IMGT Unique Numbering for Standardized Contact Analysis of Immunoglobulin/antigen and T cell receptor/peptide/MHC Complexes

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ABSTRACT: Immunoglobulins (IG) , T cell receptors (TR) and major histocompatibility complex (MHC) are major components of the immune system. Their experimentally determined three-dimensional (3D) structures are numerous and their retrieval and comparison is problematic. IMGT, the international ImMunoGeneTics information system® (http://imgt.cines.fr), has devised controlled vocabulary and annotation rules for the sequences and 3D structures of the IG, TR and MHC. Annotated data from IMGT/3Dsructure-DB, the IMGT 3D structure database, are used in this paper to compare 3D structure of the domains and receptor, and to characterize IG/antigen, peptide/MHC and TR/peptide/MHC interfaces. The analysis includes angle measures to assess receptor flexibility, structural superimposition and contact analysis. Up-to-date data and analysis results are available at the IMGT Web site, http://imgt.cines.fr.

1 INTRODUCTION

The adaptive immune response that appeared 450 million years ago in vertebrates involves B and T cells, and specific receptors, the antibodies or immunoglobulins (IG) and the T cell receptors (TR). Whereas IG recognize soluble antigens in a native form, TR recognize antigens as peptides bound to major histocompatibility complex (MHC). It is therefore of the highest importance to analyze the contacts and study the interface in IG/antigen and TR/peptide/MHC complexes. Owing to the huge diversity of the antigen receptors (10^{12} IG and 10^{12} TR per individual [1,2]) and to the high degree of the MHC polymorphism, specialized databases and tools were needed.

IMGT, the international ImMunoGeneTics information system® (http://imgt.cines.fr) [3,4], created in 1989 at Montpellier, France, is a high quality integrated knowledge resource specialized in IG, TR, MHC of human and other vertebrates, and related proteins of the immune system (RPI) that belong to the immunoglobulin superfamily (IgSF) and to the MHC superfamily (MhcSF). IMGT has developed IMGT-ONTOLOGY [5], the first ontology in immunogenetics and immunoinformatics. Based on the IMGT-ONTOLOGY concepts, the IMGT Scientific chart provides the controlled vocabulary and the annotation rules necessary for the identification, the description, the classification and the numbering of the IG, TR, MHC and RPI. The IDENTIFICATION concept refers to the IMGT standardized keywords indispensable for the sequence and three-dimensional (3D) structure assignments. The DESCRIPTION concept provides the IMGT standardized labels used to describe the structural and functional regions that compose IG, TR, MHC and RPI sequences and 3D structures. The CLASSIFICATION concept provides immunologists and geneticists with a standardized nomenclature per locus and per species. The NUMERATION concept provides the IMGT unique numbering for (i) the V-DOMAIN of IG and TR, and V-LIKE-DOMAIN of the IgSF proteins other than IG and TR [6], (ii) the C-DOMAIN of IG and TR, and C-LIKE-DOMAIN of the IgSF proteins other than IG or TR [7], and (iii) the G-DOMAIN of MHC, and G-LIKE-DOMAIN of the MhcSF proteins other than MHC [8]. The IMGT unique numbering for each domain type relies on the high conservation of the corresponding domain structure and allows to align domain and to compare sequences and corresponding 3D structures.

IMGT/3Dstructure-DB [9], developed as part of IMGT, is a specialized database that expertly identifies the genes and alleles which encode the IG, TR and MHC proteins and that provides a standardized analysis of their 3D structures. IMGT/3Dstructure-DB also provides affords renumbered coordinate files according to the IMGT unique numbering and detailed contact analysis of interface interactions. The high level of standardization allows to investigate many aspects of the managed proteins. Here we have used IMGT/3Dstructure-DB to compare domain and receptor 3D structures and to characterize IG/antigen and TR/peptide/MHC interfaces. These data are particularly useful to identify and to characterize the specific 3D structure features of a given antigen receptor

For IG/antigen, the flexibility of the IG antigen binding fragment (Fab) was measured by four characteristic angles and the number of atomic contacts with antigen was summed at each position. For peptide/MHC, the conformational variability of MHC upon peptide binding and that of peptides of different lengths were measured. The peptide/MHC contacts were analyzed and lead to the definition of IMGT peptide contact sites [10]. For the TR/peptide/MHC, the TR orientation on peptide/MHC and the TR/MHC contacting positions were analyzed.

