REPORT OF THE IUIS NOMENCLATURE SUBCOMMITTES

Nomenclature subcommittee on The Immunoglobulins (IG), T Cell Receptors (TR) and Major Histocompatibility (MH)

Chair: Marie-Paule Lefranc (Marie-Paule.Lefranc@igh.cnrs.fr)
Université Montpellier

Web page: www.imgt.org

In 2012, the SubCommittee has become 'The Immunoglobulins (IG), T Cell Receptors (TR) and Major Histocompatibility (MH) Nomenclature SubCommittee', to take into account the work of standardization for these proteins.

Véronique Laurens from Dijon (France) has joined the SubCommittee during the year. The other members remained unchanged.

The major outcomes have been the following:

1) The IMGT booklet (144 pages) edited by Cold Spring Harbor Protocols (CSHP) and available in 'IMGT References' on the IMGT web site (http://www.imgt.org).

It is a booklet with 11 papers:
-1 on IMGT(R), the international ImMunoGeneTics information system(R),
-5 information panels on the IMGT-ONTOLOGY concepts of identification (standardized keywords), concepts of description (standardized labels), concepts of classification (standardized immunoglobulin and T cell receptor nomenclature), concepts of numerotation (IMGT unique numbering and IMGT Collier de Perles),
-5 chapters on tools using the WHO/IUIS/IMGT nomenclature approved by Human Genome Organization (HUGO) Nomenclature Committee (HGNC): IMGT/V-QUEST, IMGT/Junction Analysis,
IMGT/Collier-de-Perles, IMGT/DomainGapAlign, IMGT/3Dstructure-DB.

Generously and for educational purposes, CSHP specifically edited this booklet and authorized IMGT to have it freely available on the IMGT site.

2) The SubCommittee has established standardized rules for the description of MH class I (MH1) and MH class II (MH2) from any vertebrate from fish to mammalians. The nomenclature of MH1 and MH2genes of Onchorhynchus mykiss_ has been completed (in the frame of the programme FLAVORES) and the one from mouse is near completion.Nomenclature is available on the IMGT site in IMGT Repertoire (MH) 'From genes to proteins'.

3) IMGT/HighV-QUEST, a web portal (created in November 2010 and freely available for academics) for the analysis of Next Generation Sequencing (NGS) data for the study of repertoires of immunoglobulins and T cell receptors in normal and pathological situations (150.000 sequences per batch, statistical analysis per set of 450.000 sequences) promotes the use of the WHO/IUIS/IMGT IG and TR nomenclature for genes and alleles.

Nomenclature subcommittee on allergen

Chair: Heimo Breiteneder (heimo.breiteneder@meduniwien.ac.at)
University of Vienna

Web page: www.allergen.org

The allergen nomenclature sub-committee met on June 13, 2011 during the EAACI meeting in Istanbul. 16 of the 20 current members were present. There were 5 major items on the agenda list that were discussed in detail.

1. Election of a new secretary.

2. Revision of database entries

a. Need for new publication that updates IUIS nomenclature and publication of old and new names for those that have been published.

b. Suggestion to provide the name of the allergen submitter in the IUIS data information table.

c. Suggestion to have 3 instead of 2 reviewers per allergen submission.

d. Revision of current entries:
d1. Change entry Sec c 1 to Sec c 28
d2. Delete Hor v 1 entry as it is the same as Hor v 15
d3. Replace incorrect Tri a 19 sequence by correct one
d4. Accept gamma gliadin as Tri a 20
d5. Merge Hor v 21 and Hor v 20 entries
d6. Rename Cyn d 15 to Cyn d 2
d7. Rename Ara h 4.0101 to Ara h 3.0201
d8. Rename Lyc e 1 and Lyc 4 to Sola l 1 and Sola l 4 following the new taxonomy
d9 Split cow's milk Bos d 8 casein entry into Bos d 8 alpha S 1 casein,
Bos d 9 alpha S 2 casein, Bos d 10 beta casein, and Bos d 11 kappa casein
d10. Deleting the Equ c 5 entry as the fragments are identical to Equ c 4
d11. Restructure the Chirnonous thummi thummi hemoglobins

3. Allergen Nomenclature
3a. Decision on Ara h 4: this number will not be available (although its entry will eb deleted) to avoid confusions in the future.
3b. Revision of inclusion criteria for accepting new allergens
3c. Discussion of naming convention.
3d. Decision to stick with the NCBI/UniProt taxonomy
3e. Discussion on constancy of allergen number for specific protein types
3f. Allergen and isoallergens based on percent identity
3g. Allergen and isoallergens based on amino acid versus silent mutations

4. Need of an expert - expertise list for each member of the sub-committee

5. Further changes to database

Besides these intensive annual meetings, the members of the subcommittee occupy themselves with the current submissions and stay in contact via e-mail or Skype.

