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REVIEW
ОБЗОР

Typing of adaptive immunity cells: markers of populations and their functional significance

Anton A. Fedorov[1] ✉, **Anastasia A. Fedorenko**[1], **Marina R. Patysheva**[1], **Tatiana S. Gerashchenko**[1, 2]

[1] Cancer Research Institute, Tomsk National Research Medical Center, *Tomsk, Russian Federation*
[2] RUDN University, *Moscow, Russian Federation*
✉ anton.fedorov.2014@mail.ru

Abstract. *Relevance.* Single-cell sequencing technologies (scRNA-seq) provide unique opportunities for studying the heterogeneity of immune populations, enabling the analysis of expression profiles, ligand-receptor interactions, and differentiation trajectories at the single-cell level. However, the quality of cell typing significantly depends on the accuracy of data annotation. Marker ambiguity, variability in their expression depending on physiological context, limitations of automated tools such as CellTypist, Azimuth, and SingleR, and the incompleteness of databases like PanglaoDB and CellMarker, including insufficient information on the functional roles of markers, substantially hinder the identification of cell populations and require additional efforts to achieve meaningful results. *Aim.* To systematize markers of T- and B-cells of the adaptive immune response to facilitate scRNA-seq data annotation. *Materials and Methods.* An analysis of 30 scientific publications from PubMed, Scopus, and Web of Science (2008–2024) and marker data from PanglaoDB and CellMarker was conducted. *Results and discussion.* Key and additional T-cell (*CD3D, CD3E, CD3G, CD4, CD8A, CD8B, FOXP3, GZMA, TBX21*) and B-cell (*CD19, MS4A1, CD27, IGHM, IGHD*) markers, their roles in immune processes, including activation, cytotoxicity, and regulation, were examined. Subpopulations such as Th1 cells (T-bet, IFN-γ), follicular helper cells (CXCR5, BCL-6), and regulatory B-cells (CD24, IL-10) and their functions in health and disease were described. *Conclusion.* The systematization of T- and B-cell markers was developed to improve the quality of single-cell sequencing data annotation and is applicable for enhanced typing of cell functional states in health and pathological conditions, including infectious, autoimmune, and oncological diseases. This opens opportunities for a deeper understanding of immune processes and the development of immunotherapy approaches, such as CAR-T therapy. However, the limited specificity of markers and the lack of standardized annotation algorithms highlight the need for further research to refine typing methods.

Keywords: T-cells, B-cells, adaptive immunity, single-cell sequencing, immune markers, typing, immunotherapy

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Introduction

Deciphering immune cell composition and function is key to understanding both normal immunity and its disruption in disease [1]. Modern sequencing technologies, such as single-cell RNA sequencing (scRNA-seq), provide unprecedented opportunities to investigate immune populations by enabling the analysis of gene expression profiles, ligand–receptor interactions, and differentiation trajectories at single-cell resolution [2]. In the field of cancer research, the analysis of immune cell types through scRNA-seq holds great importance, as the makeup and functional traits of the tumor microenvironment (TME) affect molecular diagnostics, the creation of targeted treatments, and the prognosis of the disease. For instance, identifying T-cell subpopulations with exhaustion markers (PD-1$^+$, LAG-3$^+$) in the TME indicates immunosuppression, making immune checkpoint inhibitors, such as anti-PD-1 antibodies, a preferred therapeutic strategy to restore immune function. High infiltration of CD8+ cytotoxic T cells is associated with favorable prognosis in breast cancer and other malignancies, whereas a predominance of regulatory T cells (FOXP3$^+$, CD25$^+$) may necessitate combined approaches, such as CTLA-4 inhibitors or CAR-T cell therapies, to overcome immunosuppression [1, 3]. Identifying markers such as CXCR5$^+$ and BCL-6$^+$ for follicular helper T cells aids in assessing humoral immune activity and selecting patients likely to respond to immunotherapy [3, 4].

The advancement of single-cell sequencing technologies has led to the development of numerous computational tools, including automated annotation methods such as CellTypist, Azimuth, and SingleR, which aim to streamline and standardize this process [5–7]. While these tools are widely used for basic immune cell population typing, they have limitations in performing detailed subpopulation analysis. They often lack information on expression variability across different physiological states and do not provide insights into the origin or functional roles of specific markers. As a result, accurately distinguishing clusters into biologically meaningful cell populations can be challenging. To achieve higher-resolution annotations, manual reclustering is frequently required, typically guided by expert knowledge and supported by curated cell marker databases such as PanglaoDB, CellMarker, and MonacoImmuneData [8–10]. However, these resources often lack detailed information on the functional roles and expression contexts of markers, limiting the depth and accuracy of annotations and necessitating additional manual literature searches. Emerging tools such as CellMeSH, which utilize indexed scientific literature for probabilistic cell type annotation, offer a promising solution to these challenges but have not yet become part of standard practice [11].

