Direktoratet for e-helse

Nyheter
Norsk laboratoriekodeverk

Norsk laboratoriekodeverk versjon 7280.69

Dato	23.09.2023
Frist for implementering	01.11.2023

Generelt

Kodene er gyldige fra publiseringsdato og skal være implementert senest 01.11.2023.

I CSV-filen er nye og endrede koder markert med publiseringsdato 23.09.2023.

Koder som blir satt ugyldige markeres med dato fem uker frem i tid for at helsetjenesten skal få tid til å utføre tilpasningene.

NLK publiseres fem ganger i året, med publisering i januar, mars, mai, september og november. Neste versjon av NLK blir publisert i november 2023.

Kodeendringer i denne versjonen av NLK

Det er **123 nye koder** i denne versjonen av NLK.

50 koder er satt ugyldig i denne versjonen av NLK.

69 koder er endret, se kolonne F for hvilke kolonner det er gjort endringer i.

Fagspesifikke endringer:

Medisinsk biokjemi

Etter anbefaling fra Seksjon for medfødte metabolske sykdommer ved OUS, og i samråd med referansegruppen, settes følgende NOR-koder ugyldig i NLK uten erstatningskoder: NOR15165 og NOR15181.

Klinisk farmakologi

Det er opprettet 16 nye koder for måling/påvisning av legemidler/metabolitter.

Immunologi og transfusjonsmedisin

Det er opprettet ny kode som skal benyttes til aktiveringstest for diklofenak: NPU62125. I tillegg settes NPU61109 ugyldig i NLK, da denne koden har feil egenskapsart i forhold til analysen som utføres i Norge i dag.

Det er også opprettet seks nye koder for CAR-T behandling. CAR-T behandling (*Kimerisk antigenreseptor-T-celleterapi*) er en avansert form for immunterapi hvor pasientens egne T-celler reprogrammeres til å gjenkjenne spesifikke antigener på kreftcellenes overflate (jmf. legemiddelhandboka.no). De seks nye kodene som er opprettet er for CAR-T celler som er modifiserte til å være målstyrte mot CD19-positive celler.

Endringer som følge av IUPAC-prosjektet: «NPU codes for characterizing subpopulations of the hematopoietic linage, described from their Clusters of Differentiation (CD) markers»

I denne versjonen opprettes, endres og lukkes mange koder for blodceller, i tråd med vedlagte IUPAC-prosjekts anbefalinger («IUPAC Technical Report 2023» ligger som vedlegg nederst i dette dokumentet). Dette har vært et samarbeidsprosjekt mellom Norge, Danmark og Sverige, for å gjøre analysekodene som benyttes for undersøkelser av blodceller mer entydige og presise. Med denne endringen vil cellepopulasjoner defineres ved hjelp av CD-markører i stedet for trivialnavn som for eksempel «helper», «virgin».

Mange av de nye og endrede kodene gjelder tilfeller der man analyser cellesubpopulasjoner som en fraksjon av en hovedpopulasjon. For disse kodene vil hovedpopulasjonen (for eksempel CD4 T-celler i blod) utgjøre systemet i kodedefinisjonen, mens cellesubpopulasjonen beskrives i posisjonen til komponenten (CD45RA+ T-lymfocytter). Siden det er gitt at hovedpopulasjonen er CD4 T-celler, gjentas ikke denne informasjonen når komponenten beskrives. Kodedefinisjonen til en analyse for måling av absolutt-tallet til en cellepopulasjon vil derfor være bygget opp annerledes enn en analyse der man måler en %-andel av en hovedpopulasjon.

Eksempel:

NPU62142

Bruksnavn: T-lymc(CD4+; B)-Naive T-celler (CD45RA+) %

Kodedefinisjon: T-lymcs(CD4+;B)—T-lymphocytes(CD45RA+); num.fr. = ? %

Det vil si at man i NPU62142 analyserer antallfraksjonen (prosentandelen) av CD45RA-positive T-lymfocytter blant de CD4-positive T-lymfocyttene i blod.