2 MATERIAL AND METHODS

2.1 Data

The IG antigen binding site is an assembly of two domains, the VH domain that belongs to the heavy chain and the V-KAPPA or V-LAMBDA domains that belongs to the light

chain (Figure 1). The assembly of VH with V-KAPPA or V-LAMBDA is termed V-DOMAIN partners. C-DOMAIN partners refer in this paper to the assembly of the CH1 domain of the heavy chain with the C-KAPPA or C-LAMBDA domain of the light chain. The percentage of sequence identity was computed between all V-DOMAIN partners, and the *hclust* algorithm with the *complete* method, implemented in R environment (http://www.R-project.org), was used to make clusters with more than 90% of sequence identity. A representative domain was chosen on each cluster on the basis of its completeness (few positions without coordinate) and its crystallographic resolution. X-Ray structures were preferred upon RMN structures, and theoretical models were discarded. A list of 256 different IG V-DOMAIN partners 3D structures were thus extracted from IMGT/3Dstructure-DB. A list of 164 different IG Fab fragments 3D structures were selected in the same way.
A set of 20 groups of 3D structures containing the same MHC (98% sequence identity) binding different peptides was selected, that comprise 14 groups and 93 peptide/MHC-I 3D structures and 6 groups and 31 peptide/MHC-II 3D structures. For the peptide conformational variability analysis and peptide/MHC contact analysis 137 peptide/MHC-I 3D structures (40 with a 8 amino acid long peptide, 85 with a 9 amino acid peptide and 12 with a 10 amino acid peptide), and 44 peptide/MHC-II 3D structures were selected.
The currently available 18 TR/peptide/MHC experimental 3D structures were used for the analysis (15 TR-ALPHA_BETA/MHC-I and 3 TR-ALPHA_BETA/MHC-II).
The lists of selected structures are available on-line at the IMGT Website in the IMGT/3Dstructure-DB analysis pages.

2.2 Structural alignments

Domain structural alignments were performed using the MacLahclan algorithm [11] as implemented in the ProFit program, with a sequence alignment according to the IMGT unique numbering of the corresponding domain [6,7,8]. The alignment of domain partners was also performed with ProFit and an alignment of both domains corresponding to the IMGT unique numbering.
Regions of variable lengths were not included in the structural alignments. They comprise, for V-DOMAIN, the complementarity determining regions (CDR) positions (positions 26 to 39, positions 55 to 66 and positions 104 to 118, for C-DOMAIN, the positions of the BC loop (26 to 39), the CD strand (positions 42 to 77) and the GF loop (positions 104 to 118), for G-DOMAIN, the AB (positions 14 to 18) and CD (positions 38 to 42) loops and C-terminal parts (positions 88 to 92).
Peptide/MHC superimposition was performed by first aligning the 3D structure of the two G-DOMAIN.
The root mean square deviation (RMSD) of a position shared by several 3D structures was computed from the distance between shared positions in all pairs of aligned 3D structures.

2.3 Angle definition and measure

To characterize the IG V-DOMAIN partners and C-DOMAIN partners, the angle between the planes of external and internal beta sheets were measured (Figure 1). The V-DOMAIN internal sheet contained the B, D and E strands, and the external sheet contained the C, F and G strands [6]. The C-DOMAIN partners (CH1 and C-KAPPA or C-LAMBDA) have a reverse arrangement, the internal sheet contained the C, F and G strands, and the external sheet contains the B, D and E strands [7]. The plane corresponding to the sheet containing the B, D and E strands is defined by one vertex in the B strand, whose the first extremity is at the center of the alpha carbons of positions 18, 19 and 20, and the second extremity is at the center of the alpha carbons of positions 24, 25 and 26, and by a second vertex between the alpha carbons of the positions 7 and 79. The plane corresponding to the sheet containing the C, F and G strands is defined by one vertex in the F strand between the alpha carbons of positions 101 and 104.
The angle between the two vertices that are perpendicular to the external sheets and the angle between the two vertices that are perpendicular to the internal sheets were computed. It will be referred as the *plane angle*. To measure *rotation angle* between external sheets and between internal sheets, the angle between the first vertex in the first domain and the project of the first vertex in the second domain on the sheet plane was computed.