Given the limitations of current automated annotation methods and the incomplete characterization of immune cell markers in existing databases, this review aims to systematize key markers of T and B lymphocytes within the adaptive immune system, taking into account their developmental origin,

functional roles, and transcriptional context. As central mediators of adaptive immunity, T and B lymphocytes play critical roles in shaping the antitumor immune response, thereby influencing treatment outcomes and disease prognosis. Markers of innate immune cells will be discussed in a forthcoming publication. This review serves as a complementary resource for the accurate annotation and interpretation of single-cell RNA sequencing (scRNA-seq) data, supporting more reliable identification of immune cell populations.

T cells

T cells are central components of the adaptive immune system, providing protection against pathogens and maintaining immune homeostasis. They originate in the bone marrow from a common lymphoid progenitor (CLP) and undergo maturation in the thymus through processes of positive and negative selection, ultimately giving rise to functionally competent $CD4^+$ and $CD8^+$ T cells (Figure) [3].

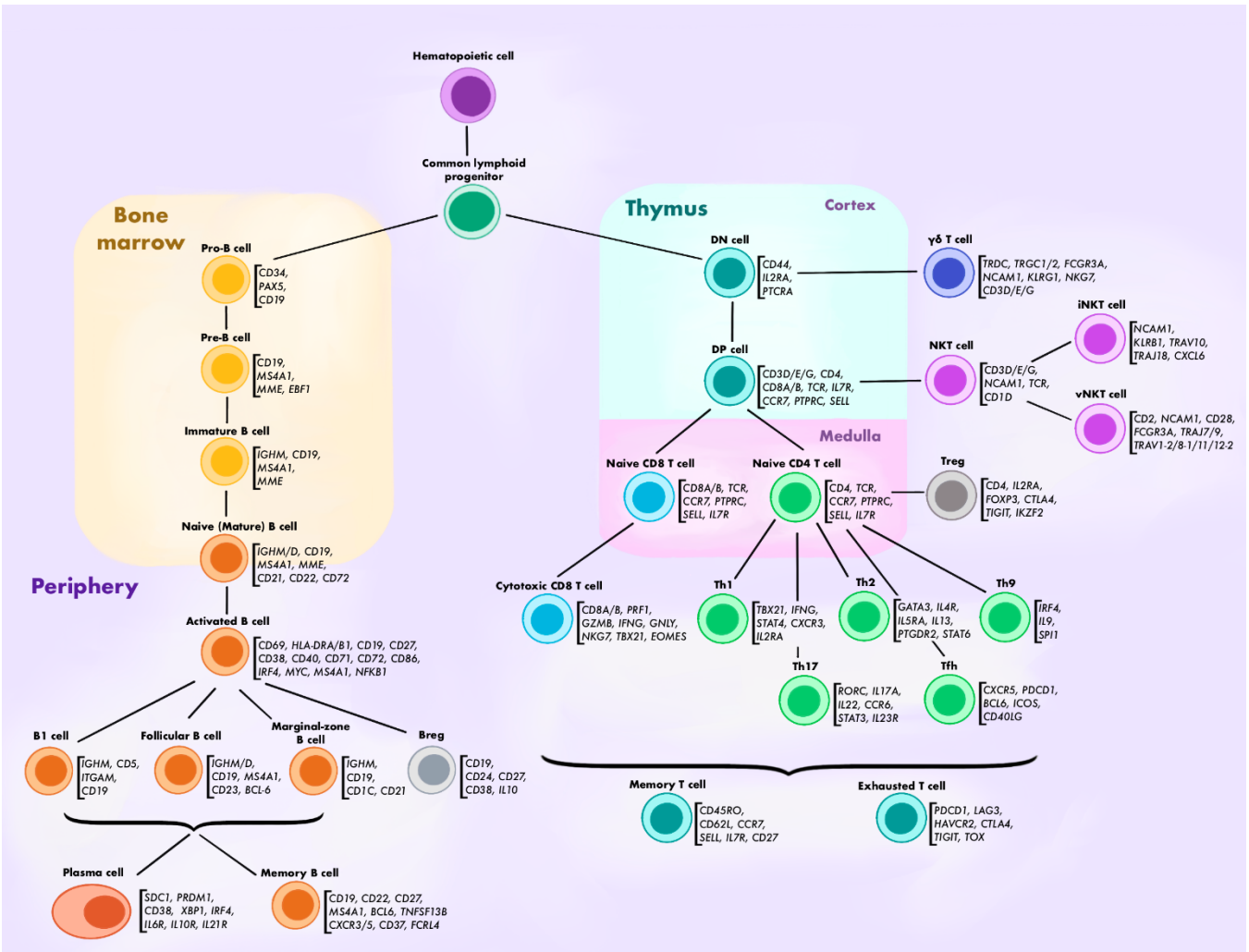

Figure. Markers of adaptive immune cell populations. The figure shows a scheme of adaptive immune cell differentiation, with key markers indicated at various stages. Colors represent the maturation sites of different cell populations

T-cell development in the thymus

T cell differentiation begins with the migration of hematopoietic progenitor cells from the bone marrow to the thymus, where they undergo maturation and selection. In the thymus, thymocytes undergo development through three main stages: double-negative (DN), double-positive (DP), and single-positive (SP).

At the double-negative stage (DN, DN1-DN4), thymocytes lack expression of *CD4* and *CD8A*/*CD8B* coreceptors but exhibit variable levels of *CD44* and *IL2RA*. A critical milestone is the DN3 stage, where the proto-TCR (*PTCRA*) begins to be expressed, enabling progression to the double-positive stage [3, 12].

During the double-positive (DP) stage, T cells co-express *CD4* and *CD8A/CD8B* and undergo selection based on the specificity of their T cell receptor (TCR). Depending on the outcome, cells differentiate into $CD4^+$ or $CD8^+$ lineages. At this stage, molecules such as *CCR7* and *PTPRC* are expressed, playing key roles in cell migration and functional maturation [13].