For målinger av absolutt antall vil kodeoppbygningen være som øvrige NLK-koder

Eksempel:

NPU62170

Bruksnavn: B-B-celler (CD20+)

Kodedefinisjon: B—B-lymphocytes(CD20+); num.c. = ? × 109/L

Det vil si at man i NPU62170 analyserer antallkonsentrasjonen av CD20-positive B-lymfocytter i blod.

Medisinsk mikrobiologi

Norsk bruksnavn endres på alle koder for apekoppevirus, som i eksempelet under:

Kode	Norsk_bruksnavn	Kodedefinisjon
NPU60731	~~Us-Apekoppevirus DNA~~	Syst(spec.)—Monkeypox virus(DNA); arb.c.(proc.) = ?
NPU60731	Us-Apekoppevirus DNA (mpox)	Syst(spec.)—Monkeypox virus(DNA); arb.c.(proc.) = ?

Det er også opprettet fem nye koder for resistensundersøkelser, etter ønske fra Nasjonal kompetansetjeneste i Tromsø.

Medisinsk genetikk

Det er i denne versjonen opprettet seks nye koder for preimplantasjonstesting.

Høring om meldingsprofil for medisinsk genetikk

I samarbeid med referansegruppen for medisinsk genetikk, er det etablert en ny meldingsprofil som ligger ute til høring på ehelse.no. Profilen inneholder krav til hvordan standarden «Svarrapportering av medisinske tjenester v1.4» skal benyttes når laboratorier sender svarrapportmeldinger innen fagområdet medisinsk genetikk.

Svarfrist for høringen er 14. desember 2023.

Anatomisk lokalisasjon (ID=8352)

I versjon 11 er det opprettet to nye koder etter ønske fra fagmiljøet for medisinsk mikrobiologi:

OVK	Overkjeve
NEV	Neovagina

En kode settes ugyldig:

UPK	Urin, permanent kateter

Prøvemateriale (ID=8351)

I versjon 18 er det opprettet tre nye koder etter ønske fra fagmiljøet i medisinsk mikrobiologi:

UNF	Urin, nefrostomikateter
URU	Urin, urostomi
DVA	Dialysevann

Tekstlige resultatverdier (ID=8340)

I versjon 5 er det opprettet tre nye koder etter ønske fra fagmiljøet for medisinsk mikrobiologi:

T035	Gram labile staver
T036	Gram positive diplokokker
T037	Gram negative diplokokker

IUPAC Technical Report 2023

INTERNATIONAL FEDERATION OF CLINICAL CHEMISTRY

AND LABORATORY MEDICINE

SCIENTIFIC DIVISION

COMMITTEE ON NOMENCLATURE FOR PROPERTIES AND UNITS (C-NPU) *
and

INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY

CHEMISTRY AND HUMAN HEALTH DIVISION (VII)

SUBCOMMITTEE ON NOMENCLATURE FOR PROPERTIES AND UNITS (SC-NPU) †

Project Number: 2021-022-1-700

PROPERTIES AND UNITS IN THE CLINICAL LABORATORY SCIENCES PART XXVIII. NPU codes for characterizing subpopulations of the hematopoietic linage, described from their Clusters of Differentiation (CD) molecules

(IUPAC Technical Report)

Evita Maria Lindholm[1], Eli Taraldsrud[2], Jakob Thaning Bay[3], Mats Bemark[4], Jens Magnus Bernth

Jensen[5], Rebecca Ceder[6], Elisabeth Abrahamsen[1], Fatma Meric Yilmaz[7], Sridevi Devaraj[8], Eline van der Hagen[9], Helle Møller Johannessen[10]

The Norwegian Directorate of eHealth, Oslo, Norway[1], Oslo University Hospital, Rikshospitalet, Oslo,

Norway[2], Dept. of Clinical Immunology, Zealand University Hospital, Region Zealand, Denmark[3],

University of Gothenburg, Göteborg, Sweden[4], The Danish Society of Clinical Immunology, Aarhus,