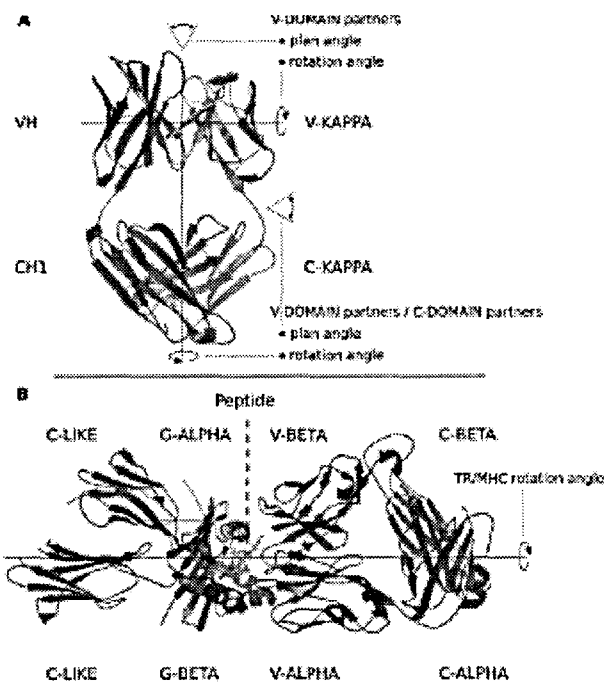

Figure 1: Angle definition used in the analysis. (A) IG Fab fragment and angle definition for the internal flexibility measure. (B) TR/peptide/MHC and TR rotation angle on peptide/MHC. The vertices and plane are defined in the text with positions on each domain type according to the IMGT unique numbering for V-DOMAIN, C-DOMAIN and G-DOMAIN [6,7,8]. The IG V-DOMAIN partners comprise VH and V-KAPPA (or V-LAMBDA) domains. The IG C-DOMAIN partners comprise CH1 and C-KAPPA (or C-LAMBDA) domains. The MHC-II partners comprise two G-DOMAINs G-ALPHA and G-BETA (the MHC-I partners comprise G-ALPHA1 and G-ALPHA2). The TR V-DOMAIN partners comprise V-ALPHA and V-BETA domains. The TR C-DOMAIN partners comprise C-ALPHA and C-BETA domains.

The angle between the IG V-DOMAIN partners and the C-DOMAIN partners was measured by computing a plane and rotation angle (similarly as defined above) from two

planes, a plane that characterizes the V-DOMAIN partners with two vertices whose extremities are alpha carbons of positions 104 and 50 of each domain, and a plane that characterizes the C-DOMAIN partners with two vertices whose extremities are the alpha carbons of positions 104 and 19.
To measure the orientation of TR on peptide/MHC, two planes were defined. The plane corresponding to the MHC sheets is defined by two vertices, whose extremities are the alpha carbons of positions 27 and 21 of each G-DOMAIN. A plane globally perpendicular to the TR sheets was defined by two vertices whose extremities are the alpha carbons of positions 47 and 104 of each V-DOMAIN.

2.4 Contact analysis

IMGT/3Dstructure-DB provides a detailed contact analysis of each position in a 3D structure [9]. The number of atom contacts is recorded and detailed in polar or apolar contacts, hydrogen bond, covalent bond or non covalent and disulfide bridge. The location of each atom in the backbone or side chain is taken into account and used for each contact type.
The V-DOMAIN positions that are in contact with the antigen were summed from the IMGT/3Dstructure-DB contacts analysis. The contacts were summed separately for each CDR (CDR1-IMGT, CDR2- IMGT and CDR3- IMGT) and for each CDR length, and for the framework [1,2].
For peptide/MHC-I contact analysis, the pairwise contacts between MHC-I positions and peptide positions were summed for each peptide length. The pairwise peptide/MHC-II pairwise contacts between MHC-II positions and the nine peptide positions in the MHC-II binding groove were summed.
For TR/peptide/MHC, the pairwise contacts between TR and MHC were summed.

3 RESULTS

3.1 IG/antigen

3.1.1 IG internal angle variations

The rotation angle between V-DOMAIN partner sheets is of 13 degrees with a standard deviation (sd.) of 5 degrees for the internal sheet, and of 126 degrees with 10 sd. degrees for the external sheet. The plane angle between the internal sheets is of 22 degrees with 5 sd. degrees and the plane angle between external sheets is of 66 degrees with 5 sd. degrees. These values indicate that the external sheets are V shaped, the opening being in the antigen direction. These numbers do not vary between the type of IG V-DOMAIN partners, VH and V-KAPPA, or VH and V-LAMBDA (data and results available on-line). The rotation angle between the V-DOMAIN partners and the C-DOMAIN partners (see materials and methods) is of 28 degrees with 8 std. degrees for the Fab fragments. The bent angle between V-DOMAIN partners and C-DOMAIN is of 24 degrees with 13 std. degrees for Fab fragments. These mean values reveal the most frequent Fab conformation in known 3D structures, and they may be used to identify 3D structures with unusual Fab conformation.