At the single-positive stage (SP), T lymphocytes acquire either a $CD4^+$ or $CD8^+$ naive T-cell phenotype. The differentiation trajectory is determined by TCR interactions with MHC class I or II molecules. The cytokine microenvironment and activation of transcription factors, such as *Runx3* for $CD8^+$ and *GATA-3* for $CD4^+$, are pivotal in this process [14]. Following the SP stage, NKT cells may emerge, serving regulatory functions at the interface of innate and adaptive immunity.

Peripheral activation and memory cell formation

Following their maturation in the thymus, naïve T cells circulate to peripheral lymphoid tissues, where antigen presentation triggers their activation and differentiation into effector T cells. Some activated T cells directly eliminate pathogens or infected cells, while others differentiate into memory T cells, including central memory, effector memory, and tissue-resident memory subsets. These memory cells persist in lymphoid organs and tissues, ensuring a faster and more effective response upon re-exposure to antigens. During memory formation, both $CD4^+$ and $CD8^+$ T cells may express similar markers, such as *SELL*, *CCR7*, and *PTPRC* [13].

T-cell activation and specialization are orchestrated by networks of transcription factors (e.g., *TBX21*, *GATA3*, *FOXP3*), epigenetic mechanisms (e.g., DNA methylation, histone modification), and metabolic shifts, such as transitions between glycolysis and oxidative phosphorylation [14].

$CD4^+$ T-helper cells differentiate into various subpopulations under the influence of specific cytokines and signaling pathways: Tfh, Th1, Th2, Th9, Th17, and Tregs. Follicular helper T cells (Tfh), expressing *CXCR5*, *PDCD1*, and *BCL6*, regulate B-cell maturation and germinal center formation [3, 15]. Th1 cells, characterized by *TBX21* expression and IFN-γ production, are critical for defense against intracellular pathogens by activating macrophages [3]. Th2 cells express *GATA3* and produce IL4, IL5, and IL13, promoting humoral immunity and stimulating B cells to produce antibodies [3]. Th9 cells, associated with *IRF4*, *SPI1*, and *IL9*, contribute to defense against helminths and are involved in allergic responses [14]. Th17 cells, expressing *RORC* and producing IL17A and IL22, protect mucosal surfaces against fungi and bacteria [3]. Regulatory T cells (Tregs), expressing *CD4*, *IL2RA*, and *FOXP3*, suppress excessive immune responses and prevent autoimmune reactions by secreting IL-10 and TGF-β [3, 16, 17].

