# ImYoo Participant Report

*v1.08b*

This report was prepared for

**s3**

**28/07/2023**

# Contents

# 1 Introducing your immune army

Your blood is made up of many different cell types. In our lab we remove red blood cells and focus on checking the state of white blood cells. Below are different types of cells that comprise the white blood cells in your sample. The inner circle represents the top level hierachy and the outer circles show a breakdown of subtypes within those major cell types. Below are definitions of major cell types and their functions.

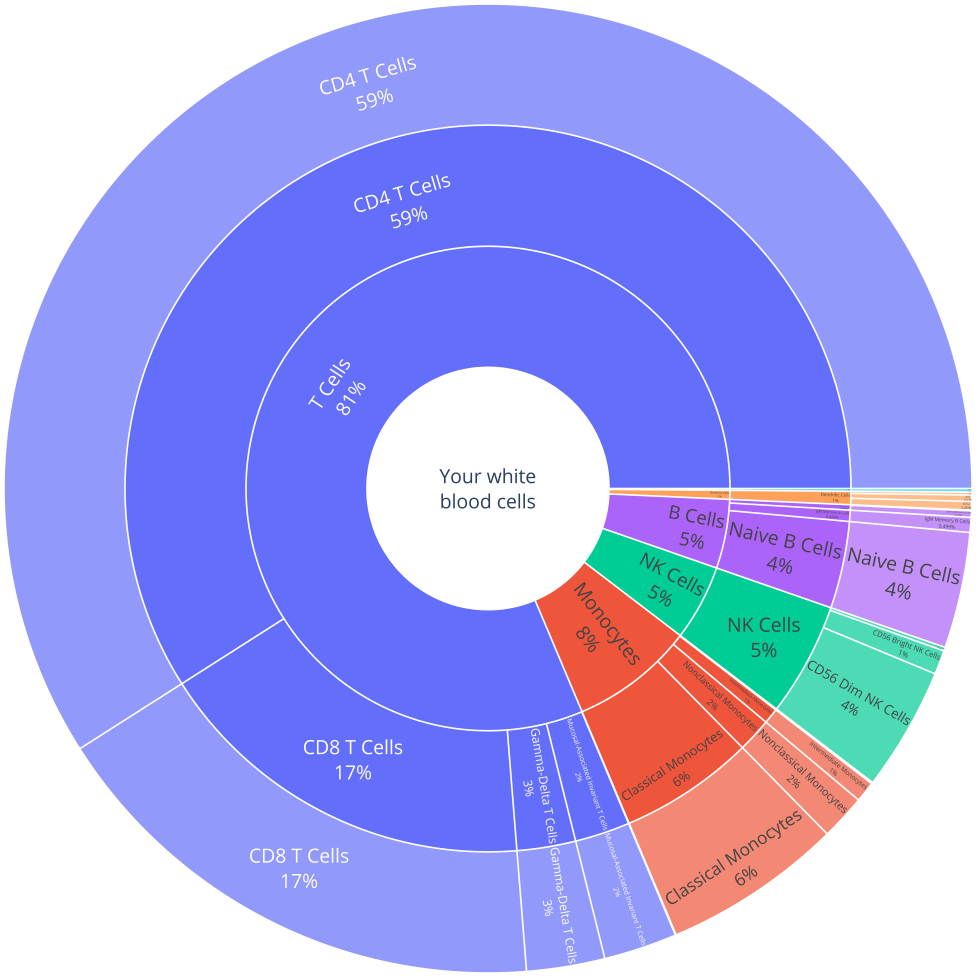



**Figure 1.** Your immune army

- **T cells** are specialized cells belonging to the adaptive immune system which are responsible for recognizing pathogens.
- **B cells** are part of adaptive immune system and are responsible for making different types of antibodies that bind to pathogens.
- **Monocytes** migrate into tissue and turn into macrophages. They engulf pathogens and present the pathogen chunks to cells like T cells to activate them and initiate the adaptive immune response.
- **Natural killer (NK) cells** recognize and kill cells that are harmful to the rest of the body, such as virus-infected cells and cancer cells.
- **Dendritic cells** are specialized antigen-presenting cells of the immune system that capture, process, and present antigens to T cells, thereby initiating and regulating adaptive immune responses.

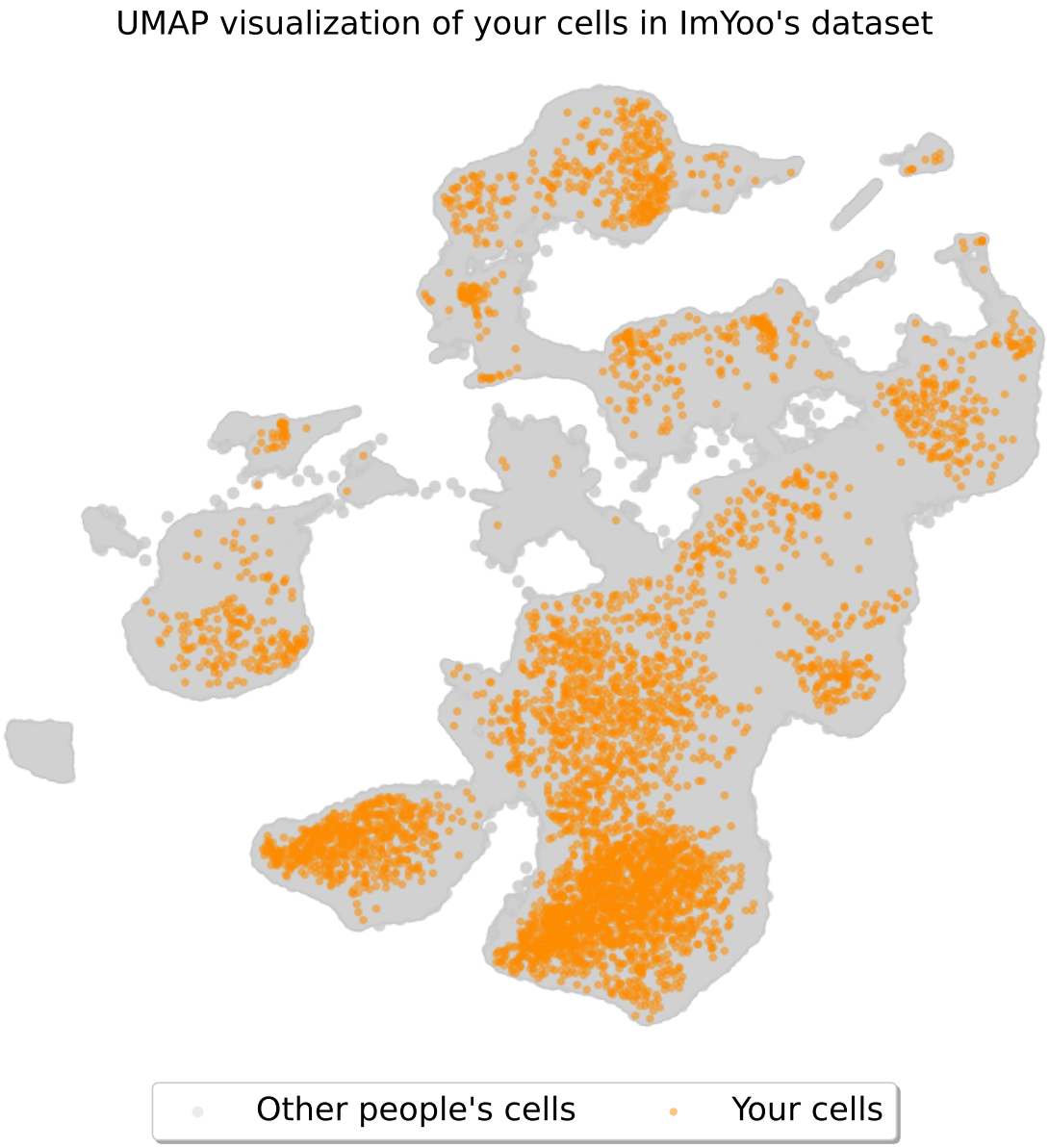
## 2 Embeddings - Visualizing your cells

Your cells are now a part of ImYoo's human reference transcriptome database.

In the following embeddings each dot is one of your cells, and how close they are to each other represents how similar they are to each other.

Cells that group together are often cells of a common type, such as T Cells. By growing our reference database, you are helping us discover more rare and unique cell types and states.

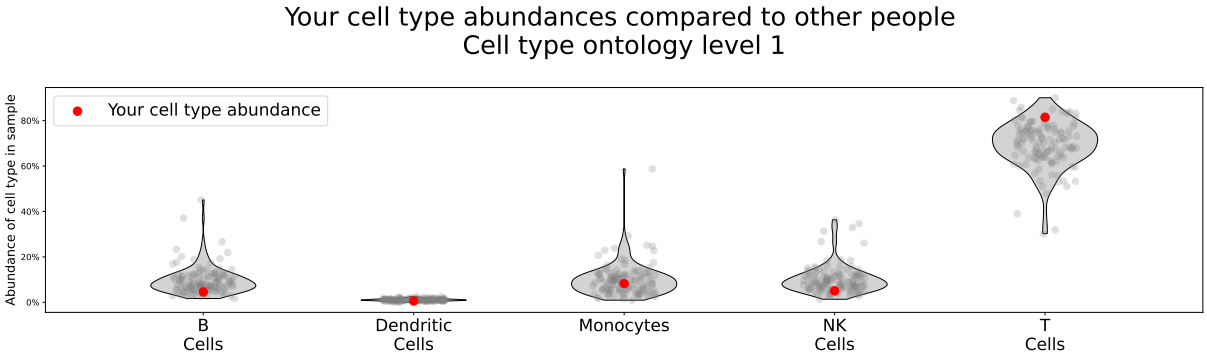
UMAP stands for "Uniform Manifold Approximation and Projection". UMAP is a non-linear dimensionality reduction technique that aims to preserve the structure and relationships in high-dimensional data, such as single-cell RNA sequencing (scRNA-seq) data, while representing it in a lower-dimensional space.