Denmark[5], Equalis AB, Uppsala, Sweden[6], Ankara Yildirim Beyazit University, Ankara, Turkey[7], Baylor

College of Medicine, Houston, USA[8], Queen Beatrix Hospital MCA Laboratory, Winterswijk, The

Netherlands[9], Danish Health Data Authority, Copenhagen, Denmark[10]

Abstract: This document describes how the Nomenclature for Properties and Units (NPU) terminology can be applied to differentiate between cell subpopulations of the hematopoietic lineage. The Clusters of Differentiation (CD) molecules are included in the NPU syntax, together with its correct affiliations to indicate their presence or absence. This

allows for identification and isolation of cell populations, subsets, and differentiation stages, which is essential for correct diagnosis and treatment of several malignancies and autoimmune diseases.

Keywords: B-lymphocytes, T-lymphocytes, Clusters of Differentiation (CD) molecules, NPU terminology

Content

1. Preface

The present document is Part XXVIII of a series on properties and units in the clinical laboratory sciences initiated in 1987. The series currently comprises:

I.	Syntax and semantic rules [1]
II.	Kinds-of-property [2]
III.	Elements (of properties) and their code values [3]
IV.	Properties and their code values [4]
V.	Properties and units in thrombosis and hemostasis [5]
VI.	Properties and units in IOC-prohibited drugs [6]
VIII.	Properties and units in clinical microbiology [7]
IX.	Properties and units in trace elements [8]
X.	Properties and units in general clinical chemistry [9]
XI.	Coding systems: structure and guidelines [10]
XII.	Properties and units in clinical pharmacology and toxicology [11]
XIII.	Properties and units in reproduction and fertility [12]
XVI.	Properties and units in clinical allergology [13]
XVIII.	Nomenclature, properties, and units in clinical molecular biology [14]
XIX.	Properties and units for transfusion medicine and immunohematology [15]
XXIII.	The NPU terminology, principles, and implementation – A user's guide [16]
XXIV.	Properties and units in clinical molecular genetics [17]
XXVII.	Properties and units in the clinical laboratory sciences. Online dynamic NPU manual [18]

2. Introduction

Examination results from clinical laboratories in the health area has increased through the last decades. Coding of laboratory analyses is an efficient way of securing standardized and accurate recording of patient information, which can then serve as an invaluable resource for clinical treatment decisions, improved patient care and medical research. The Nomenclature for Properties and Units (NPU) terminology was developed to support correct and standardized exchange of data across laboratories and ehealth systems. To achieve this, each NPU definition (described under section 3.1), needs to contain information that ensures similar interpretation of results between laboratories, and even across countries. The NPU terminology has also been employed for the characterization of hematopoietic cells. However, due to certain limitations in the terminology's rules and syntax, it has so far not been able to capture the complexity and phenotypic differences between subpopulations.

By the end of 1960, T- (thymus-dependent) and B- (bursa-independent) lymphocytes were described as two distinct lymphocyte populations, with distinct roles in the immune response. Prior to antigen stimulation, B- and T-lymphocytes appear morphologically similar, and differentiation of the two populations proved difficult. Several studies therefore failed to produce an easy and consistent method to differentiate functionally unique lymphocyte populations [19-21]. This changed with the development of monoclonal antibodies specific to Clusters of Differentiation (CD) molecules present on the lymphocyte cell surface, which could differentiate B- and T-lymphocytes much more effectively. In the decades that followed a rapid increase in new CD molecules were discovered, further unfolding the complexities in lymphocyte development and function. Due to the rapid increase of the number of discovered CD molecules, and the absence of studies to differentiate whether the same molecule was recognized by other antibodies, the Human Leukocyte Differentiation Antigens (HLDA) Workshops were initiated in 1982. The first workshop was sponsored by the International Union of Immunology Societies (IUIS) and the World Health Organization (WHO), and over the years these HLDA workshops have used antibodies to characterize many of the molecules involved in immunological processes [22]. In addition, they have provided the CD nomenclature system, which is universally used and acknowledged. Currently, more than 350 different CD molecules have been identified [23], which enables identification of different cell types and the stage of differentiation.