$CD8^+$ cytotoxic T cells are key in eliminating virus-infected and transformed cells through the production of cytotoxic proteins (granzymes, perforin) and antiviral cytokines, such as IFN-γ. Upon activation, they form pools of effector and memory cells, regulated by transcription factors *TBX21* and *EOMES* [3].

Additional subpopulations include γδ T cells, which express *TRDC*, *TRGC1*, *TRGC2* and are capable of rapid antigen recognition independent of MHC presentation. [18, 19]. These cells are divided into subsets such as $V\delta1^+$ (tissue surveillance) and $V\delta9V\delta2^+$ (mucosal protection). NKT cells combine features of NK and T cells, expressing *CD3D*, *CD3E*, *CD3G* and NK markers (*NCAM1*) [20]. They recognize lipid antigens presented by *CD1D* and differentiate into functional subsets: NKT1 (*TBX21*, *IFNG*), NKT2

(*GATA3*, *IL-4*), and NKT17 (*RORC*, *IL-17*) [21]. Two types of NKT cells are distinguished: invariant NKT (iNKT) and variable NKT (vNKT). iNKT cells express an invariant TCR composed of the *TRAV10*, *TRAJ18* α-chain and co-express markers such as *CD3D*, *CD3E*, *CD3G*, *NCAM1*, *KLRB1*, and *CXCR6*. They recognize lipid antigens via *CD1D* and swiftly secrete diverse cytokines such as IFN-γ, IL-4, and IL-17, bridging innate and adaptive immunity [20,22]. vNKT cells have more diverse TCRs (e.g., *TRAV12–2*, *TRAJ9*, *TRAV1–2*, *TRAJ7*, *TRAV8–1*, *TRAV11*) and express *CD3D*, *CD3E*, *CD3G*, *NCAM1*, *FCGR3A*, *CD2*, and *CD28*. These cells produce proinflammatory mediators such as TNF-α and IL-2, playing a significant role in infection control and tumor immune surveillance [20].

T-cell functional activity is defined by various markers. Cytotoxicity is characterized by the expression of granzymes (*GZMA*, *GZMB*), *PRF1*, *FASLG*, and *TNFSF10*, particularly in $CD8^+$ and γδ T cells [23]. Cytokine secretion, such as IFN-γ, TNF-α, IL-2, and IL-17, varies by subpopulation, with Th1 cells producing IFN-γ and Th2 cells producing IL-4 and IL-5 [1]. T-cell activation and proliferation are accompanied by the expression of *IL2RA* and *MKI67*, reflecting cell division in response to antigenic stimulation. Apoptosis is regulated by molecules such as *FAS*, *TNFRSF10A*, *TNFRSF10B*, and *CASP*, preventing excessive inflammation [3]. In conditions of chronic antigenic stimulation, such as viral infections or tumors, T cells may exhibit exhaustion, marked by the expression of inhibitory receptors like PD-1, CTLA-4, TIM-3, and LAG-3 [24]. A list of T-cell subpopulation markers and their functional significance is provided in Table 1.

Table 1

Markers and functional significance of T-cell subpopulations

Subpopulation/Stage	Main markers	Additional markers	Functional significance of markers	References
Double negative cells (DN1–DN4)	*CD44, IL2RA* (CD25), *PTCRA* (pre-TCRα)	–	Absence of CD4 and CD8 indicates early development; CD44 and CD25 regulate migration and proliferation on DN1–DN4 substages; PTCRA on DN3 initiates transition to DP stage	[3, 12]
Double positive cells (DP	*CD4, CD8A, CD8B, TCR, CCR7, PTPRC* (CD45RA), *SELL* (CD62L), *CD3D, CD3E, CD3G, IL7R* (CD127)	–	Simultaneous expression of CD4 and CD8 reflects TCR specificity testing; CD3D/E/G form TCR complex; CCR7 supports migration	[13]
Single positive cells (SP), naive T-cells	*CD4, CD8A/CD8B, TCR, CCR7, PTPRC* (CD45RA), *SELL* (CD62L), *IL7R* (CD127)	CD27, CD28	Differentiation into CD4+ or CD8+ upon interaction with MHC–II or MHC–I; CCR7 and CD62L ensure migration to lymphoid organs	[14]
$CD4^+$ Tfh (follicular helper)	*CXCR5, PDCD1* (PD-1), *BCL6, ICOS, CD40LG* (CD40L)	MAF, IL21R	Support B-cell maturation and germinal center formation; ensure antibody class switching	[3 ,15]
$CD4^+$ Th1	*TBX21* (T-bet), *IFNG* (IFN-γ), *STAT4, CXCR3, IL2RA* (CD25)	IL18R1, IL18RAP, CXCR6	Activate macrophages; form antiviral immunity and immunity against intracellular infections	[3]
$CD4^+$ Th2	*GATA3, IL13, PTGDR2* (CRTH2), *STAT6, IL4R, IL5RA*	*IL10, IL1RL1*(ST2)	Support humoral immunity; stimulate antibody production (IgE)	[3]
$CD4^+$ Th9	*IRF4, SPI1* (PU.1), *IL9*	*STAT5, STAT6, TGFBR1* (TGF-βR)	Protection against helminths; participation in allergic reactions	[3,14]