# 3 Cell type abundance distributions

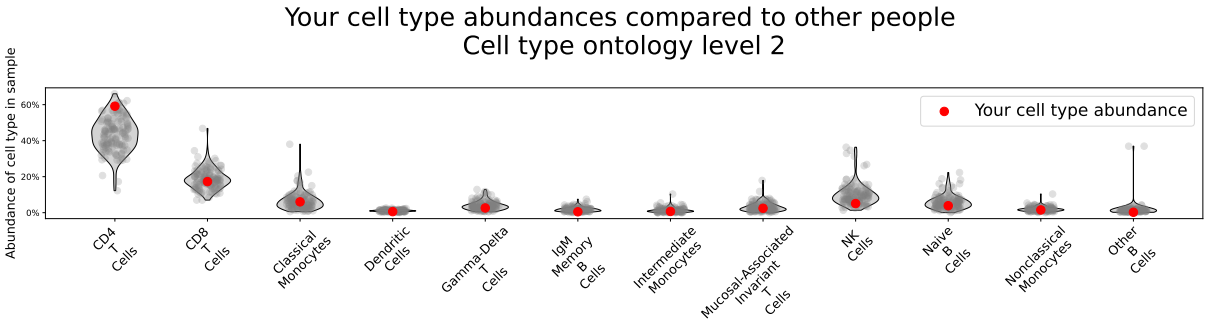
Here you can see the different immune cells captured in your capillary blood and how much each of them contributes to your white blood cells, and how it compares to other people, at three different levels of our cell type taxonomy.

## Cell types - taxonomy level 1



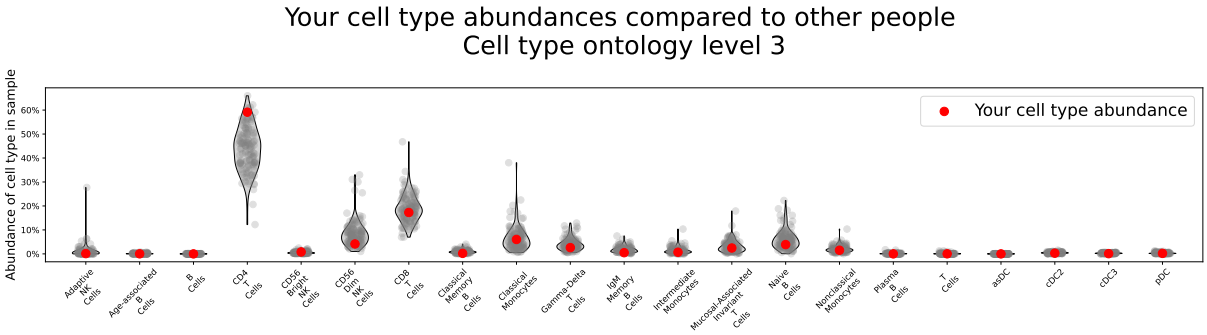

- **T cells** are specialized cells belonging to the adaptive immune system which are responsible for recognizing pathogens.
- **B cells** are part of adaptive immune system and are responsible for making different types of antibodies that bind to pathogens.
- **Monocytes** migrate into tissue and turn into macrophages. They engulf pathogens and present the pathogen chunks to cells like T cells to activate them and initiate the adaptive immune response.
- **Natural killer (NK) cells** recognize and kill cells that are harmful to the rest of the body, such as virus-infected cells and cancer cells.
- **Dendritic cells** are specialized antigen-presenting cells of the immune system that capture, process, and present antigens to T cells, thereby initiating and regulating adaptive immune responses.

## Cell types - taxonomy level 2




- **Naive B Cells :** A type of B lymphocyte that has been produced in the bone marrow but has not yet been exposed to an antigen, they are ready to respond to infections.
- **NK Cells :** A type of lymphocyte (white blood cell) and a component of the innate immune system which can rapidly respond to viral-infected cells and tumor formation.
- **CD8 T Cells :** Also known as cytotoxic T cells, these cells are part of the adaptive immune system and are capable of killing cancer cells, cells that are infected, or cells that are damaged in other ways.
- **CD4 T Cells :** Known as helper T cells, they assist other white blood cells in immunologic processes, including maturation of B cells into plasma cells and memory B cells, and activation of cytotoxic T cells and macrophages.
- **Mucosal-Associated Invariant T Cells :** These are a type of T cell that play a role in the mucosal immune response and can recognize a broad range of infectious microbes as well as cancer cells.
- **IgM Memory B Cells :** A subpopulation of B cells that have been previously exposed to antigens, primed to mount aN effective immune response upon re-exposure.
- **Gamma-Delta T Cells :** A small subset of T cells that possess a distinct T-cell receptor (TCR) on their surface. They are involved in the immune response to certain types of infections and diseases, including some cancers.
- **Other B Cells :** B cells that have other kinds of receptors against other antigen families.
- **Nonclassical Monocytes :** These are a subset of monocytes, a type of white blood cell, that display distinct functions, such as tissue repair and inflammation regulation, compared to other monocyte subsets.
- **Classical Monocytes :** These are the most common subset of monocytes that circulate in the blood. They play a role in immune surveillance and response, as they can differentiate into macrophages or dendritic cells to combat infection.
- **Dendritic Cells :** These are powerful antigen-presenting cells that are able to initiate a primary immune response. They process antigen material and present it on their surface to T cells, triggering an adaptive immune response.
- **Intermediate Monocytes :** These are a transitional subset of monocytes between classical and nonclassical monocytes. They are involved in antigen presentation and inflammatory responses.

## Cell types - taxonomy level 3




- **Naive B Cells :** These are B lymphocytes that have been produced in the bone marrow but have not yet been exposed to an antigen, hence are prepared to respond to infections.
- **CD56 Dim NK Cells :** A subset of Natural Killer (NK) cells, characterized by low surface expression of CD56 and high cytotoxic capability, playing a key role in the innate immune response to tumors and virally infected cells.
- **CD8 T Cells :** Also known as cytotoxic T cells, these cells are a part of the adaptive immune system and have the capability to kill cancer cells, cells that are infected, or cells that are damaged in other ways.
- **CD4 T Cells :** Known as helper T cells, these cells assist other white blood cells in immunologic processes, including maturation of B cells into plasma cells and memory B cells, and the activation of cytotoxic T cells and macrophages.
- **Mucosal-Associated Invariant T Cells :** : These are a type of T cell that plays a role in the mucosal immune response and has the capacity to recognize a broad range of infectious microbes and cancer cells.
- **IgM Memory B Cells :** These are a subpopulation of B cells that have been previously exposed to antigens and are primed to mount a more rapid and effective immune response upon re-exposure.
- **Gamma-Delta T Cells :** These are a small subset of T cells that possess a distinct T-cell receptor (TCR) on their surface and are involved in the immune response to certain types of infections and diseases, including some cancers.
- **CD56 Bright NK Cells :** A subset of Natural Killer (NK) cells, characterized by high surface expression of CD56. These cells have less cytotoxic activity but produce significant amounts of immune regulatory cytokines.
- **T Cells :** These are a type of white blood cell that are key players in the immune system, particularly in adaptive immunity. They attack cells infected with pathogens and help coordinate the immune response.
- **Classical Memory B Cells :** These are B cells that have previously encountered and responded to a specific antigen, and can respond more quickly and robustly if they encounter the same antigen again.
- **B Cells :** These are a type of white blood cell that produce antibodies against antigens, playing a crucial role in the adaptive immune system.
- **Age-associated B Cells :** These are a distinct subset of B cells that accumulate with age and chronic inflammatory conditions. They have unique signaling and functional characteristics.
- **Adaptive NK Cells :** These are NK cells that have gained memory-like properties, allowing them to respond more effectively upon re-exposure to a previously encountered pathogen or tumor cell.

- **Nonclassical Monocytes :** These are a subset of monocytes, a type of white blood cell, with distinct functions like tissue repair and inflammation regulation compared to other monocyte subsets.
- **Classical Monocytes :** These are the most common subset of monocytes, involved in immune surveillance and response. They can differentiate into macrophages or dendritic cells to combat infection.
- **cDC2 :** Conventionally, Dendritic Cell type 2, or cDC2, is a type of dendritic cell known for its high capability of antigen presentation to helper T cells, and plays a crucial role in the activation and shaping of the adaptive immune response.
- **cDC3 :** Conventionally, Dendritic Cell type 3, or cDC3, is another subtype of dendritic cells, although as of my last update in 2021, there's limited information about this particular subtype.
- **pDC :** Plasmacytoid Dendritic Cells, or pDCs, are a unique subset of dendritic cells known for their ability to produce large quantities of type I interferon, a protein that has antiviral properties, in response to a viral infection.
- **Plasma B Cells :** These are B cells that have been activated and have differentiated into cells that secrete large volumes of antibodies. They play a crucial role in the immune system's response to infection.
- **Intermediate Monocytes :** These are a transitional subset of monocytes that sit between classical and nonclassical monocytes. They are involved in antigen presentation and inflammatory responses.
- **asDC :** Activated Stromal Dendritic Cells, or asDCs, are dendritic cells that are activated and interact with stromal cells, which are cells that contribute to the physical support of tissues. They are involved in immunity and inflammation responses, however, as of my last update in 2021, detailed information about asDCs is limited.

# 4 About Differential Gene Expression - Volcano plots and MA plots

**Gene expression** is the process by which information stored in our DNA is used to create proteins. Our DNA is made up of units called genes, which contain the instructions to produce specific proteins. The process of gene expression has two main steps : transcription and translation. During transcription, a molecule called RNA is created from the DNA template. This RNA molecule is called messenger RNA (mRNA) and carries the genetic information to the next step, translation. In translation, the mRNA is read by structures called ribosomes, which create the desired protein using the mRNA as a guide.