Nomenclature subcommittee on CD molecules

Chair: Pablo Engel (pengel@ub.edu)

Web page: www.hcdm.org

1) Results of HLDA9 Workshop studies have been published in a special issue of Immunological Letters (Proceedings of the 9th International Workshop on Human Leukocyte Differentiation Antigens; Volume 134, Issue 2, 2011). This issue contains 13 papers.

2) Validation files of monoclonal antibodies have been published at the HLDA web page.

New Council:

Pablo Engel (Spain)
(President)
Laurence Boumsell (France)
(Honorary President
Robert Balderas (USA)
Armand Bensussan (France)
Georgina Clark (Australia)
Gilbert Faure (France)
David Fox (USA)
Valter Gattei (Italy)
Bo-Quan Jin (China)
Frank Mortari (USA)
Hannes Stockinger (Austria)
Menno C. van Zelma (Holland)
Heddy Zola (Australia)

Goals for 2012:

1) To establish a documents with the requirements to establish new CD molecules.
2) To establish a systematic validation protocols for monoclonal antibodies against CD molecules. These protocols will guide researches when testing new monoclonal antibodies against both intracellular and extracellular leukocyte markers.
3) Improve the HCDM web page by adding information about the structure, expression and function of the CD molecules.
3) Start the organization and collection of new monoclonal antibodies for HLDA10 meeting that will be held in Sidney (Australia) in 2014 chaired by Georgina Clark.

Nomenclature subcommittee for monocytes and dendritic cells in blood

Chair: Loems Ziegler-Heitbrock, (Ziegler-Heitbrock@helmholtz-muenchen.de)
Helmholtz Zentrum München

Use of the new nomenclature

The crucial paper for the new nomenclature is the publication in BLOOD journal in 2010[1] As of April 1, 2012 this paper has been referenced 31 times[2]

In order to reflect the use of the new nomenclature for monocytes we searched in Google Scholar for publications that use the terms "nonclassical monocyte or classical monocyte" and this revealed 37 publications.

As a criterion to track the use of the new nomenclature for DCs we performed a search in Google Scholar for "CD1c+ myeloid DC" and this revealed 28 publications.

Hence it appears that the new nomenclature is being used in the community. The changes suggested for DCs are not very extensive in that we suggest omitting the designation pre-, immature or precursor and we advise to use CD rather than BDCA names and therefore its introduction may be less of a hurdle. For monocytes we have suggested new terms and scientists may tend to stick to their old nomenclature. Still the new names are being used increasingly for monocytes, as well.

Promoting the new nomenclature

The nomenclature had been initially published in BLOOD (***Blood*.2010;116:e74-e80**) and under the IUIS home page (http://www.iuisonline.org/iuis/images/stories/docs/monosdc.pdf). In order to publicise the new nomenclature further we have entered a brief description under Wikipedia.org. Here under monocyte the section "monocyte subpopulations" was introduced and under the dendritic cell section we added a paragraph with the title "dendritic cells in blood". This was done along with the relevant references. For your information please see: http://en.wikipedia.org/wiki/Monocyte and http://en.wikipedia.org/wiki/Dendritic_cell.

Updating the new nomenclature

For monocytes the original nomenclature document has listed proliferating monocytes and 6-sulfo LacNAc+ and FcepsiolonRI+ monocytes as potential future additions. To date no additional manuscripts, which characterise monocytes with these features, have appeared.

A new candidate has emerged with cells showing high CD14 and no CCR2, i.e. CD14++CD16- CCR2- monocytes (Gama et al JLB, 2012). These cells increase with immunodeficiency virus infection and they are functionally distinct from the CD14++CD16- CCR2+ monocytes. They will be considered for inclusion pending confirmation and further characterization by independent groups.