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Subpopulation/Stage	Main markers	Additional markers	Functional significance of markers	References
CD4⁺ Th17	*RORC* (RORγt), *IL17A* (IL-17), *IL22, CCR6, STAT3, IL23R*	IL21, CCL20	Protection of mucosal surfaces from fungi and bacteria; regulation of neutrophil recruitment and activation	[3]
Treg (regulatory T-cells)	*CD4, IL2RA* (CD25), *FOXP3, CTLA4, TIGIT, IKZF2* (Helios)	*CD127, IL10, TGFB1* (TGF-β)	Suppression of autoimmune reactions; maintenance of tolerance to autoantigens (via IL-10, TGF-β)	[3, 16]
CD8+ cytotoxic (effector T-cells)	*CD8A, CD8B, PRF1* (Perforin), *GZMB* (Granzyme B), *IFNG* (IFN-γ), *GNLY, NKG7, TBX21* (T-bet), *EOMES*	GZMK, KLRG1	Destruction of infected and tumor cells via perforin and granzymes; participation in antiviral immunity (via IFN-γ synthesis)	[3, 23]
γδ T-cells	*TRDC, TRGC1, TRGC2, FCGR3A* (CD16), *NCAM1* (CD56), *CD3D, CD3E, CD3G, KLRG1, NKG7*	IL17A, CCR5	Rapid antigen response without MHC presentation; tissue surveillance (Vδ1+) and mucosal protection (Vδ9Vδ2+)	[18, 19]
NKT-cells	*CD3D, CD3E, CD3G, NCAM1* (CD56), *TCR, CD1D*		Combine functional properties of T- and NK-cells; secretion of cytokines (IFN-γ, IL-4, IL-17) in response to lipid antigens	[20, 21]
iNKT (invariant)	*CD3D, CD3E, CD3G, NCAM1* (CD56), *TRAV10, TRAJ18* (TCR Vα24-Jα18), *KLRB1* (CD161), *CXCR6, NCAM1*	*IFNG* (IFN-γ), *IL4, IL17A* (IL-17)	Immunoregulation, rapid cytokine response, antitumor activity.	[20, 22]
vNKT (variable)	*TRAV12–2, TRAJ9, TRAV1–2, TRAJ7, TRAV8–1, TRAV11* (TCR Vα3.2-Jα9, Vα1-Jα7, Vα8, Vα11), *FCGR3A* (CD16), *CD3D, CD3E, CD3G, NCAM1* (CD56), *CD2, CD28*	TNF, IL2	Antiviral and antitumor activity, immune response modulation.	[20]
Memory T-cells	*CD45RO, CD62L, CCR7, SELL* (CD62L), *IL7R* (CD127), *CD27*	KLRG1, CX3CR1	Ensure enhanced and rapid secondary immune response; divided into central (TCM), effector (TEM), and resident (TRM) cell	[3]
Exhausted T-cells	*PDCD1* (PD-1), *CTLA4, HAVCR2* (TIM-3), *LAG3, TIGIT, TOX*	*EOMES, CD244* (2B4)	Indicate T-cell dysfunction under chronic antigenic stimulation (tumors, viral infections); loss of effective proliferation and cytotoxic response	[3, 24]

Notes: Main markers are associated with the specific subpopulation, functionally relevant, and used for cell identification in flow cytometry and scRNA-seq. Additional markers are less specific, support biological interpretation, may vary depending on the cell state, and are validated by the CellMarker 2.0 and PanglaoDB databases.

B cells

B cells are key components of adaptive immunity, responsible for humoral responses through antibody secretion and antigen presentation. Derived from CLPs they mature in the bone marrow through immunoglobulin (Ig) gene rearrangement, forming unique B-cell receptors (BCR). Their heterogeneity is reflected in diverse functional subtypes, differentiation stages, and activation statuses, identifiable by distinct surface and transcriptional markers [25, 26].