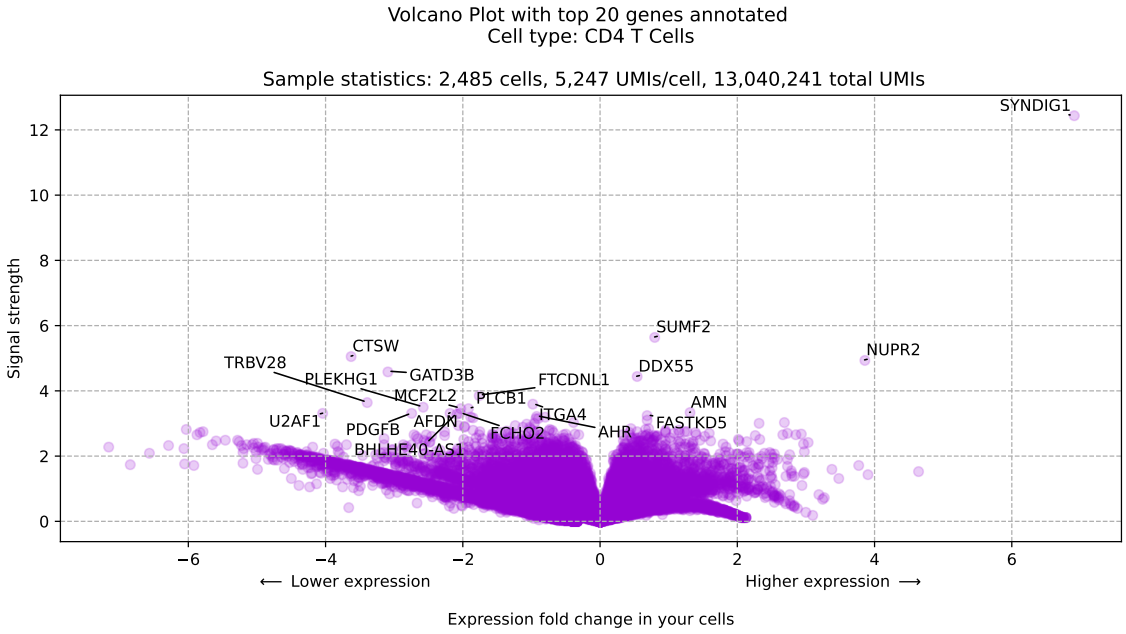
**Differential gene expression analysis** is a technique used by researchers to compare gene expression levels between different biological conditions or groups, such as healthy and diseased tissues. By measuring the abundance of messenger RNA (mRNA) molecules produced from each gene in the different samples, researchers can identify genes that show significant changes in expression levels. These changes may provide insights into the underlying molecular mechanisms of various biological processes, diseases, or responses to external stimuli, and can potentially lead to the discovery of novel therapeutic targets or biomarkers.

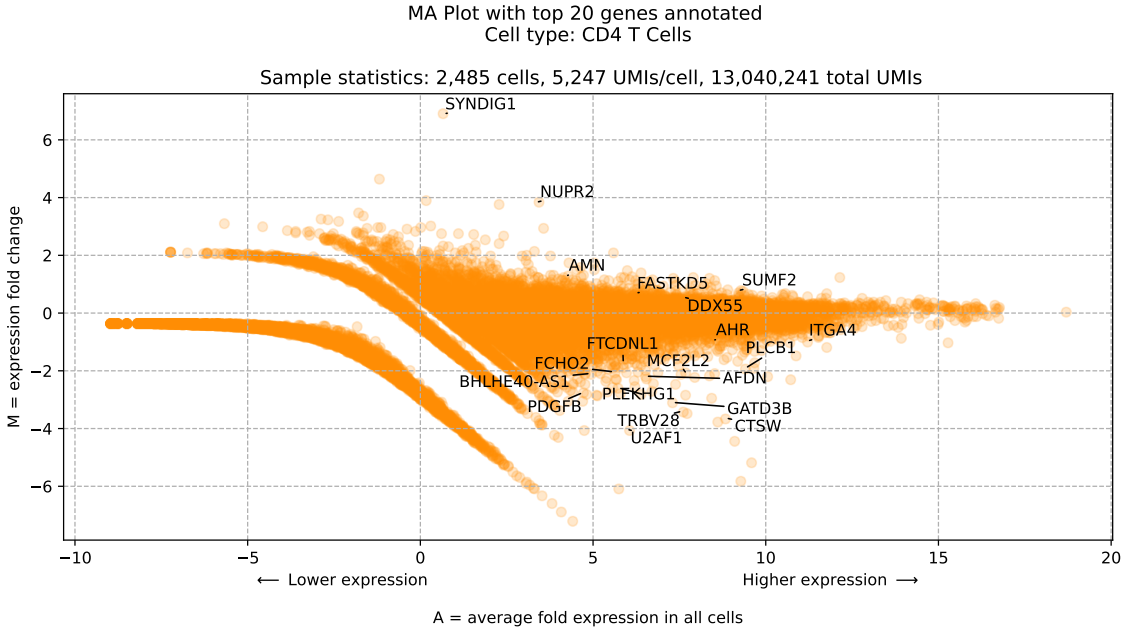
**A volcano plot** is a type of graph used in biology to visualize and compare gene expression changes in two different conditions, such as a healthy versus a diseased state. The x-axis represents the difference in gene expression (log2 fold change) between the two conditions, while the y-axis represents the signal strength of the observed change. The name "volcano plot" comes from its shape, which resembles a volcano, with highly significant genes appearing towards the top and genes with large expression differences appearing on the sides.

**MA plots**, short for "M (log ratio) vs. A (mean average)" plots, are another type of graph used to analyze gene expression data. They plot the relationship between the average expression level of a gene (A) and the ratio of expression levels between two conditions (M). The x-axis represents the average expression level across both conditions, and the y-axis represents the log2 fold change between the two conditions. MA plots help researchers visualize the overall distribution of gene expression changes and identify any systematic biases in the data. They can also help identify differentially expressed genes that deviate from the expected distribution.

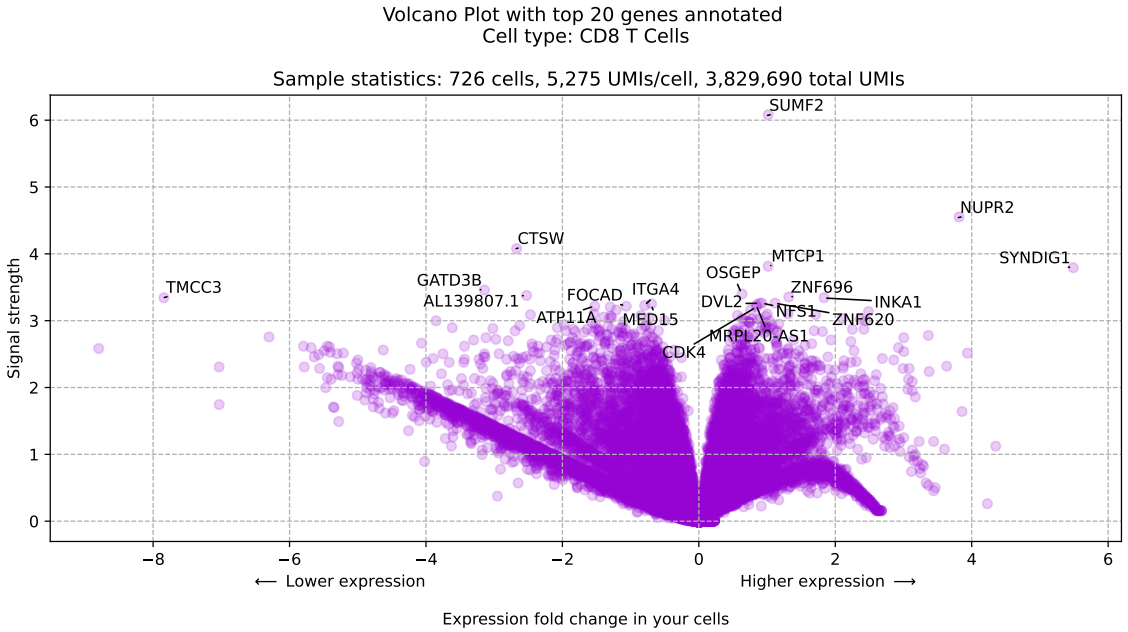
# 5 Differential expression results

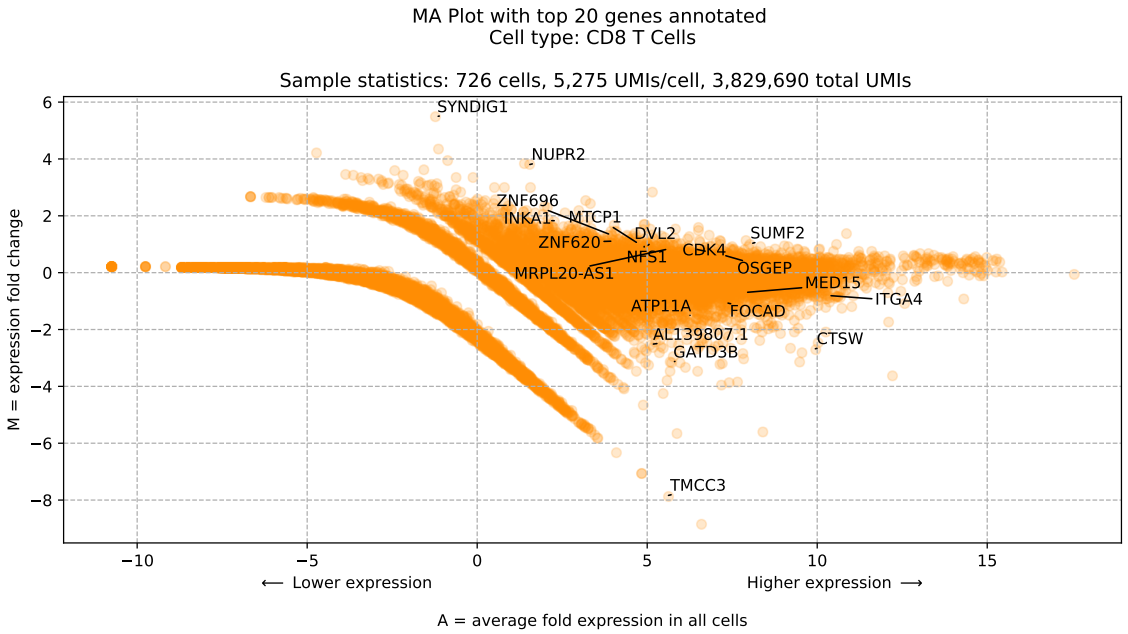
## CD4 T Cells - Differential gene expression