In addition to the different subtypes of B- and T-lymphocytes, analysis of other cell types such as NK cells, dendritic cells, monocytes, etc. are equally important in current laboratory diagnostics [24-26]. This illustrates the need to extend the field of application of such codes beyond B- and T-lymphocytes, and in this respect, it is appropriate to use the CD nomenclature to characterize all subpopulations of the hematopoietic lineage [27]. Although identification and quantification of lymphocyte subpopulations by CD-specific antibodies and flow cytometry has been considered the most exact and reliable procedure to assess immunocompetence, leukocyte subsets and their specialized functions have also been characterized through sequencing and, more recently, gene microarrays [28].

Numerous diseases are associated with alterations in peripheral blood lymphocyte subpopulations, including primary or congenital immunodeficiencies, in which certain lymphocyte subpopulations are absent or reduced [29], secondary immunodeficiencies,

including HIV infection, which destroys the CD4+ T-cell subpopulation [30], systemic autoimmune diseases [31], infections [32] and cancer [33]. The need to communicate the different cell types and differentiation states is therefore of outmost importance for clinical decisions in diagnosis, prognosis, and patient monitoring. This report describes how the NPU terminology can adapt to the CD nomenclature, so results can be communicated in a precise and standardized way.

3. Objective

The objective of this project is to define rules and principles to establish NPU definitions for describing subpopulations of the hematopoietic cell lineage by applying the CD nomenclature as reference terminology.

3.1 The NPU terminology syntax and semantic content

The NPU terminology is an international medical laboratory terminology that presents and communicates millions of laboratory results yearly in various health care systems, supporting clinical decisions in diagnosis, prognosis, and patient monitoring. The NPU terminology is used for the communication of laboratory results between laboratory information systems, hospital patient records, GPs, and local and national data repositories, for health care professionals and citizens in the Scandinavian countries. In addition to local use in some other countries. In addition to the NPU terminology, LOINC (Logical Observation Identifiers Names and Codes) represents another terminology for laboratory results, issued by the Regenstrief Institute (US) and with extensive use across both Europe and USA. In contrast to NPU, which is based on metrological concepts with strict rules regarding the coding of the measurand and the result value, LOINC provides codes for analyses as offered by the laboratory.

Use of the NPU terminology allows clinical examination results to be recognized, compared, reused in calculations, extracted for research or statistics, and stored for documentation, without loss of meaning. The terminology has been developed since the 1990's with support from the international organizations IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) in collaboration with IUPAC (International Union of Pure and Applied Chemistry).

The rules and principles for establishing NPU definitions is that all terms within the NPU definition are from an international approved terminology or classification. This secures a stable and unambiguous understanding of each concept used.

The NPU concept model identifies examined properties of a patient, independent of the technology or procedure used to obtain the information. The NPU terminology consists of a code value of five unique numbers, and a unique NPU definition. The NPU definition encompasses essential information about an examination result or a measurement in a formal structure, identifying:

- The part of the universe that is studied (the system), for example plasma

- The component examined in that system, for example sodium ion
- The estimated kind-of-property (k-o-p) of the component in that system, for example substance concentration
- The measurement unit, preferrable SI, is added quantitative measures. For example, milligram per litre

This is expressed through a prescribed syntax and identified with a NPU definition:

NPUXXXXX System—Component; kind-of-property = measurement unit

Examples:

NPU03431 U—Sodium ion; subst.c. = ? mmol/L

The result describes the concentration ("subst.c."; substance concentration) of sodium ion in urine ("U"), where the result value should be returned in millimole per litre.

NPU02321 Ercs(B)—Haemoglobin(Fe); subst.c. = ? mmol/L

The result describes the concentration ("subst.c."; substance concentration) of haemoglobin in erythrocytes in blood ("Ercs(B)"), where the result value should be returned in millimole per litre.