B-cell development in the bone marrow

B-cell development is divided into early (pro-B, pre-B) and late (immature, mature) stages. In the bone marrow, pro-B cells, characterized by *CD34*, *CD19*, and the transcription factor *PAX5*, initiate heavy-chain immunoglobulin gene rearrangement under the influence of EBF1 and RAG1/2 enzymes [25,27]. Successful heavy-chain rearrangement leads to pre-B cells, which express C*D19*, *MS4A1*, *MME,* and components of the pre-B cell receptor (pre-BCR) including *IGHM* (μ chain), *VPREB1* and *IGLL1* (λ-like chain). The pre-BCR comprises an immunoglobulin μ heavy chain and a surrogate light chain formed by VPREB1 and λ5 proteins. Interactions between these components activate signaling pathways via adapter molecules Igα and Igβ, promoting pre-B cell proliferation and initiating light-chain gene rearrangement [25, 28]. During B cell development, cells expressing *IGHM*, *CD19*, *MS4A1*, *MME*, and *CD22*, undergo negative selection to eliminate autoreactive clones, a process mediated by BCR recognition of autoantigens and signaling through *CD79A* [25, 28]. Mature B cells, co-expressing IgM and IgD, complete maturation and migrate to peripheral lymphoid organs, such as lymph nodes and the spleen, guided by chemokines like CXCR4 [25, 27]. Mature B cells remain naïve until antigen encounter and are generally defined by the absence of CD27 and the presence of IGHD expression [25].

Peripheral activation and memory cell formation

In peripheral lymphoid organs, mature B cells are activated upon antigen binding to the BCR, triggering signaling cascades via *CD79A*/*CD79B* and activation of transcription factors such as *NFKB1* and *IRF4*. T-dependent activation requires co-stimulation from T-helper cells through CD40-CD40L interactions and cytokine secretion (e.g., IL-4, IL-21, BAFF), activating STAT5 and STAT6 pathways to promote proliferation and differentiation. This process leads to germinal center formation, where B cells expressing *BCL6* undergo somatic hypermutation and class-switch recombination, producing high-affinity antibodies of IgG, IgA, or IgE isotypes. T-independent activation, induced by polyvalent antigens like bacterial polysaccharides, relies on signals through CD21 and Toll-like receptors, activating NF-κB. Activated B cells express *CD69* and *HLA-DRA*/*HLA-DRB1*, reflecting their proliferative and antigen-presenting status [25, 28].

Upon activation, B cells differentiate into plasma cells expressing *SDC1* and *PRDM1*, which secrete antibodies (IgM, IgG, or IgA) to neutralize pathogens. Others become memory B cells, marked by *CD27* and *BCL6*, ensuring faster and stronger immune responses during subsequent encounters with the same antigen [25, 29].

B cells demonstrate considerable functional and phenotypic diversity, resulting in the formation of specialized subpopulations with unique immunological functions (Figure 1). Follicular B cells, expressing *FCER2* and *BCL6*, localize in lymph nodes and participate in T-dependent immune responses, forming germinal centers. Marginal zone B cells, predominantly in the spleen, express high levels of *CR2*, *IGHM* and *CD1c*, providing rapid T-independent responses to blood-borne pathogens. B1 cells, located in serous cavities, produce natural antibodies (IgM^{hi}) and express *CD5*, playing a key role in early immune responses to infections [25, 27].

Regulatory B cells (Bregs) are critical for maintaining immune tolerance, suppressing excessive Th1/Th17 responses through the secretion of IL-10, TGF-β, and IL-35. They express *CD19*, *CD24*, *CD38*, and *CD27* and are activated by CD40L, CpG, and IL-21 signals [26, 30, 31].

B-cell functional activity encompasses three main roles. First, antibody production is carried out by plasma cells expressing *SDC1* and *PRDM1*, which secrete IgM, IgG, or IgA antibodies to neutralize pathogens. Second, antigen presentation is mediated by activated B cells expressing *HLA-DRA*/*HLA-DRB1* and *CD69*, which efficiently interact with T-helper cells to enhance adaptive immune responses. Third, immunosuppression is driven by Bregs and transitional B cells through IL-10, TGF-β, and IL-35 secretion, as well as PD-L1 expression, suppressing effector T cells and preventing autoimmune reactions. These functions are regulated by transcription factors (*PAX5*, *BCL6*, *PRDM1*, *IRF4*, *NFKB1*) and epigenetic modifications, such as DNA methylation [25, 29]. A list of B-cell subpopulation markers and their functional significance is provided in Table 2.