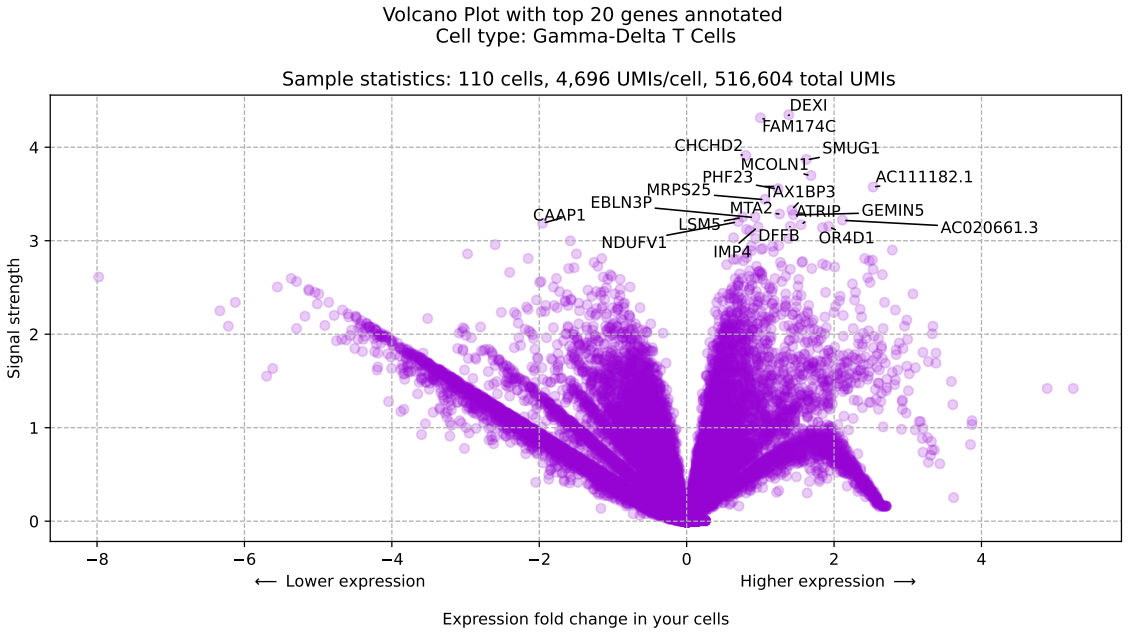



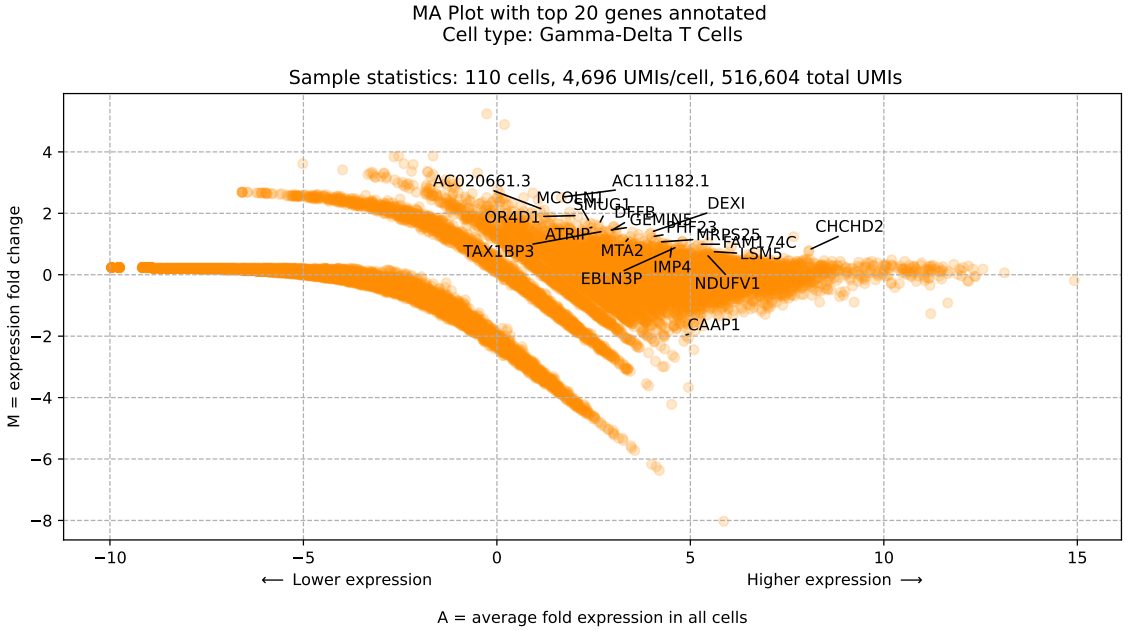
## CD8 T Cells - Differential gene expression



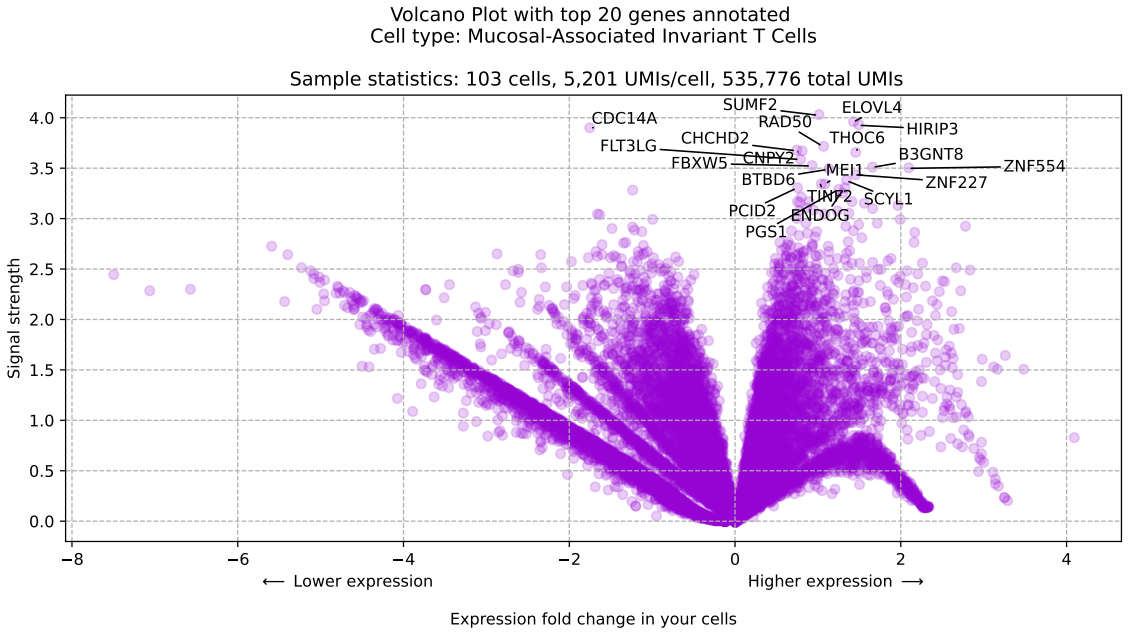



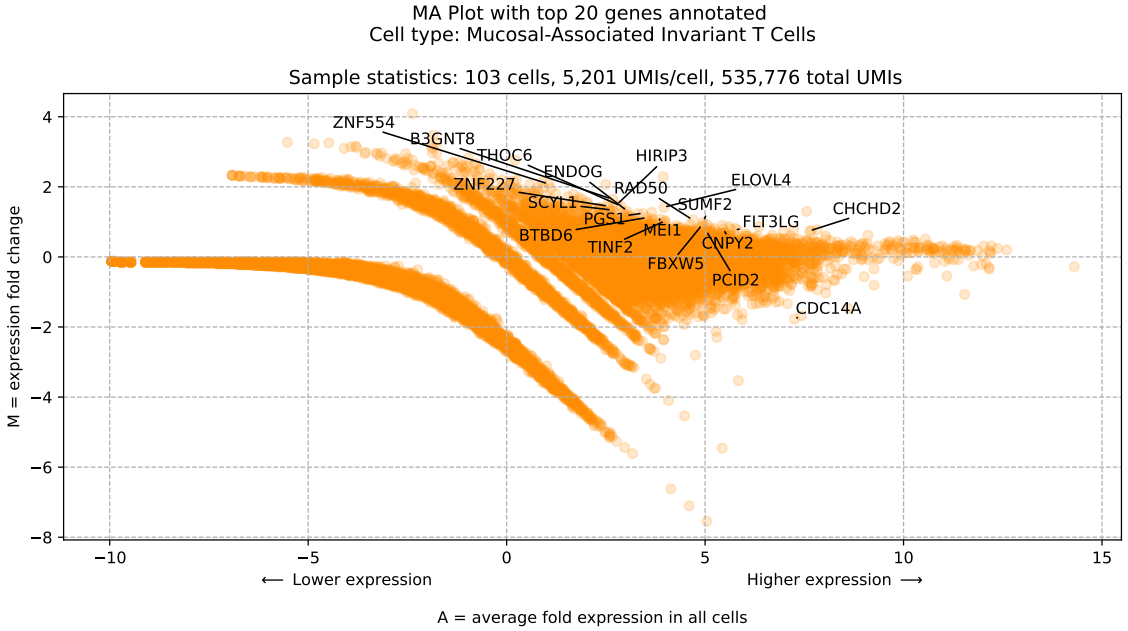
## Gamma-Delta T Cells - Differential gene expression