NPU56029 Marrow—Hematopoietic Stem Cells; num.c. = ? × 106/L

The result describes the concentration ("num.c."; number concentration) of hematopoietic stem cells in bone marrow, where the result value should be returned in concentration of 10^6 cells per litre.

3.2 CD molecules as preferred terms in NPU definitions for describing hematopoietic cells

Most cells can be identified by the proteins they express. The Universal Protein Resource (UniProt) is a knowledge data base for protein sequence and annotation of data, and this data base has become an important source for annotating proteins. This data base is also the primary choice when establishing NPU definitions for other proteins.

As described above, the CD nomenclature was established by the Human Leukocyte Differentiation Antigens (HLDA) Workshops [23]. This nomenclature has been universally adopted by the immunological community and is officially approved by the International Union of Immunological Societies (IUIS) and sanctioned by the World Health Organization [34], for identification and isolation of leukocyte populations, subsets, and differentiation stages. To further emphasize the international credibility of the use of CD molecules and their role in the immune system, the U.S. Food and Drug Administration (FDA) have requested that, for a monoclonal antibody to be used as a diagnostic reagent, it should be evaluated by the HLDA Workshops. The list of CD molecules can be found on the Human Cell Differentiation

Molecules (HCDM) (http://www.hcdm.org/) homepage. Each molecule is listed with their “CD name”, as well as their “NCBI name”, “Gene name” and “NCBI other name”.

To avoid misclassification based on different understanding of terms for the hematopoietic cell populations, and based on the universal acceptance of the CD nomenclature, NPU definitions will be developed based on the expression of CD molecules, whenever these are available. This will provide consistency and uniformity in analyses referring to identical molecules. Furthermore, based on the international consensus on describing CD molecules with the abbreviation “CD”, this abbreviation will also be used when creating NPU definitions. For example, CD40 ligand will be referred to as CD154 in NPU definitions.

This principle will also apply for NPU definitions where cell populations are clinically known through “common names”, like “helper”, “memory” etc. This is important, as there are currently no concise and established nomenclature defining lymphocyte populations precisely. Therefore, a “helper, memory T-lymphocyte” can potentially be defined with different sets of CD molecules, as the publications of Valiathan and Apoil illustrates [35, 36].

3.3 CD molecules as separate terms within the NPU definitions

To enable NPU definitions to reflect the complexity in lymphocyte phenotypes through different expression of CD molecules, new NPU definitions will be developed with the appropriate cell type, i.e. B- or T-lymphocytes, as component, and with the different CD molecules as component specifications. This will allow both the component and the specifications to have their individual international approved term references. For example:

NPUXXXXX B—T-lymphocytes(CD4+;CD45RA-;CD197+); num.c. = ? × 10^9/L

The result describes the concentration (“num.c.”; number concentration) of CD4 positive, CD45RA positive or CD45RO negative and CD197 positive T-lymphocytes in blood, where the result value should be returned in concentration of 10^9 cells per litre.

As described in section 3.10, CD molecules which are known to always be expressed by the cell listed as component, will be omitted from the NPU definition. Therefore, CD3 is not included in the example above, as T-lymphocytes are listed as the component and CD3 is therefore assumed to be present.

3.4 Annotation of shared phenotypic characteristics between the main populations within the system and the subpopulation in the component

T-lymphocytes are identified through the cell surface molecule CD3 and are mainly comprised of two predominant subsets, which are either positive in their expression of CD4 or CD8. The CD4 positive cells are known as T-helper lymphocytes, while the CD8 positive cells are known as cytotoxic Tlymphocytes. Several phenotypes of both the CD4 positive and

the CD8 positive T-lymphocytes have been identified, and these subpopulations are frequently calculated as relative proportions of CD4 or CD8 positive T-cells. This means that the CD4 positive or the CD8 positive lymphocytes often represent the NPU “system”. As the investigated subpopulation is implied to have some of the phenotypic characteristics as the main population, shared characteristics between the main population and the subpopulation will not be repeated in the “component” when developing NPU definitions. This is true whenever the kind-of-property is defined with "fraction".