For the intermediate monocytes a series of publications has appeared since its delineation in the original nomenclature document. This included transcriptome studies which show unique signatures (Wong, Blood, 2011, Zawada, Blood, 2011) and several reports on their increase in clinical settings and a study of their induction by TLR7/8 ligands in non-human primates(Kwissa Blood, 2012). While it appears that these cells are, in fact, in transition, their definition as a separate cell population also for clinical purposes is warranted.

Tie2-expressing monocytes have been defined earlier in man and mouse (Da Palma 2005) and here Tie2 expression was found in CD16-positive monocytes (Venneri Blood, 2007) and more specifically in the intermediates (Murdoch JIM 2007). The recent study by Zawada et al has shown that the intermediate monocytes are the cells with a higher tie2 protein expression. An update of the nomenclature will draw attention to this finding and may suggest the use of the term intermediate monocyte for the tie2 expressing monocytes.

Among dendritic cells the CD141+ myeloid blood DCs have been further characterized and the expression of markers like XCR1, Clec9A and the transcription factor IRF8 have strengthened the view that these DCs and the mouse CD8-positive DCs are homologous cells and share the property to cross-present exogenous antigen to CD8 T cells (Contreras J Immunol. 2010;185:3313-25. Crozat K. J Exp Med. 2010;207:1283-92. Bachem A J Exp Med. 2010;207:1273-81). Of note, in blood the respective mouse DCs do not express the CD8 antigen on the cell surface. XCR1 has been recently identified as a conserved universal marker for these DCs across tissues and species (for review see Villadangos and Shortman, JEM 2010). Studies using monoclonal antibodies against XCR1 are required in order to determine the usefulness of this marker for definition of these cells in flow cytometry.

For the CD1c+ myeloid DC in human blood it had been noted earlier that there are CD14- and CD14low cells and these have not been characterized further. In the mouse the homologous blood DCs appear to be the $CD11c^{+}CD11b^{+}CD45RA^{-}$ cells, which are the CD8- DCs in the spleen. Splenic CD8- DCs can be subdivided into $Clec12A^{high}$ DCIR2 $(Clec4a4)^{low}$ and the $Clec12A^{low}$ $DCIR2(Clec4a4)^{high}$ (Kasahara, JLB, 91:437, 2012). Also, in mouse blood the $CD11c^{+}CD11b^{+}CD45RA^{-}$ DCs can be subdivided into CD172a+ (Sirpalpha+, 70%) and CD172a- (Sirpalpha-, 30%) DCs (Proietto PNAS 2008). Hence it appears that for mouse blood DCs a further subdivision emerges but better and selective markers are needed to support this.

Other species: non-human primates

As mentioned in the original nomenclature document the anti-human reagents can be used directly for non-human primates and they give similar patterns for blood leukocytes. The CD16-positve monocyte subset was originally reported for Macaca fascicularis by Munn et al (Blood 1990) and Otani (AIDS Res Human Retro viruses 1998) expanded on this in the context of retrovirus infection.

For Macaca mulatta the Williams team also reported on monocyte subsets and they identified and characterized the intermediate monocytes (Kim, JLB, 2011). For DCs the CD1c+, CD141+ and CD303+ DCs have been identified and similar functional properties were reported (cross-presentation for CD141+DCs, high type I IFN for

CD303+ DCs). These findings support a suggestion to recommend the human nomenclature also in non-human primates.

Other species: rat and pig

No new information is available for the rat monocytes. For the pig early work had shown that antihuman CD14 antibodies can stain pig monocytes (Ziegler-Heitbrock Scand J Immunol 1994;40:509-14) and there were monocytes with high and low CD14. A clear demonstration of monocyte subsets was provided by the Dominguez lab, which described CD14+CD163+ MHC ClassII+ and CD14++CD163- MHC classII- subsets (Sanchez, 162:5230, 1999). Also, Ondrackova et al (Vet. Res. (2010) 41:64) have found two subsets based on CD14 and CD163 and Fairbairn et al (JLB 89:855, 2011) have confirmed subdivision of porcine monocytes based on CD14 and CD163 with a CD14+CD163+ and a CD14++CD163- subset.

