
Sub-Committee on CD Molecules
Chair: Pablo Engel (pengel@ub.edu)
University of Barcelona (Spain)

Website: www.HCDM.org

List of current committee members

Pablo Engel
(President HCDM and IUIS Nomenclature Chair)

Laurence Boumsell (France)
(Honorary President)

Robert Balderas (USA)
Armand Bensussan (France)
Georgina Clark (Australia)
Valter Gattei (Italy)
Tomas Kalina (Czech Republic)
Bo-Quan Jin (China)
Fabio Malavasi (Italy)
Frank Mortari (USA)
Hannes Stockinger (Austria)
Menno C. van Zelm (The Netherlands)

Menno C. van Zelm will become new chair in 2021.
Bo-Quan Jin (China) and Fabio Malavasi (Italy) will step down form the council.
HCDM will actively reach for new council members.

I. Objective
To establish the nomenclature and validation of monoclonal antibodies against leukocyte cell-surface molecules and other cell-surface molecules of the immune system

II. Recent Accomplishments

-The CD Maps project.
The second phase of the CD maps project has been started. This project aims to define the expression of all CD molecules on mayor leukocyte and lymphocytes subsets.

The results of the first phase of the study, which included CD molecules from 1 to 100, were published in Frontiers as part of IUIS Special Issue on Nomenclature (van Zelm MC, Ziegler-Heitbrock L, Collins AM, Chan SK, Engel...
The paper Kalina T, et. al. CD Maps-Dynamic Profiling of CD1-CD100 Surface Expression on Human Leukocyte and Lymphocyte Subsets. Front Immunol. 2019 Oct 23;10:2434 that show these results have had an enormous impact since the paper has received more than 20,000 visits since its publication.

- The publication a chapter that summarizes information about all CD molecules


-HCDM web
The HCDM/HLDA web www.hcdm.org has received more than 9 million visits since its establishment in 2016.

It contains a link to an interactive database generated with the results from the CDMaps project that is open to the public (http://bioinformin.cesnet.cz/CDmaps/)

The contribution of the IUIS is acknowledged at the web page.

III. Education
The following talks have been presented in different international meetings.

Engel P Antibody validation for flow cytometry. Reproducible Science Week (ABCAM) Cambridge (UK). 1st June. 2020 (virtual meeting)

Engel P Reproducibility Crisis and Antibody Validation for Flow Cytometry ISAC Webinar. 3rd March 2021 (virtual meeting)

Publication of a paper about relevance of antibody validation:

III. Ongoing Projects

-HLDA11. In 2018, we will start the organization of HLDA11 Workshop focused on Seven-span receptors and ion channels. During 2018 the panel of mAb to be studied will be collected. The goal is to have a panel of antibodies of around 200 mAbs. We have already secured the commitment of the major antibody producers both academic and companies to submit mAb to the HLDA11 workshop.

The aim of this workshop is to study, and give CD nomenclature to the newly validated monoclonal antibodies. We foresee that we will able to define a minimum of 30 new CDs.
Unfortunately, this project has been considerably delayed due to the pandemic crisis. However, we expect to finish during 2022.

- Publishing the results of the CDMaps project and database.


**IV. Future Directions**

- Continue ascribing CD names to molecules recognized by well validated monoclonal antibodies.

- Publish a database of actual expression profiles by FACS analysis of CD molecules on all known leukocyte and lymphocyte subsets. Make this database freely available to academic groups.

- Continue with the CDMaps project and complete the analysis of the expression of CD101 to CD371.

- Publication of nomenclature papers about CD molecules

- Prepare guidelines for monoclonal antibody standardization and validation.
ANNEX

Example information added to the HCDM web page:

**STRUCTURE**

CD5 is a type 1 transmembrane glycoprotein of the scavenger receptor cysteine-rich family. Its extracellular region contains 3 scavenger receptor cysteine-rich domains in tandem.\(^1\) The cytoplasmic tail displays a pseudo-ITIM domain, proximal to the membrane, and a pseudo-ITAM domain, distal to the membrane, involved in signaling.\(^2,3\) CD5 is also present as a soluble form.\(^4\)


**LIGANDS**

**Extracellular**

Presumably, CD72, IgVH, CD5, gp40-80, zymosan, β-D-glucans and gp150. It also interacts with CD6 in cis.\(^7\)

**Intracellular associate molecules**

Lck, TCR/CD3 complex, fyn, PI3K, c-cbl, ras GAP, SHP-1, CKII, AP2, CAMK II and BCR complex.\(^17\)


**EXPRESSION**

CD5 is expressed on mature T lymphocytes. It is also present on thymocytes and its levels are proportional to the stage of differentiation. B-1a cells and B regulatory cells also display CD5. It can also be induced on B-2 cells of mice. Apart from that, CD5 expression has been reported in certain types of dendritic cells.


**FUNCTION**

The receptor CD5 can act as an inhibitory or stimulatory molecule depending on the cell type and stage of maturation. For instance, CD5 inhibits Ig-mediated signaling in B-1 cells. Similarly, CD5 participates in thymocytes development and selection through negative regulation of the TCR-mediated signaling. However, in mature T cells, CD5 enhances T cell receptor signaling transduction. Furthermore, it participates in Th17 and Th2 differentiation and promotes survival of B cells and T cells.

CD5 is also involved in the maintenance of the immunological tolerance. It regulates T cell responsiveness and anergy. CD5 governs extrathymic Treg cells and nTreg development. In addition, CD5 signaling inhibits autoimmune responses through negative regulation of Ig receptor signaling in anergic B cells.
Last, CD5 acts as a receptor for PAMPs.\textsuperscript{12}


APPLICATIONS

Cell marker

CD5 is a pan-T-cell marker but also a marker of B-1a B cells.1-2

CD5 immunophenotyping is used for the diagnosis of chronic lymphocytic leukemia, mantle cell lymphoma, T-cell precursor acute lymphoblastic leukemia/lymphoma, T-cell chronic lymphoproliferative diseases and NK-cell chronic lymphoproliferative diseases.3-5 In diffuse large B-cell lymphoma, CD5 expression is associated with a poorer prognosis.6


Therapeutic

In the context of cancer, phase 1 studies have been performed with T101 antibodies against CD5 for treatment of chronic lymphocytic leukemia and cutaneous T-cell lymphoma.1-2 Furthermore, injection of soluble CD5 delayed tumor progression in a preclinical model of melanoma.3
In rheumatoid arthritis, administration of anti-CD5 antibodies led to a response rate of 22-25% at 6 months in phase II studies.\(^4\) In a mice model of type I diabetes, anti-CD5 therapy protected against diabetes onset.\(^5\) Consistent with this, anti-CD5 therapy displayed a dose-dependent effect in preserving β-cell function in a preliminary study of type I diabetes.\(^6\) Targeting CD5 have also been studied in other autoimmune diseases including multiple sclerosis, autoimmune nephropathy, systemic lupus erythematosus and inflammatory bowel disease.\(^7\)

In addition, the administration of T101 antibodies have been assessed in human pilot studies of graft-versus-host disease.\(^8\)-\(^9\)