Table 2

Markers and functional significance of B-cell subpopulations

Subpopulation/Stage	Main markers	Additional markers	Functional significance of markers	References
Pro-B cells	CD34, CD19, PAX5	*DNTT* (TdT), *RAG1, RAG2*	Initiate heavy chain immunoglobulin rearrangement for BCR formation	[25, 27]
Pre-B cells	*CD19, MS4A1* (CD20), *MME* (CD10), *EBF1*	*CD79A* (Igα), *CD79B* (Igβ)	Complete light chain rearrangement, forming a functional BCR	[25, 27, 28]
Immature B-cells	*IGHM* (IgM), *CD19, MS4A1* (CD20), *MME* (CD10)	*CD22, CD79A* (Igα)	Undergo negative selection to eliminate autoreactive clones	[25, 27, 28]
Naive (Mature) B-cells	*IGHM* (IgM), *IGHD* (IgD), *CD19, CD21, CD22, CD72, PAX5, TCL1A, IL21R, TNFRSF13C* (BAFFR)	*PTPRC* (CD45), *CD79A* (Igα), *CD79B* (Igβ), *MS4A1* (CD20)	Maintain antigen-independent status, readiness for activation in peripheral lymphoid organs	[25, 27, 28]
Follicular B-cells	*CD19, MS4A1* (CD20), *CD23, IGHM* (IgM), *IGHD* (IgD)	BCL6	Participate in T-dependent responses, form germinal centers	[25, 27]
Marginal zone B-cells	*CD19, CD21, IGHM* (IgM), *CD1C*	*MS4A1* (CD20)	Provide T-independent response to pathogens circulating in peripheral blood	[25, 27, 29]
B1-cells	*CD19, CD5, ITGAM* (CD11b), *IGHM* (IgM)	CD43	Produce natural antibodies, participate in early immune response	[25, 27]
Memory B-cells	*CD19, CD27, MS4A1* (CD20), *BCL6, CD22, TNFSF13B* (CD30L), *CD37, CD39, CD44, CD73, CD80, CD86, CXCR3, CXCR5, FCRL4*	*CD72, CD79B* (Igβ), *CD82, FAS* (CD95), *EBI2, ITGAX* (CD11c), *PDCD1* (PD-1), *CD274* (PD-L1), *TBX21* (T-bet), *ZEB2*	Secondary immune response, reaction to repeated antigen	[25, 27, 29]
Plasma cells	*SDC1* (CD138), *PRDM1* (BLIMP-1), *XBP1, IRF4, CD38, IL6R, IL10R, IL21R*	*BHLHE40, CD19, CD27, CD45RO, ITGA4* (CD49d), *CD69, CD71, FAS* (CD95)	Produce antibodies after terminal differentiation	[25, 27, 29]
Regulatory (Breg)	CD19, CD24, CD38, CD27, IL10	*CD274* (PD-L1), *TGFB1* (TGF-β), *CD5*	Suppress inflammatory reactions	[26, 29, 31]
Activated B-cells	*CD19, CD69, CD86, NFKB1, MS4A1* (CD20), *CD21, CD22, CD23, CD27, CD38, CD39, CD40, CD71, CD72, HLA-DRA, HLA-DRB1* (HLA-DR), *IRF4, MYC*	AICDA, BACH2	Ensure proliferation and antigen presentation	[25, 28]

Notes: Main markers are associated with the specific subpopulation, functionally relevant, and used for cell identification in flow cytometry and scRNA-seq. Additional markers are less specific, support biological interpretation, may vary depending on the cell state, and are validated by the CellMarker 2.0 and PanglaoDB databases.

Conclusion

The rapid development of scRNA-seq has enabled deeper insights into cellular heterogeneity and immune cell function. Yet, the value of these insights' hinges on precise and reliable cell type annotation. This review provides a systematic overview of markers for adaptive immune cells, ranging from early progenitors to functionally specialized subpopulations. These marker panels can significantly improve the accuracy of automated annotation by reducing the rate of false positives and false negatives. Such standardization has important practical implications in oncoimmunology, facilitating a better understanding of disease pathogenesis, more accurate prediction of responses to immunotherapy, and the identification of novel therapeutic targets. Nevertheless, a comprehensive understanding of the immune system requires the analysis of both adaptive and innate immune compartments. The systematization of markers for innate immune cells will be the focus of future work.