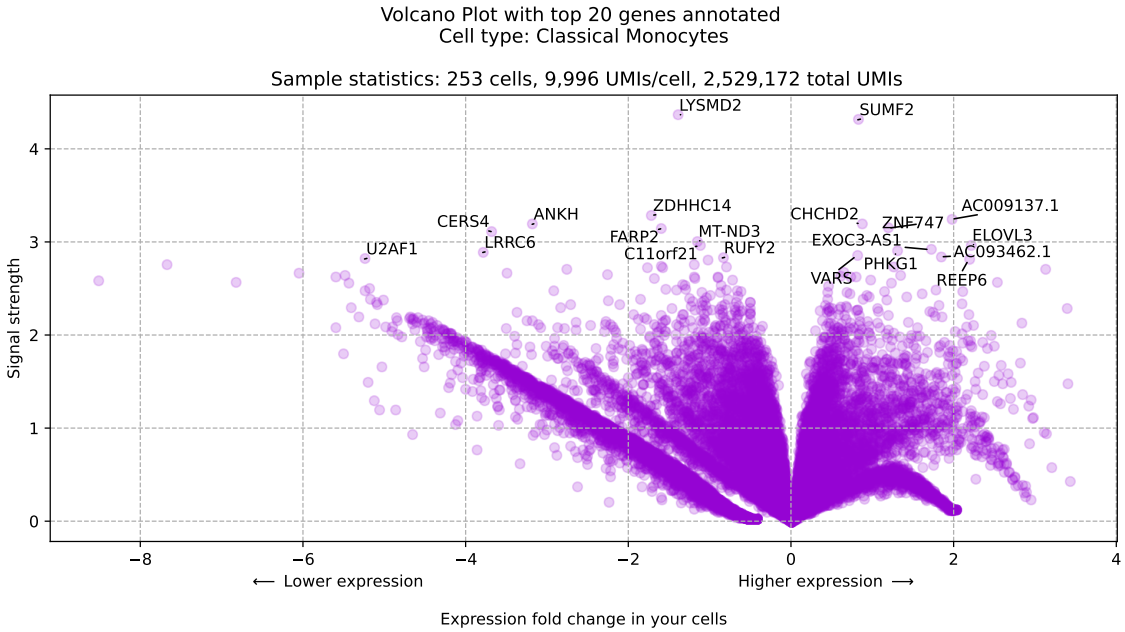



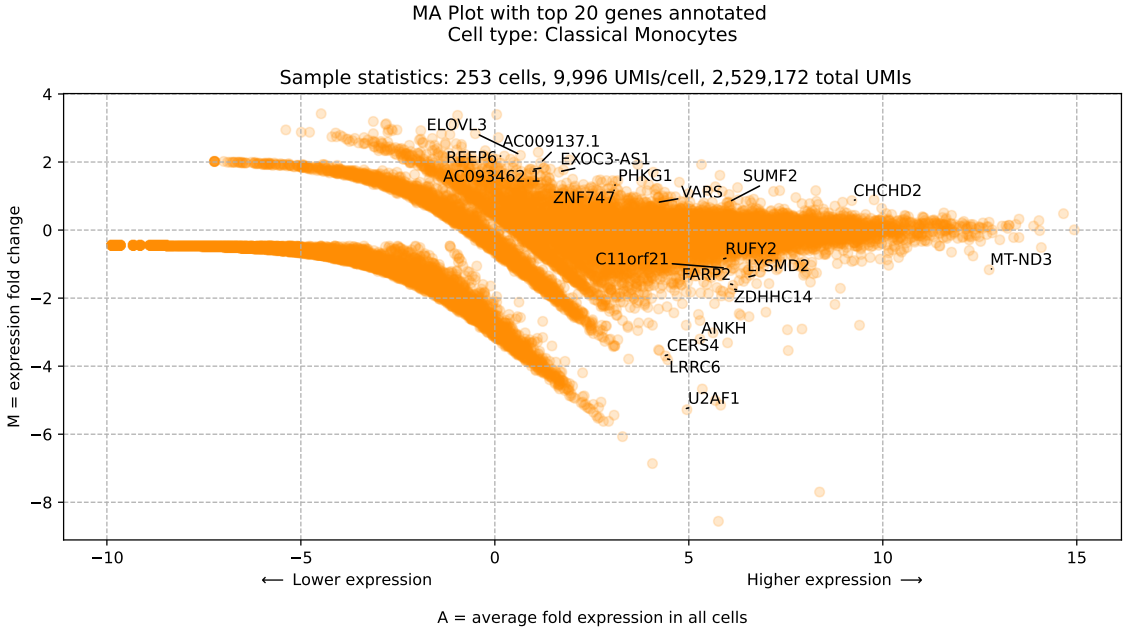
## Mucosal-Associated Invariant T Cells - Differential gene expression



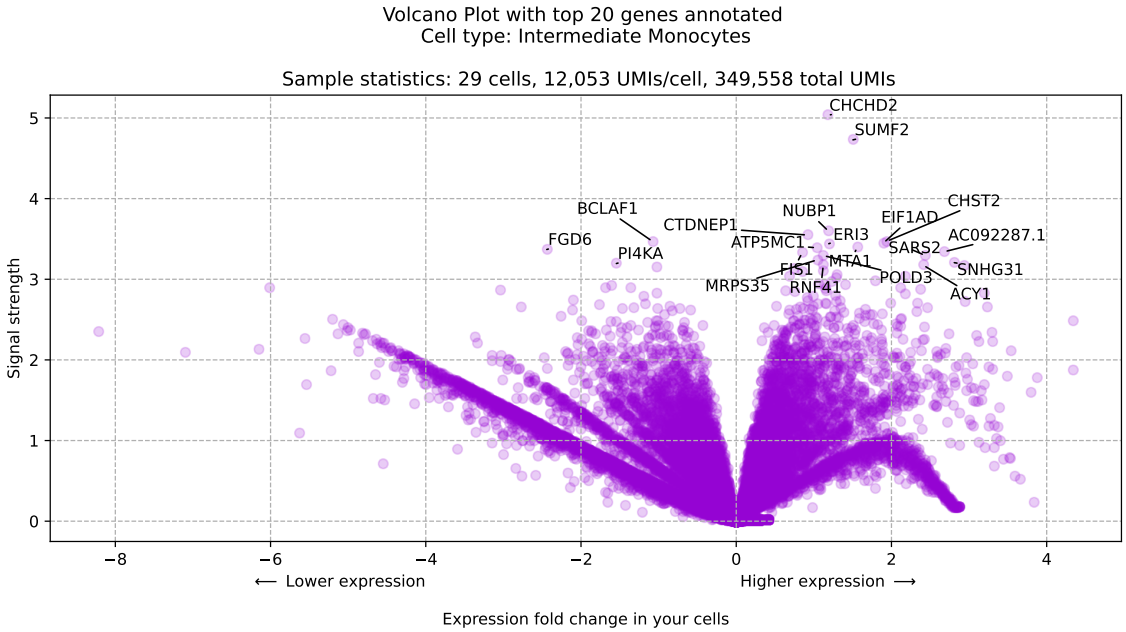



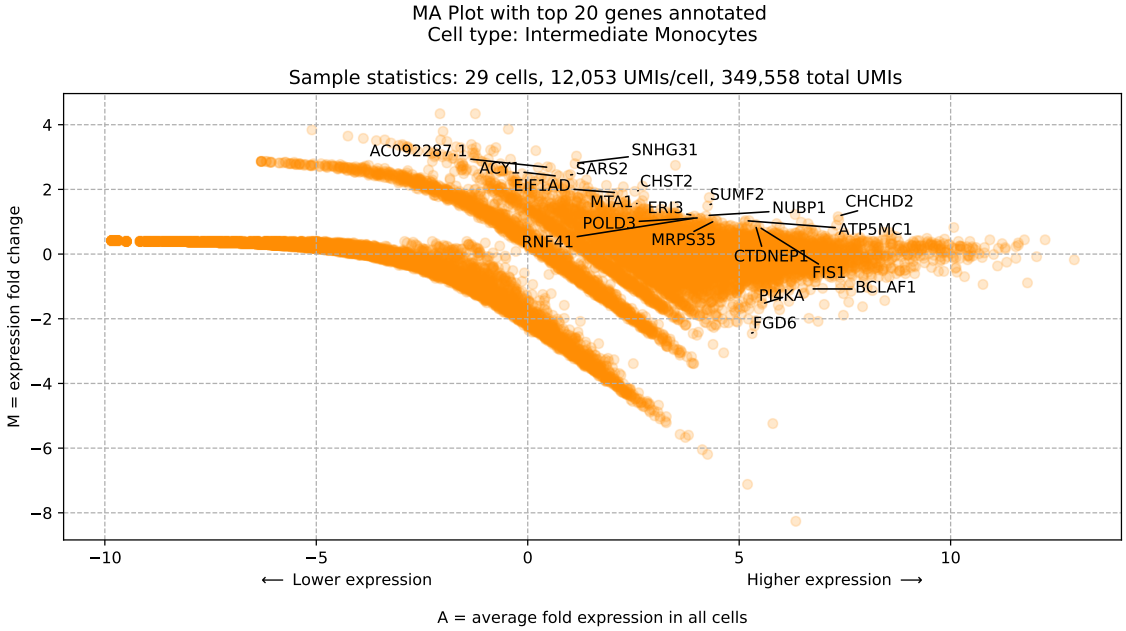
## Classical Monocytes - Differential gene expression



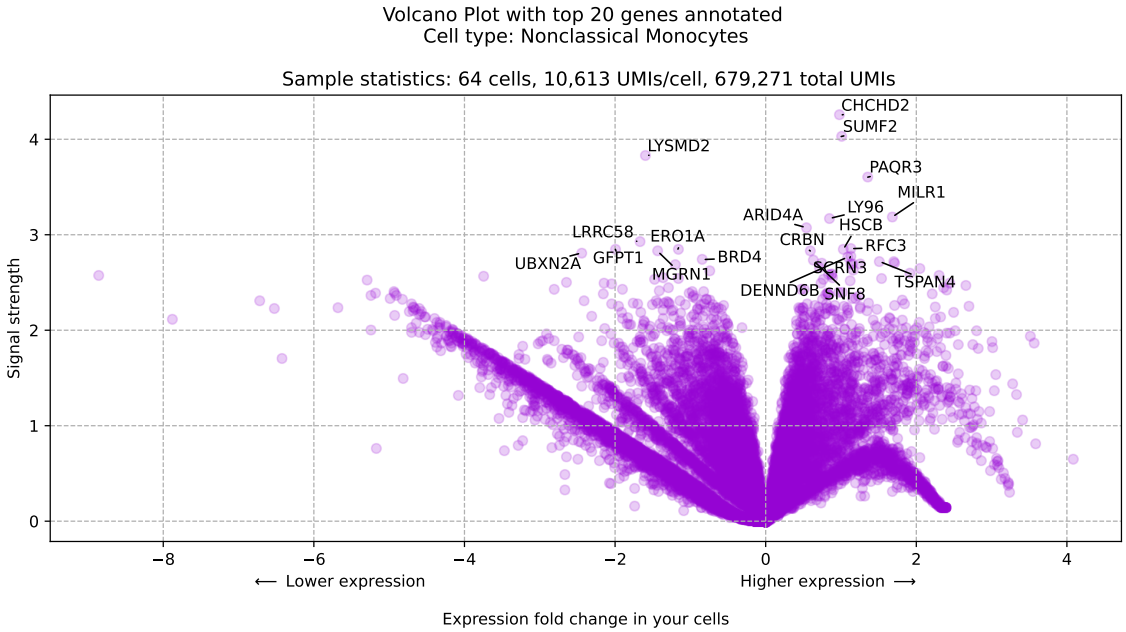



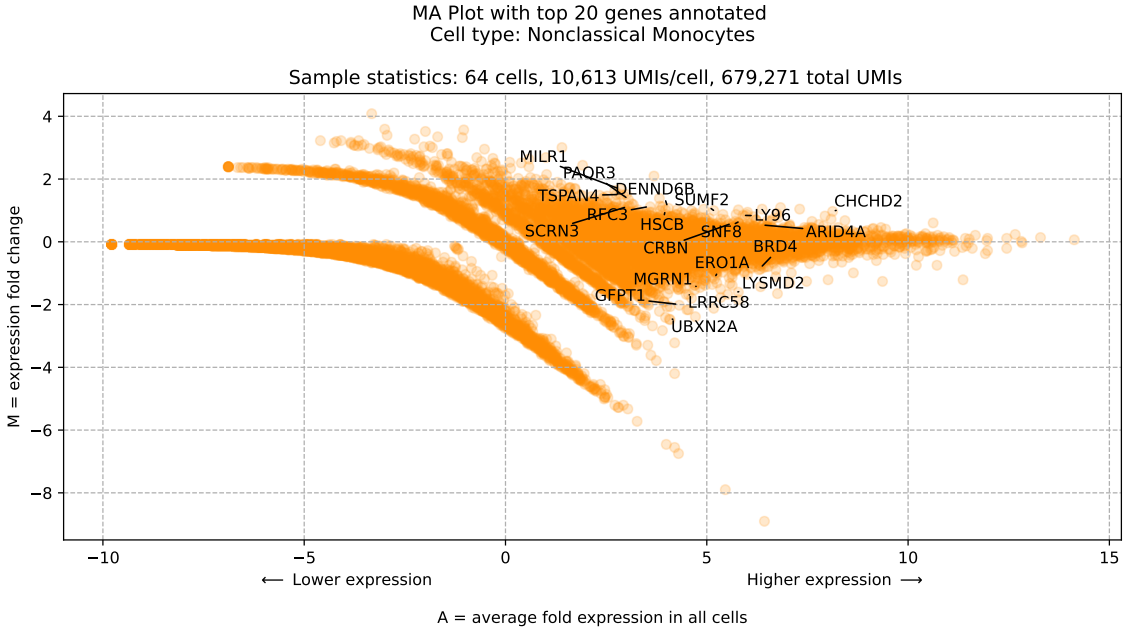
## Intermediate Monocytes - Differential gene expression