3.1.2 IG contact analysis

The CDRs are the main contact regions with the antigen but framework positions could also be involved (Figure 2), especially with small antigens which are known to be deeply buried in the IG binding site. For all domain type, the framework positions which are the more frequently in contact with the antigens are the CDR2 anchor positions 55 and 66 and the position 40, that mainly interact with their side chain. For the V-KAPPA and V-LAMBDA, the positions 67, 68 and 69 on the C" strand, for V-LAMBDA position 80 and 84, and for V-KAPPA positions 58 and 118 are also significantly found in interaction with the antigen.
The CDR interactions have been analysed for each CDR length and domain type. The second part of the CDR1 make more contacts with the antigen than the first part, whatever the domain (VH, V-KAPPA or V-LAMBDA) or the CDR1 length. All positions of the CDR2 could be implicated in the antigen recognition, whatever the domain and CDR2 length. The CDR3 could also contact the antigen with almost all its positions whatever the domain and the CDR3 length. Even with longer CDR3 (up to 24 amino acids in the data set) the contacting positions could be at the tip positions as well as near the anchor positions. The on-line visualization tool (http://imgt.cines.fr) provides useful information about positions that are frequently found in a specific interaction with the antigen (hydrogen bond or polar contact of side chain).

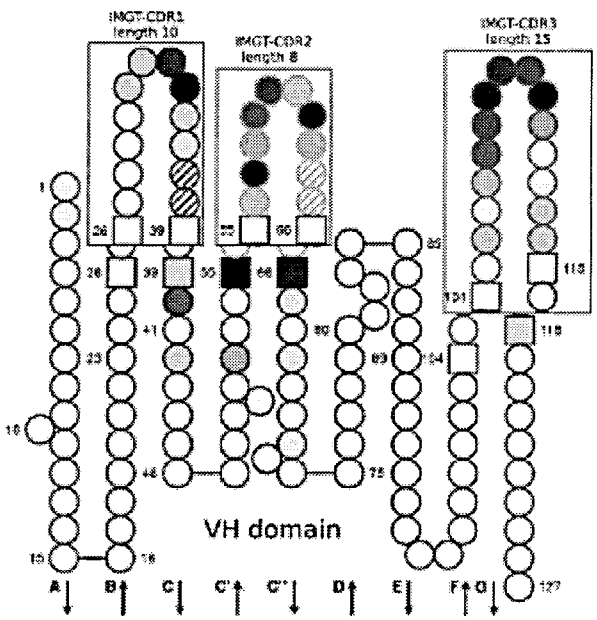

Figure 2: VH IMGT Collier de Perles with positions the most frequently in contact with antigens. Three hundred and seventeen VH 3D structures have been analyzed for the framework, 30 3D structures for the CDR1-IMGT of length 10, 182 3D structures for the CDR2-IMGT of length 8 and 22 3D structures for the CDR3-IMGT of length 15. Positions which most frequently are in contact with the antigen are the darker. Be aware that the scale of the gray is different for CDR and frameworks.