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Типирование клеток адаптивного иммунитета: маркеры популяций и их функциональное значение

А.А. Федоров[1] ✉, А.А. Федоренко[1], М.Р. Патышева[1], Т.С. Геращенко[1,2]

[1] Научно-исследовательский институт онкологии, Томский национальный исследовательский медицинский центр, *г. Томск, Российская Федерация*
[2] Российский университет дружбы народов, *г. Москва, Российская Федерация*
✉ anton.fedorov.2014@mail.ru

Аннотация. *Актуальность.* Технологии секвенирования единичных клеток (scRNA-seq) открывают уникальные возможности для изучения гетерогенности иммунных популяций, позволяя анализировать экспрессионные профили, лиганд-рецепторные взаимодействия и траектории дифференцировки на уровне отдельных клеток. Однако качество типирования клеток существенно зависит от точности аннотации данных. Неоднозначность маркеров, вариабельность их экспрессии в зависимости от физиологического контекста, ограничения автоматических инструментов, таких как CellTypist, Azimuth и SingleR, а также неполнота баз данных PanglaoDB и CellMarker, включая недостаток сведений о функциональной роли маркеров, значительно затрудняют идентификацию клеточных популяций и требуют дополнительных усилий для достижения значимых результатов. *Цель.* Систематизировать маркеры Т- и В-клеток адаптивного иммунного ответа для упрощения аннотации данных scRNA-seq. *Материалы и методы.* Проведен анализ более 30 научных публикаций из баз PubMed, Scopus и Web of Science за 2008–2024 годы, а также данных маркеров из баз PanglaoDB и CellMarker. *Результаты и обсуждение.* Рассмотрены ключевые и дополнительные маркеры Т-клеток (*CD3D, CD3E, CD3G, CD4, CD8A, CD8B, FOXP3, GZMA, TBX21*) и В-клеток (*CD19, MS4A1, CD27, IGHM, IGHD*), их роль в иммунных процессах, включая активацию, цитотоксичность и регуляцию. Описаны субпопуляции, такие как Th1-клетки (T-bet, IFN-γ), фолликулярные хелперы (CXCR5, BCL-6), регуляторные В-клетки (CD24, IL-10), и их функции в норме и патологии. *Выводы.* Систематизация маркеров Т- и В-клеток разработана для улучшения качества аннотации данных секвенирования единичных клеток и применима для расширенного типирования функциональных состояний клеток в норме и при патологии (инфекционные, аутоиммунные и онкологические заболевания). Это открывает возможности для углубленного понимания иммунных процессов и разработки подходов к иммунотерапии, включая CAR-T-терапию. Однако ограниченная специфичность маркеров и отсутствие стандартизированных алгоритмов аннотации подчеркивают необходимость дальнейших исследований для совершенствования методов типирования.

Ключевые слова: Т-клетки, В-клетки, адаптивный иммунитет, секвенирование единичных клеток, иммунные маркеры, типирование

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Corresponding author: Anton A. Fedorov — PhD, Junior Researcher, Laboratory of Cancer Progression Biology, Cancer Research Institute, Tomsk National Research Medical Center, 5, Kooperativny St., Tomsk, 634009, Russian Federation. E-mail: anton.fedorov.2014@mail.ru
Fedorov A.A. SPIN 1315-8100, ORCID 0000-0002-5121-2535
Fedorenko A.A. SPIN 8092-0070, ORCID 0000-0003-3297-1680
Patysheva M.R. SPIN 5714-4611, ORCID 0000-0003-2865-7576
Gerashchenko T.S. SPIN 7900-9700, ORCID 0000-0002-7283-0092

Ответственный за переписку: Федоров Антон Андреевич — кандидат медицинских наук, младший научный сотрудник лаборатории биологии опухолевой прогрессии, Научно-исследовательский институт онкологии, Томский национальный исследовательский медицинский центр, Российская Федерация, 634009, г. Томск, пер. Кооперативный, д. 5. E-mail: anton.fedorov.2014@mail.ru
Федоров А.А. SPIN 1315-8100, ORCID 0000-0002-5121-2535
Федоренко А.А. SPIN 8092-0070, ORCID 0000-0003-3297-1680
Патышева М.Р. SPIN 5714-4611, ORCID 0000-0003-2865-7576
Геращенко Т.С. SPIN 7900-9700, ORCID 0000-0002-7283-0092