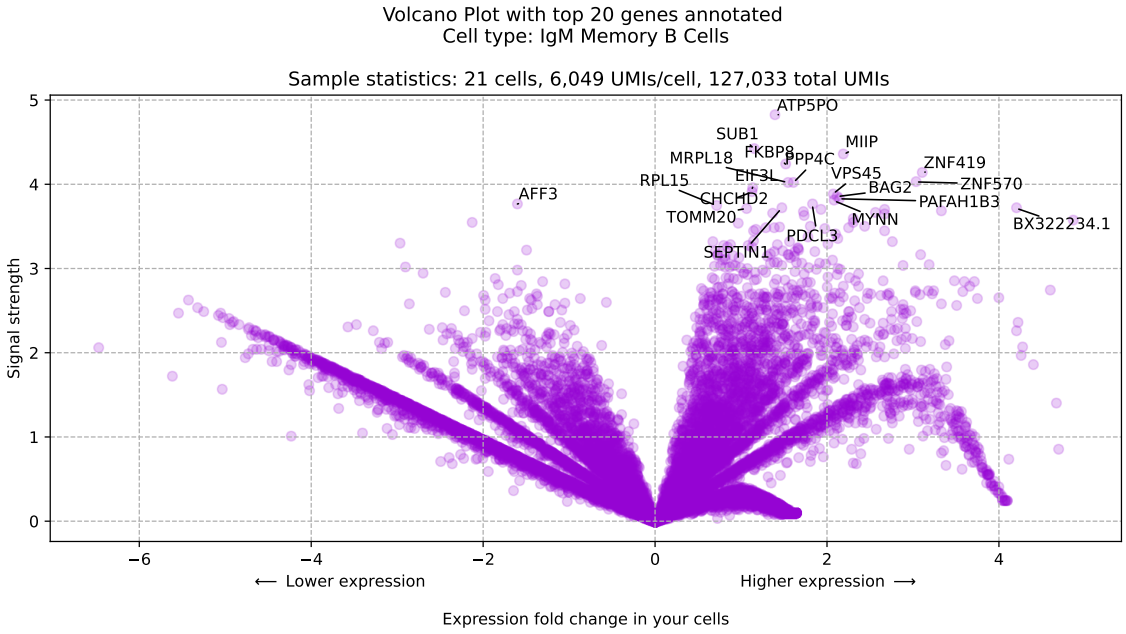



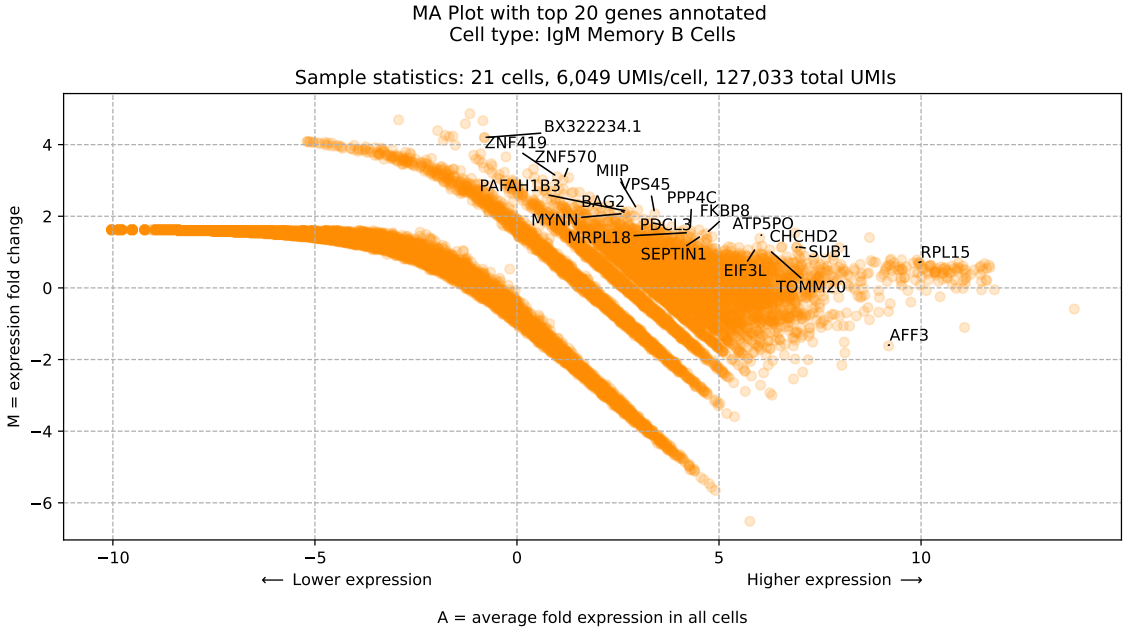
## Nonclassical Monocytes - Differential gene expression



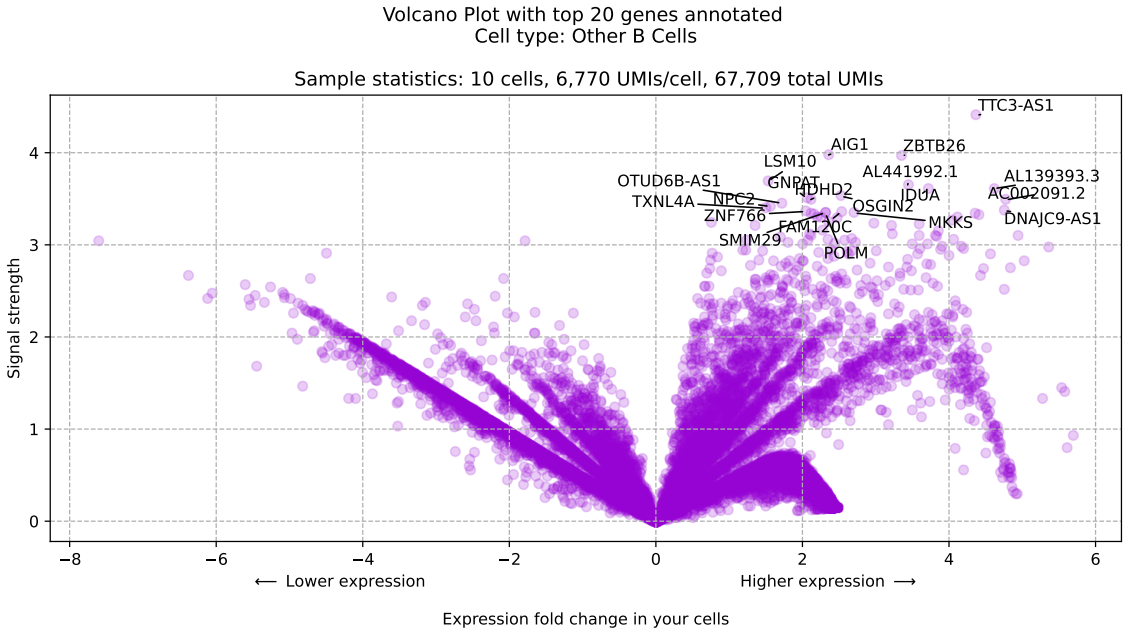



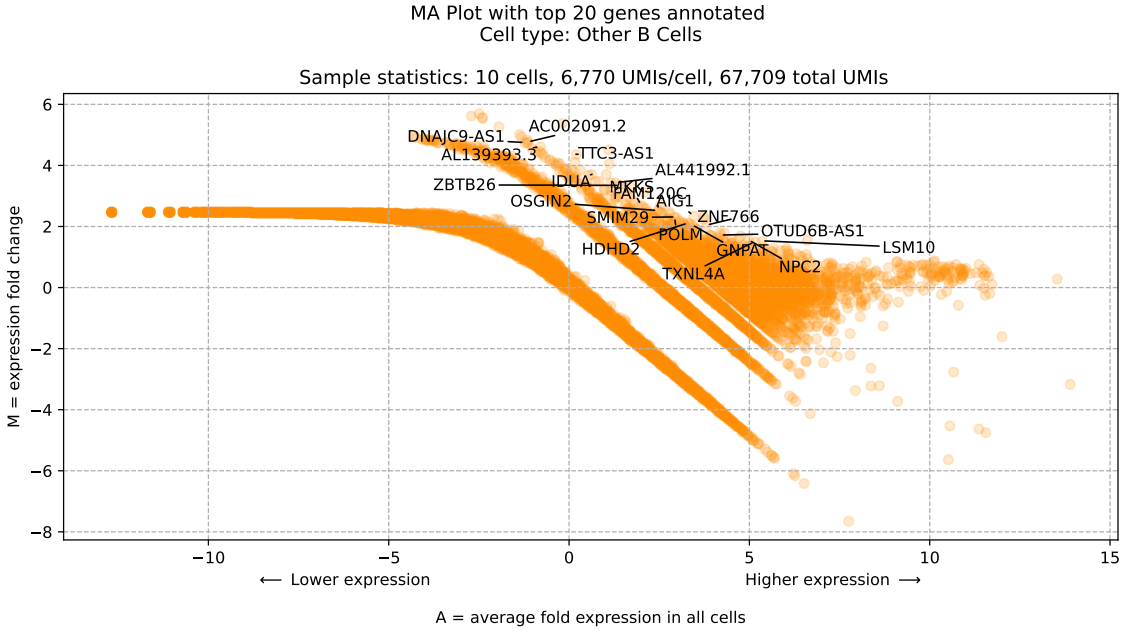
## IgM Memory B Cells - Differential gene expression