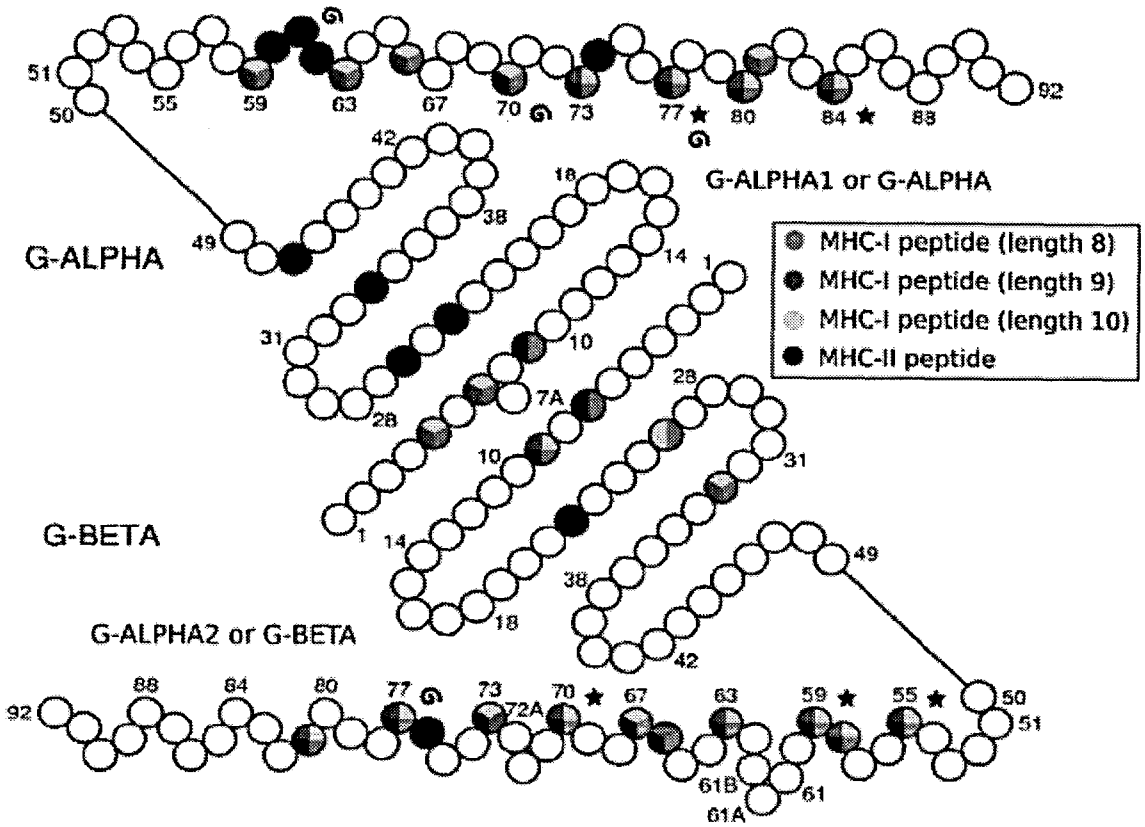

Figure 3: IMGT Collier de Perles of MHC positions found in contacts in at least 80% of studied peptide/MHC-I 3D structures for 8-residue, 9-residue and 10-residue peptides and peptide/MHC-II for nine peptide positions in MHC-II groove. The stars indicate MHC-I positions and snails MHC-II positions that make hydrogen bonds with the peptide in at least 80% of the studied structures.

3.2 peptide/MHC

3.2.1 MHC conformation

The RMSD per position was measured and the mean RMS per position was calculated on the set of 3D structures groups that comprise the same MHC binding different peptides. The G-DOMAIN AB and CD loops and C-terminal part are the more structurally variable positions but, as they do not belong to the binding groove, they are probably unrelated to peptide binding [8,10]. The two helical N terminal regions display a slightly higher RMS (0.8 Å) than the rest of the cleft (0.5 Å) which was interpreted as an induced fit required for optimal contacts with peptides [12]. The MHC-II proteins display structural displacements near the centre of the G-BETA helix, especially at positions 61A to 63 (mean RMS of 0.8 Å). This region connects the short and long helix of G-BETA. The G-ALPHA helix is also slightly flexible at similar positions 65 and 66 (mean RMS of 0.7 Å). Nevertheless, despite the small deviations discussed above, the MHC molecules seem to achieve little conformational rearrangement upon binding of different peptides.

3.2.2 Peptide conformation

The mean backbone alpha carbon RMS between G-DOMAIN is of 0.7 Å for the 137 MHC-I and 0.8 Å for the 44 MHC-II (AB and CD loops, and C-terminal parts excluded). The conformational variability of peptides bound to MHC-I clearly depends on the peptide length. The 8-residue MHC-I bound peptides display a well conserved backbone conformation (0.8 Å mean RMS with no value above 1.0 Å) whereas the 10-residue MHC-I bound peptides are more flexible (2.5 Å mean RMS), especially at positions 4 to 7. The 9-residue MHC-I bound peptides display intermediate behavior (1.8 Å overall RMS), with positions 4 to 7 being the most flexible (the largest observed deviation is 5.9 Å between peptide position 5 in peptide/MHC 3D structures 1kjm and 1e27). The peptides bind to MHC-I with a well-defined, conserved, location of the first and last two residue pairs, whatever the peptide length.