Furthermore, each term should be possible to use as both "system" and "component", to ensure similar meaning of each concept. The system should therefore be described in the same form as the component, with the CD molecules placed in parenthesis as specifications.

Based on these principles, a potential NPU definition describing the fraction of CD154 positive Tlymphocytes among the CD4 positive T-lymphocyte population in blood, after some form of stimulation (“stim.”) will be defined as follows:

NPUXXXXX T-lymcs(CD4+;B)—T-lymphocytes(CD154+); arb.num.fr.(stim.; proc.) = ?

3.5 Annotating CD molecules as present, absent or with a degree of positivity

Analysing for the presence or absence of CD molecules on cell surfaces is currently mainly performed by fluorescent labelled antibodies reacting with these cell-surface CD molecules. And the fraction of cells belonging to each immunophenotype is then measured mainly by using flow cytometry. The signs “+” (plus) and “-“ (minus) are added to the CD molecules to indicate the presence or absence, respectively, of that molecule on a cell or cell population. Designating CD molecules together with a "+" and "-" sign is according to the recommended CD nomenclature [34], and NPU definitions for these cell populations will therefore be developed accordingly. This involves that each CD molecule will require at least two term IDs when creating NPU definitions, depending on whether it is present or absent.

The CD nomenclature recommends annotating the signs "+" and "-" using superscript, for example $CD4^+$ instead of CD4+. However, to simplify the technical use of the NPU definitions in electronic health records, normal script for these signs will be employed in NPU definitions.

In some instances, CD molecules are expressed in various degrees of positivity, or antigen density, which needs to be communicated in a more detailed way than indicated by the affiliation “+”. Differences in antigen density, or expression level, can for example be due to cell activation level and functional differences, which again can affect disease or prognosis. Differences in antigen density are measured through mean fluorescence intensity (MFI) in flow cytometry. As MFI is set by the user for each experiment, and depends on fluorochrome strength, flow cytometry machine, laboratory settings etc., no exact definition can be set for the parameters that indicate the degree of positivity. In cases where the degree of positivity is important to report, the terms "high", "intermediate" and "low" (or alternatively “bright”, “mid” and “dim”) are usually added to the CD molecule, in the same way as the signs "+" and "-" [34]. Therefore, and whenever appropriate, NPU definitions will be developed with the terms "high", "intermediate" and "low" added to the CD molecule.

An example where these affiliations are necessary are within the CD21low B-lymphocyte subpopulation, which is enriched in a number of conditions with chronic immune stimulation including certain pathogenic infections (viral and parasitic) [37, 38] and autoimmune diseases

[39, 40]. The need to characterize CD markers with "high" and "low" is also true for natural killer (NK) cells, which are an important part of the immune system, contributing to the defence of both pathogens and tumours [41]. These cells can be broadly divided into two major subgroups according to the expression density of CD16 and CD56 [42, 43].

For CD21low B-lymphocytes, the following NPU definition will be developed:

NPUXXXXX B-lymcs(B)— B-lymphocytes (CD21low; CD38low); num.fr.(proc.)= ? %

The results describe the percentage of CD21 low and CD38 low B-lymphocytes among the whole Blymphocyte population in blood.

3.7 NPU definitions represents the CD molecules in order

Whenever several CD molecules are present as specifications within an NPU definition, we suggest that their sequence is ordered according to ascending order. If necessary, CD molecules should then be followed by additional proteins that are present as component specifications, in numerical and then alphabetical order.

Example:

NPUXXXXX T-lymcs(CD4+;B)—T-lymphocytes(CD38+;CD45RA+;CD197-;HLA-DR+);num.fr.(proc.) = ? % The results describe the percentage of CD38 positive, CD45RA positive or CD45RO negative, CD197 positive and HLA-DR positive T-lymphocytes among the CD4 positive T-lymphocyte population in blood.