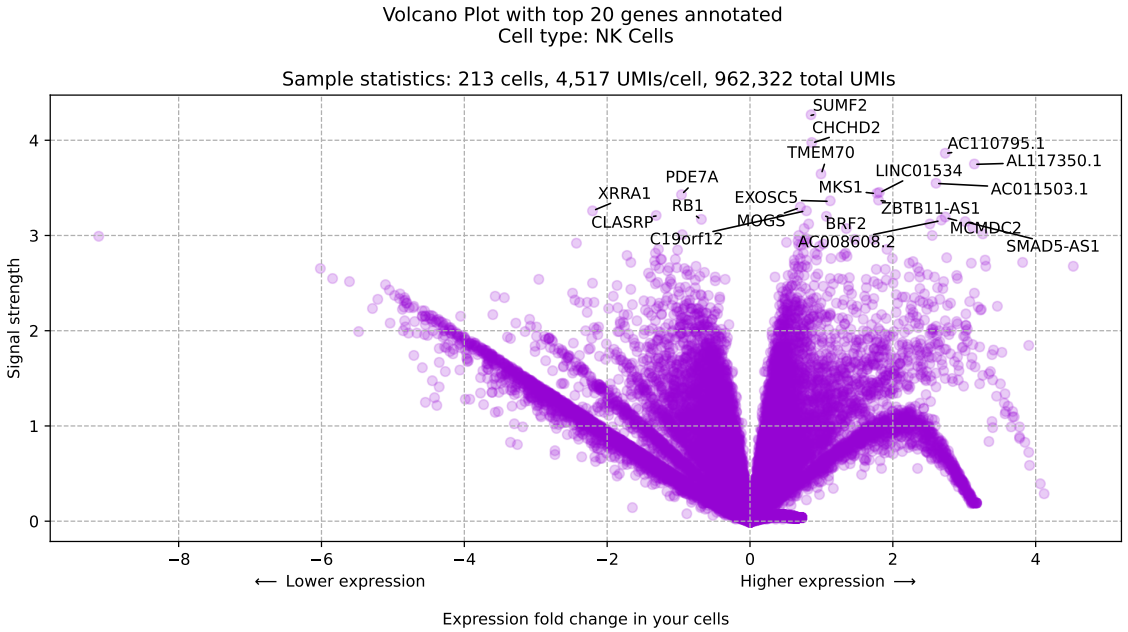



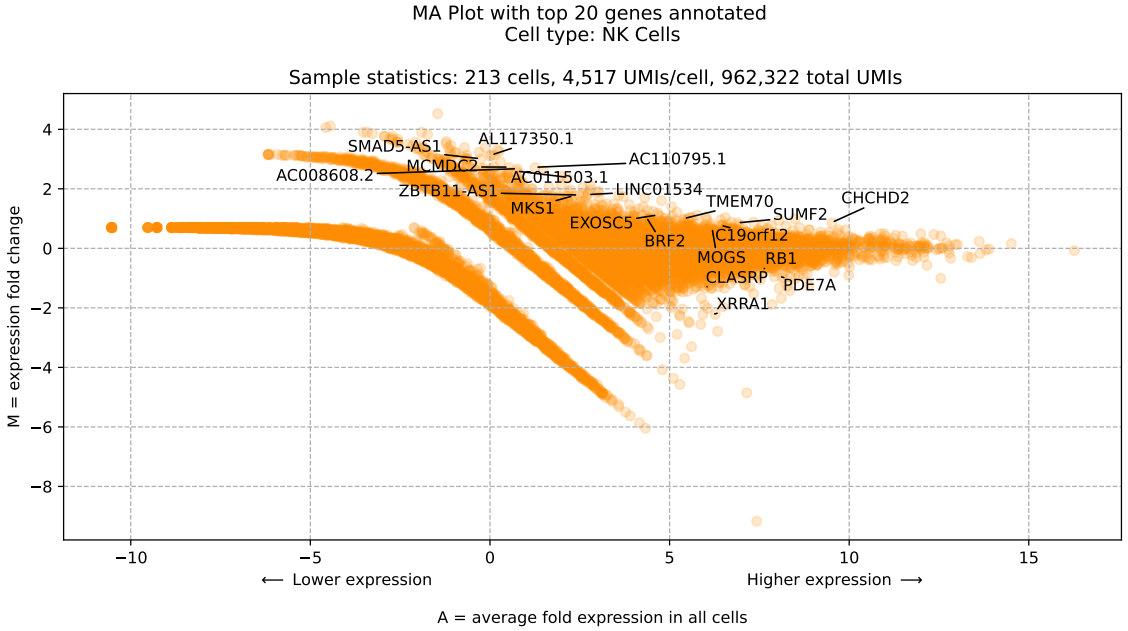
## Other B Cells - Differential gene expression



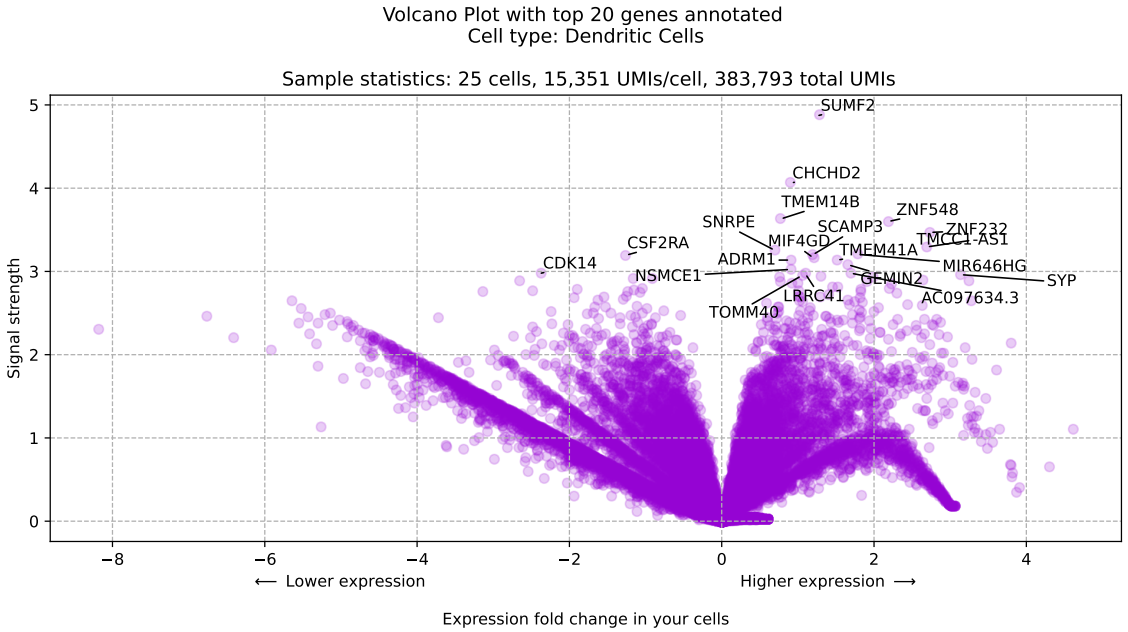



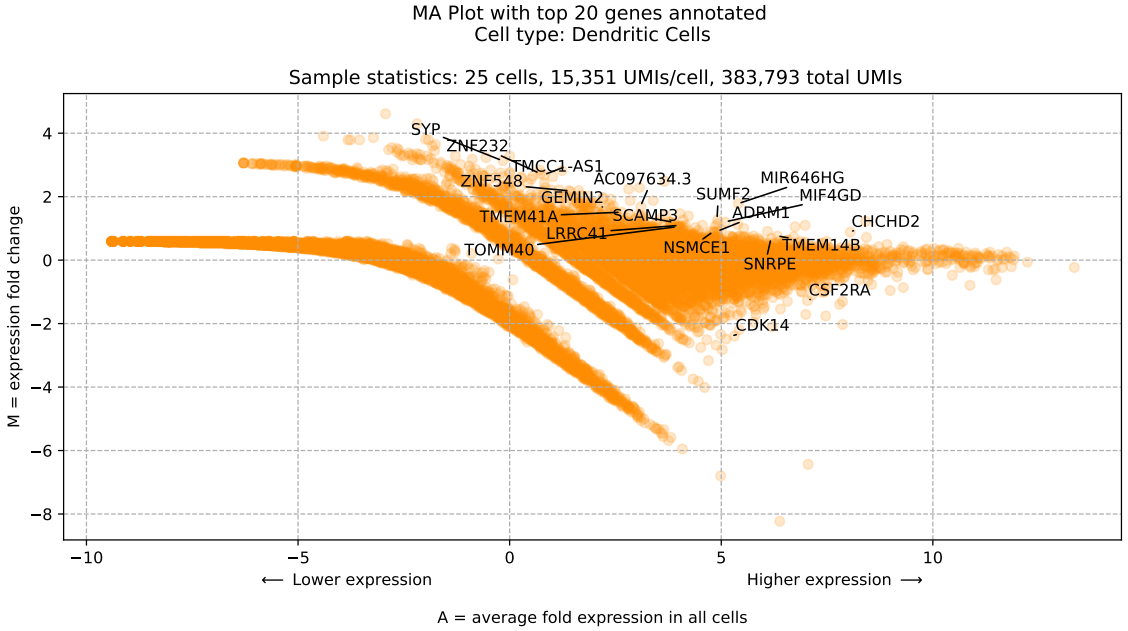
## NK Cells - Differential gene expression



## Dendritic Cells - Differential gene expression



# 6 Visualizing gene abundances across cell types with violin plots

**Violin plots** A violin plot is a type of graph used to visualize the distribution of a gene's abundance across several samples and different cell types. Each "violin" in the plot represents a specific cell type and displays the range and frequency of the gene's abundance in that cell type. The width of the violin at a particular level of abundance indicates the frequency of samples with that abundance value. Wider sections of the violin indicate higher frequency, while narrower sections represent lower frequency. By comparing the shapes and widths of the violins for each cell type, researchers can gain insights into the gene's expression patterns and how they vary across different cell populations.