The backbone atom RMS between peptide positions inside the cleft of MHC-II are less than 1.5 Å, which means that there is little conformational variability of the peptide backbone.

3.2.3 Peptide-MHC interactions

In MHC-I, conserved hydrogen bonds occur between position 70 of G-ALPHA2 and the N-terminal end of the peptide, whereas conserved hydrogen bonds occur between positions 77 and 84 of G-ALPHA1, position 59 of G-ALPHA2 and the C-terminal end of the peptide. The first and last two peptide residues participate in conserved hydrogen bonds with the MHC-I molecule. Compared to the 9-residue peptides, the 8-residue peptides display more positions with a conserved hydrogen bond (6 positions vs 4 positions), they are also more deeply buried and display reduced conformational variability.

Consistent with the well-conserved peptide backbone

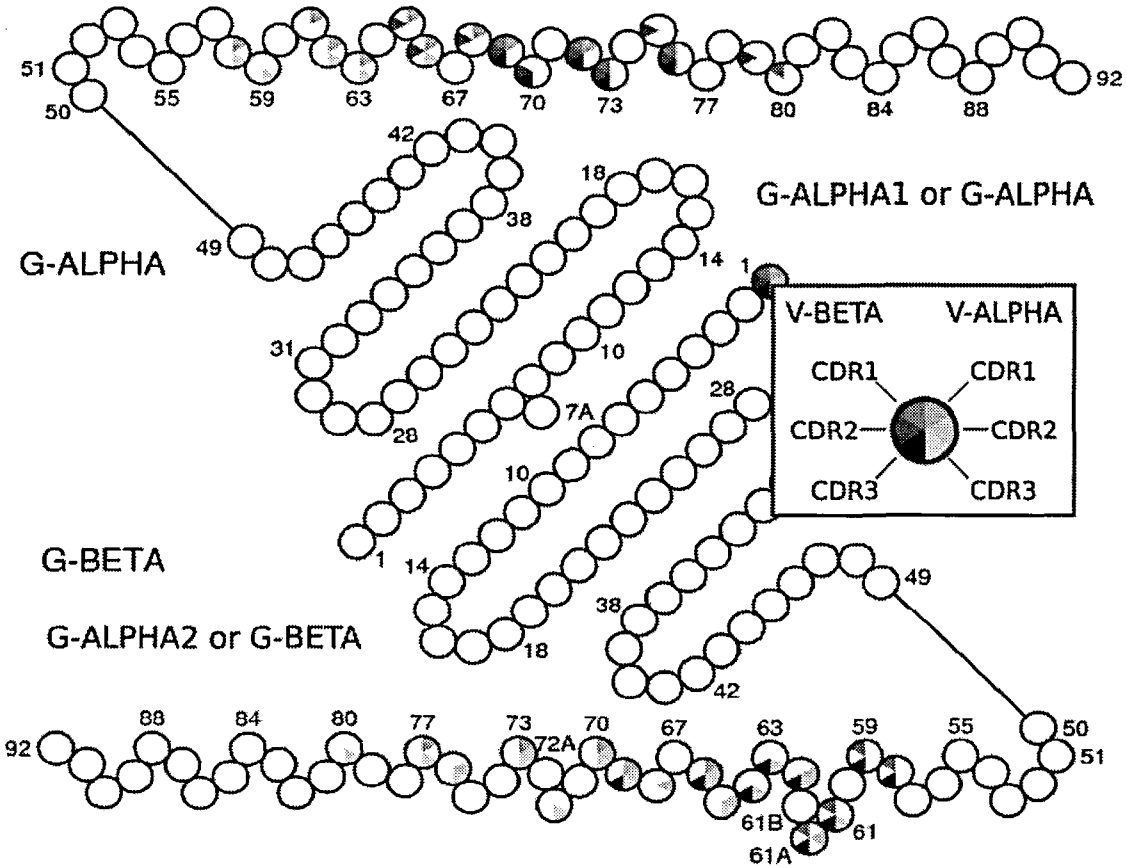

Figure 4: IMGT Collier de Perles of the MHC positions found in contacts with the TR CDR in the 18 TR/peptide/MHC 3D structures.

conformation, analysis of peptide/MHC-II interactions involves conserved hydrogen bonds that are not restricted to peptide termini.

