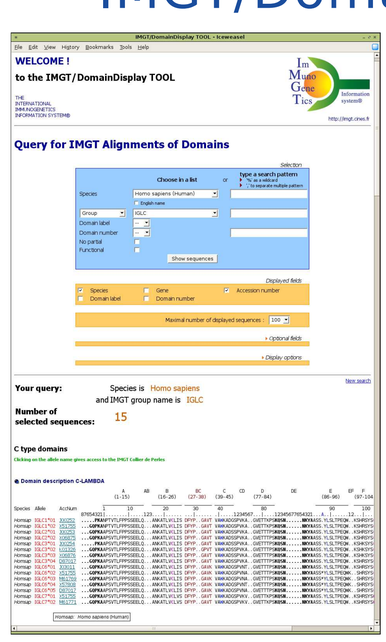


CH2 from **1igt**, with hydrogen bonds in the GFC sheet.

6. to localize amino acids **involved in ADCC** (FcR binding) [6]
7. to localize amino acids **involved in CDC** (C1q binding)
8. to localize amino acids located in **N-glycosylation sites**.

[6] *Lefranc, M.-P. and Lefranc, G. The Immunoglobulin FactsBook, Academic Press, 458 pages (2001)*

IMGT/DomainDisplay



gives access:

- to the IMGT domain reference directory (sequences from **IMGT/GENE-DB** [7] and from **IMGT Protein displays** [6])
- to IMGT Collier de Perles for each germline V sequence which allows a straightforward **comparison between germline and engineered sequences.**

[7] *Giudicelli, V. et al. Nucleic Acids Res. 33:256-261 (2005)*

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