3.8 Use of percentage (%) as unit in NPU definitions

As described above, flow cytometry has been the most used procedure to quantify lymphocyte subpopulations [44]. Within this method, cell subpopulations are often calculated as a percentage of a parent population when reporting these examinations. Within the NPU terminology the kind of property “number fraction” is used to describe the number of a component divided by the number of the system. NPU definitions for characterization of lymphocyte subpopulations as a fraction of a larger cell population will therefore be developed with “number fraction" as kind of property). Although percentage is currently not widely accepted as unit within the NPU terminology, this unit will be allowed for the NPU definitions examining immunophenotypes, to avoid confusion and misinterpretation amongst the clinicians who receive the laboratory results.

Example:

NPUXXXXX T-lymcs(CD4+; B)—T-lymphocytes(CD25+; CD127-); num.fr. = ? %

The results describe the percentage of CD25 positive and CD127 negative T-lymphocytes among the whole CD4 positive T-lymphocyte population in blood.

3.9 Adding clinically relevant search terms to ease the use of NPU definitions

The different subtypes of B- and T-lymphocytes are commonly described based on their specific function: helper/effector, cytotoxic, memory, regulatory etc. [45]. In addition, T-

lymphocytes can be characterized by physiological states through their expression of molecules for activation (HLA-DR and CD38), differentiation (CD45RA, CCR7, CD28, and CD27), senescence (CD57), exhaustion (PD1) and apoptosis (CD95, CD178 and CD102b).

Although NPU definitions represents a precise and uniform way of presenting and exchanging laboratory results, NPU definitions can be considered difficult to understand and little user friendly in clinical practice. However, the terms describing function and physiological state are interpretations of the CD molecules expressions. Since no consensus regarding which CD molecules needs to be expressed to characterize a subpopulation by these phenotypic descriptions, this information will not be included within NPU definitions. Therefore, the Scandinavian countries, which are the countries with most extensive use of this terminology, have developed separate national short names for each NPU definition. These short names make the NPU definitions more useful and easily understandable for clinicians and laboratory personal, and can refer to the subpopulations with common nomenclature (e.g., naïve, memory etc.). This could also be achieved by adding search terms to each NPU definition, which allows different and user-friendly descriptions of the subpopulation, while the NPU definitions are kept constant.

3.10 CD molecules with inferred or equivalent expression are omitted from NPU definitions

In clinical practice, the kits and methods used to detect the different subpopulations varies between laboratories. Due to the potential magnitude of new NPU definitions, certain rules are necessary to limit unnecessary NPU definitions describing the same subpopulations based on the use of different CD molecules. As seen in the examples above for T-lymphocytes, the CD3 molecule is not listed as a defining marker of this cell type. This is due to its inferred expression, as it is well acknowledged that all T-lymphocytes are CD3 positive. This is also true for CD19 in B-lymphocytes, which is known to be present on all B-lymphocytes. CD markers with inferred/unquestioned presence should be omitted from the NPU definitions whenever possible, and CD3 and CD19 are therefore omitted from the NPU definition whenever T-lymphocytes or B-lymphocytes are specified, respectively.

Some CD markers are considered equivalent in terms of detecting their presence or absence. This is true for the CD markers CD45RA and CD45RO, where CD45RA represents the long isoform of CD45 and CD45RO represents the shorter isoform. After antigen priming, T lymphocytes downregulate the longer isoform CD45RA and reciprocally upregulate the shorter isoform CD45RO. These molecules have therefore been proposed as markers for naïve (CD45RA+/RO-) and memory (CD45RA-/RO+) T lymphocytes [46]. For simplicity we have chosen to include only CD45RA in the NPU definitions for these subpopulations, but with the implied understanding that antibodies for CD45RO is considered equivalent for use. For example, for the following NPU definition the lab can choose whether they use antibodies detecting CD45RA+ or CD45RO- T-lymphocytes;

NPUXXXXX T-lymcs(CD4+;B)—T-lymphocytes(CD45RA+); num.fr. = ? %

The results describe the percentage of CD45RA positive or CD45RO negative T-lymphocytes among the whole CD4 positive T-lymphocyte population in blood.

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