3.2.4 IMGT peptide/MHC contact sites

In order to standardize the comparison between peptide/MHC contact sites each MHC position of each peptide/MHC 3D structure was assigned to a peptide position based on the interaction energy with peptide side chains [10]. Interestingly, the MHC environment of peptide side chains display significant analogy whether the peptide is bound to MHC-II or to MHC-I (8-, 9- or 10-residue peptides) [10]. This observation provided the basis for the definition of the eleven IMGT contact sites [10] which identify MHC positions that are likely to be in contact with a peptide side chain, whatever the MHC type (MHC-I or MHC-II) or the peptide length.

3.3 TR/peptide/MHC

The raw principles governing the TR binding on peptide/MHC have been defined [13,14,15] but no rules have yet been found at the atom level description. The IMGT unique numbering for V-DOMAIN [6] and G-DOMAIN [8] builds a unique frame to analyze the TR/peptide/MHC and reveals the conserved and variable features of the interactions.

3.3.1 TR orientation

The TR adopts a diagonal orientation on the peptide/MHC complexes and could slide along the MHC peptide binding groove [16]. The two highest points of the MHC that are localized between the two helix regions of the G-DOMAIN, put a geometric constraint on the TR orientation. The V-ALPHA is on top of the peptide N-terminal part and of the MHC-I G-ALPHA2 or MHC-II G-BETA helix. The V-BETA is on top of the peptide C-terminal part and of the MHC-I G-ALPHA1 or MHC-II G-ALPHA helix. The orientation angle (see material and methods) varies from 26 to 75 degrees. The MHC-I tend to have low angle values and MHC-II high angle values but their interval intersects.

3.3.2 Contact analysis

The analysis reveals no conservation of the position pair contacts at the interface but the TR and MHC positions involved are frequently implicated (Figure 4).
The TR positions implicated in the peptide recognition belong to the CDR3 and a few to the CDR1. The MHC positions implicated in the TR binding all belong to the helix regions. The majority of the TR positions in interaction with the MHC belong to the CDR1 and CDR2. The relative contribution of V-ALPHA and V-BETA is variable, for example the in LC13/peptide/HLA-B complex (1m05) the two V-DOMAINs have a nearly symmetrical contribution but in the JM22/peptide/HLA-A complex (1oga) the V-ALPHA does nearly all the contacts.

4 CONCLUSION

The IMGT standardization of the gene and allele nomenclature and the IMGT V-DOMAIN, C-DOMAIN and G-DOMAIN unique numbering [6,7,8] was applied to all related 3D structures in the IMGT/3Dstructure-DB database [9] and used to analyze each 3D structure individually. The IMGT unique numbering was used to compare IG/ antigen, peptide/MHC and TR/peptide/MHC 3D structures, by measuring internal receptor angles, by making superimposition of the receptor domain partners and by analyzing interface contacts. All these comparisons have been automated and up-to-date results are built at each new release of IMGT/3Dstructure-DB.

For IG, the angles measuring the orientation variability between V-DOMAIN partners, C-DOMAIN partners, and between group of partners in Fab fragments, do not present much variability (with a maximum of about 13 degrees standard deviation). The IG/antigen contact analysis reveals that a few framework scaffold positions are in contact with antigens. The CDR1 positions located at the C-terminal end of the loop are more often in contact but no positional preference could be seen within CDR2 and CDR3.

Upon peptide binding, the MHC-I undergo little conformational rearrangement at one extremity of the groove and the MHC-II do not rearrange significantly. MHC-I binding peptide conformations depend on its length, ranging from no conformational variability for an 8 amino acid peptide, to a 5.9Å RMSD of the central positions for a 10 amino acid peptide. MHC-II binding peptide admits little conformational variability. The conserved hydrogen bonds at the interface have been measured and the contact analysis between MHC-I and MHC-II and the binding peptide allows the definition of IMGT MHC contact sites. IMGT contact sites describe the mean environment of a peptide position side chain, whatever the peptide length and the MHC protein.

Finally the TR/peptide/MHC, despite the little number of complexes, show a global conservation of the diagonal orientation that was measured for all known complexes. The complexes do not present any conservation of pairwise contacting positions but some positions are frequently found at the interface.

The IMGT standardization, as applied in IMGT/3Dstructure-DB, is intended to allow many data comparison. The analyses described here are examples that could be easily extended to more specific queries, for instance the influence of one CDR length on other CDR contact patterns, or the correlation between antigen nature and IG framework positions present at the interface.