In functional analysis Sanchez et al (1999) reported for the CD163+ subset a higher antigen presenting activity, a higher production of TNF and a lack of IL-10 production. More recently the same team has demonstrated that the CD163+CD14+SLA-II+ monocyte subset lacks CCR2 and shows a preferential expression of CX3CR1 (Moreno, Veterinary Research, 2010), which further strengthens the homology to the nonclassical monocytes in man.

Of note, the CD14+CD163+ MHC ClassII+ monocytes in the pig show the reverse expression pattern for CD163, since the nonclassical monocytes in man are essentially CD163 negative. Also in the pig CD16 is expressed by both subsets albeit higher in the CD163+ cells. Still, all the other features studied show a similar pattern for the non-classical CD14+CD16++ monocytes in man and the CD14+CD163+ MHC ClassII+ monocytes in the pig. There is also evidence for the existence of intermediate cells.

A proposal for the use of the classical-intermediate-nonclassical nomenclature for pig monocytes will be put on the agenda for the next meeting of the nomenclature committee.

Regarding blood dendritic cells no data are available on the rat, while for the pig CD172low CD4+ DCs and CD172low CD4- interferon type I producing plasmacytoid

DCs have been described (Summerfield, Immunology 2003, Balmelli, EJI 2005). Other than that data on blood DCs in these species are scarce.

The next meeting to review the nomenclature is projected for 2014 during the conference of the European Macrophage and Dendritic Cell Society in Vienna.

[1] Nomenclature of monocytes and dendritic cells in blood Author(s): Ziegler-Heitbrock Loems; Ancuta Petronela; Crowe Suzanne; et al. Source: BLOOD Volume: **116** Issue: **16** Pages: **E74-E80** Published: **OCT 21 2010**

[2] Source: web of knowledge platform run by Thomson Reuters

Nomenclature subcommittee on B cells and plasma cells

Chair. Ignacio Sanz (Ignacio_Sanz@URMC.Rochester.edu)

Dr. Igancio Sanz is currently a Professor and Chief, Division of Clinical Immunology & Rheumatology University of Rochester Medical Center Rochester, New York .He is now moving to Emory University, where he will be named director of the Division of Rheumatology in the Department of Medicine, a professor of medicine and pediatrics in Emory University School of Medicine, and chair in human immunology).

Proposed list of members of this committee:

Thomas L Rothstein (USA)
Thomas F. Tedder (USA)
Max D. Cooper (USA)
Claudia Mauri (UK)
Stuart G Tangye (Autralia)
Ralf Küppers (Germany)
Mark J Shlomchik (USA)
Frances Lund (USA)
Jean-Claude Weill (France)
Thomas Dörner (Germany)

Andreas Radbruch (Germany)
Frances Eun-Hyung Lee (USA)

This is a new subcommittee. Its main goal is to establish a nomenclature on B cell and plasma subsets.

Goals for 2012:
Organize a first face to face meeting before the end of 2012.

MALT: Nomenclature of Mucosa Associated Lymphoid Tissue SubCommittee
Chair: Per Brandtzaeg (per.brandtzaeg@medisin.uio.no)

The chair of this committee forward this message:
"There was no activity in our mucosal committee last year and both the actual molecules and tissue structures have been published in Mucosal Immunology and the paper can be found on the IUIS website. I foresee no immediate further action on these issues, but I copy the President of the Society, Jo Viney in case she disagrees. In that case I think I should be replaced to get some fresh blood. The implementation of the nomenclature is a remaining problem, often failing even in the best journals".

No reports were received by the following subcommittees:
KIR Nomenclature SubCommittee
Chair: Steve Marsh (marsh@ebi.ac.uk)

Web page: www.ebi.ac.uk/ipd/kir

This subcommittee keeps an updated database that provides a centralised repository for human KIR sequences. Killer-cell Immunoglobulin-like Receptors (KIR) have been shown to be highly polymorphic at the allelic and haplotypic level. KIRs are members of the immunoglobulin superfamily (IgSF) formerly called Killer-cell Inhibitory Receptors. They are composed of two or three Ig-domains, a transmembrane region and cytoplasmic tail which can in turn be short (activatory) or long (inhibitory). The

Leukocyte Receptor Complex (LRC) which encodes KIR genes has been shown to be polymorphic, polygenic and complex like the MHC.

Interleukin Nomenclature SubCommittee

Chair: John Schrader (john@brc.ubc.ca)