REFERENCES

[1] M.-P. Lefranc and G. Lefranc. The immunoglobulin FactsBook. Academic Press, London UK, (458 pages), 2001.

[2] M.-P. Lefranc and G. Lefranc. The T cell receptor FactsBook. Academic Press, London UK, (398 pages), 2001.

[3] M.-P. Lefranc, V. Giudicelli, Q. Kaas, E. Duprat, J. Jabado-Michaloud, D. Scaviner, C. Ginestoux, O. Clément, D. Chaume and G. Lefranc. IMGT, the international ImMunoGeneTics information system. Nucleic Acids Res, 33, D593-D597, 2005.

[4] M.-P. Lefranc, O. Clément, Q. Kaas, E. Duprat, P. Chastellan, I. Coelho, K. Combres, C. Ginestoux, V. Giudicelli, D. Chaume, and G. Lefranc. IMGT-Choreography for Immunogenetics and Immunoinformatics. E pub *In Silico* Biology 5 0006 http://www.bioinfo.de/isb/2004/05/0006/ 24 December 2004, 5, 45-60, 2005

[5] V. Giudicelli and M.-P. Lefranc. Ontology for immunogenetics: IMGT-ONTOLOGY. Bioinformatics, *15, 1047-1054, 1999.*

[6] M.-P. Lefranc, C. Pommié, M. Ruiz, V. Giudicelli, E. Foulquier, L. Truong, V. Thouvenin-Contet and G. Lefranc. IMGT unique numbering for immunoglobulin and T cell receptor variable domains and Ig superfamily V-like domains. Dev. Comp. Immunol. 27, 55-77, 2003.

[7] M.-P. Lefranc, C. Pommié, Q. Kaas, E. Duprat, N. Bosc, D. Guiraudou, C. Jean, M. Ruiz, I. Da Piedade, M. Rouard, E. Foulquier, V. Thouvenin and G. Lefranc. IMGT unique numbering for immunoglobulin and T cell receptor constant domains and Ig superfamily C-like domains. Dev. Comp. Immunol. 29, 185-203, 2005.

[8] M.-P. Lefranc, E. Duprat, Q. Kaas, M. Tranne, A. Thiriot and G. Lefranc. IMGT unique numbering for MHC groove G-DOMAIN and MHC superfamily MhcSF G-LIKE-DOMAIN. Dev. Comp. Immunol. 2005.

[9] Q. Kaas, M. Ruiz and M.-P. Lefranc. IMGT/3Dstructure-DB and IMGT/StructuralQuery, a database and a tool for immunoglobulin, T cell receptor and MHC structural data. Nucleic Acids Res. 32, D208-D210, 2004.

[10] Q. Kaas, E. Duprat, G. Tourneur and M.-P. Lefranc. IMGT standardization for molecular characterization of the T cell receptor/peptide/MHC complex, Springer Immunoinformatics Book, 2005

[11] A.D. McLachlan, Rapid comparison of protein structures. Acta Crys. A38, 871-873, 1982

[12] K.J. Smith, S.W. Reid, D.I.Stuart, A.J. McMichael, E.Y. Jones and J.I. Bell. An altered position of the alpha 2 helix of MHC class I is revealed by the crystal structure of HLA-B*3501. Immunity 4, 203-213, 1996.

[13] G. Vasmatzis, J. Cornette, U. Sezerman and C. DeLisi. TcR recognition of the MHC-eptide dimer: structural properties of a ternary complex. J. Mol. Biol. 261, 72-89, *1996.*

[14] B.C. Sim, L. Zerva, M.I. Greene and N.R. Gascoigne. Control of MHC restriction by TCR Valpha CDR1 and *CDR2. Science 273, 963-964, 1996.*

[15] L. Kjer-Nielsen, C.S. Clements, A.W. Purcell, A.G. Brooks, J.C. Whisstock, S.R. Burrows, J. McCluskey and J. Rossjohn. A structural basis for the selection of dominant alphabeta T cell receptors in antiviral immunity. Immunity 2003, 18, 53-64, 2003.

[16] M.K. Teng, A. Smolyar, A.G. Tse, J.H. Liu, J. Liu, R.E. Hussey, S.G. Nathenson, H.C. Chang, E.L. Reinherz and J.H. Wang. Identification of a common docking topology with substantial variation among different TCR-peptide-MHC complexes. Curr. Biol. 8, 409-412, 1998.