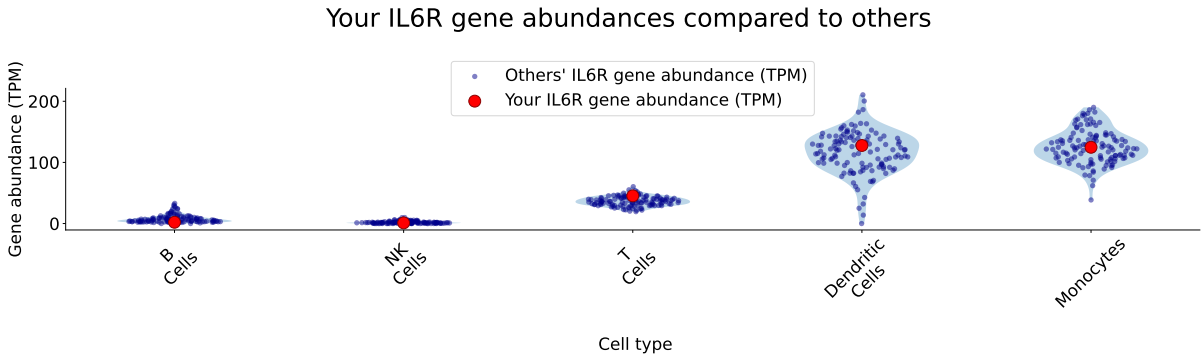
**Counting genes transcripts with TPM - Transcripts Per Million**

Transcripts Per Million (TPM) is a unit of measurement for gene expression levels in RNA-seq (RNA sequencing) experiments. It is used to describe the abundance of a specific gene's transcripts in a sample, taking into account both the gene's expression level and the total number of sequenced reads in the sample. The abundance of a gene's transcripts is an important measure of its expression level. However, raw read counts of a gene's transcripts can be influenced by various factors, such as sequencing depth (the number of reads sequenced per sample) and gene length.

You can think of TPM as the transcriptomic equivalent of PPM (parts per million), which is often used in measurements of the abundance of molecules in the air.

The main advantage of using TPM is that it allows for direct comparisons of gene expression levels between samples. It is particularly useful in experiments where the aim is to compare the expression levels of various genes across different samples, such as in differential gene expression analysis. By using TPM, researchers can obtain a more accurate and biologically meaningful understanding of gene expression changes in their experiments.

## IL6R - Interleukin 6 Receptor




### Fun Fact - IL6R, Interleukin 6 Receptor

IL6 is involved in the regulation of body temperature. It's released in response to fever and helps to increase body temperature, which can help to fight off infections. This is why people often feel hot and sweaty when they have a fever.

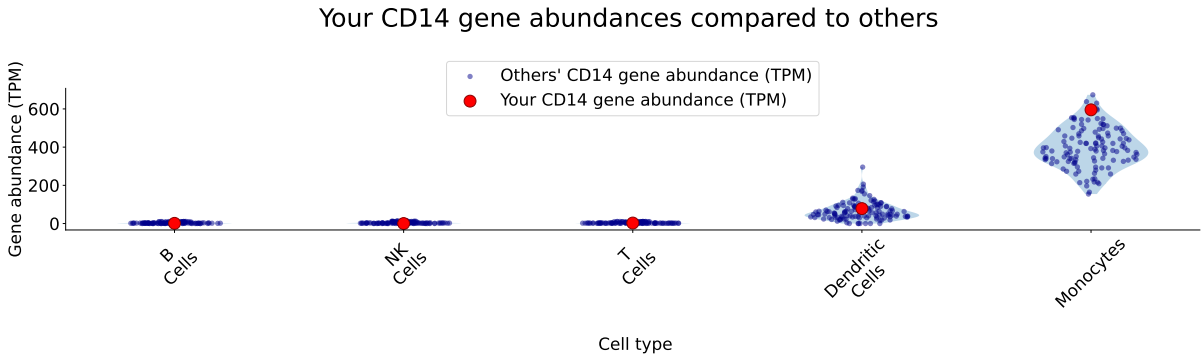
**Details for nerds**

Gene IL6, or Interleukin-6, is a cytokine that plays a crucial role in immune cell regulation, inflammation, and hematopoiesis. It is secreted by various cell types, including T cells, monocytes, NK cells, B cells, and dendritic cells. IL6 functions as a pro-inflammatory and anti-inflammatory cytokine, exhibiting pleiotropic effects on immune cell differentiation, activation, and survival. It is an essential component of the immune response, mediating the cross-talk between innate and adaptive immune cells.

In T cells, IL6 promotes the differentiation of naïve CD4+ T cells into effector T helper 17 (Th17) cells and inhibits the generation of regulatory T cells (Tregs), thus influencing the balance between pro-inflammatory and anti-inflammatory responses. In monocytes, IL6 induces their differentiation into macrophages, which are essential for phagocytosis and antigen presentation. NK cells, or natural killer cells, are affected by IL6 through the enhancement of their cytotoxic activity and the production of interferon-gamma , a critical cytokine for immune responses against viral infections and tumors. IL6 also contributes to B cell maturation and antibody production, supporting humoral immunity. In dendritic cells, IL6 promotes maturation and enhances the antigen-presenting capacity, facilitating the activation of T cells and the initiation of adaptive immune responses. Consequently, the multifaceted roles of IL6 in various immune cell types are critical for shaping the immune response and maintaining immunological homeostasis.

**References :** *Interleukin-6 is important for regulation of core body temperature during long-term cold exposure in mice*. By *Emil Egecioglu, Fredrik Anesten, Erik Schéle, and Vilborg Palsdottir* Published on Biomed Rep. 2018 Sep ; 9(3) : 206–212. doi : 10.3892/br.2018.1118 PMCID : PMC6158403, PMID : 30271595 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6158403/

## CD14 - Cluster of Differentiation 14




**Fun Fact - CD14, Cluster of Differentiation 14**

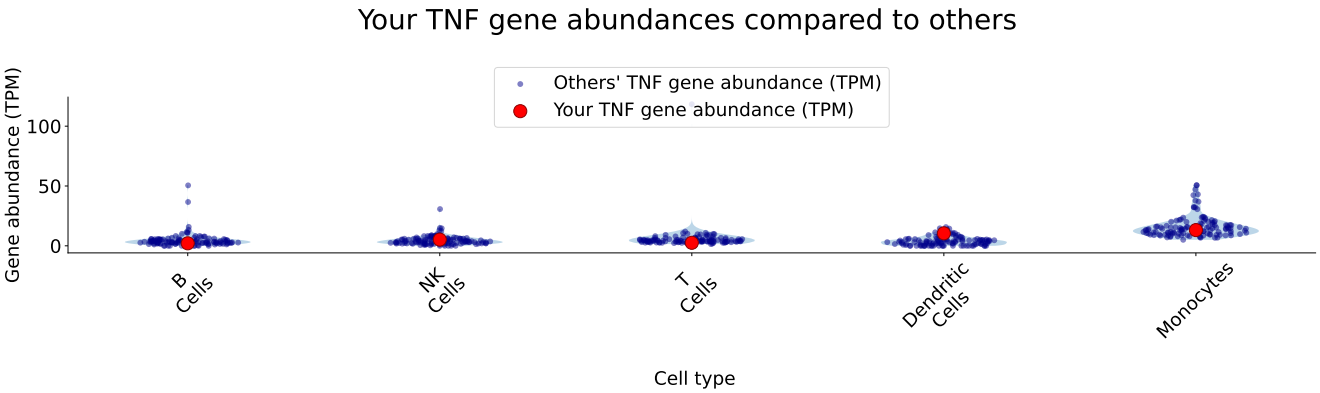
The protein made by the CD14 gene is sometimes called the "gateway to infection" because it recognizes and binds to bacterial components, triggering an immune response

**Details for nerds**

Gene CD14, or Cluster of Differentiation 14, is a cell surface glycoprotein predominantly expressed on monocytes and macrophages, functioning as a co-receptor for lipopolysaccharide (LPS) recognition and innate immune response activation. Although CD14 is mainly associated with monocytes and macrophages, it also plays a role in the interaction and modulation of other immune cells, including T cells, NK cells, B cells, and dendritic cells. In monocytes and macrophages, CD14 facilitates the recognition of LPS and other bacterial components, leading to the activation of these cells and the release of pro-inflammatory cytokines. CD14 also impacts T cells by modulating their activation and cytokine production. In NK cells, CD14 indirectly influences their activity by inducing the production of cytokines such as IL-12 and IL-18 by monocytes, which in turn stimulate NK cell activation and IFN-$\gamma$ production. Although CD14 expression is low or absent on B cells and dendritic cells, its role in these cells is related to the modulation of their functions through interactions with other immune cells. CD14 contributes to B cell activation and antibody production by promoting the release of cytokines from monocytes and macrophages, and it supports dendritic cell maturation and antigen presentation by enhancing the response to bacterial components. Overall, CD14 plays a significant role in coordinating immune responses and maintaining effective communication among various immune cell types.

**References :** *Role of cytokines as a double-edged sword in sepsis*. By *Hina Chaudhry, Juhua Zhou, Yin Zhong, Mir Mustafa Ali, Franklin McGuire, Prakash S Nagarkatti, Mitzi Nagarkatti* Published on In Vivo. 2013 Nov-Dec ;27(6):669-84. PMID : 24292568 PMCID : PMC4378830 https://pubmed.ncbi.nlm.nih.gov/24292568/

## TNF - Tumor Necrosis Factor




**Fun fact - TNF, Tumor Necrosis Factor**

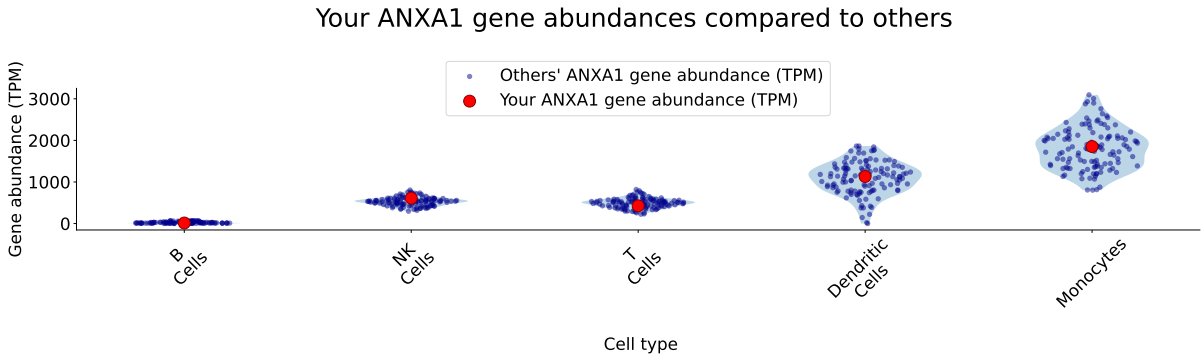
Did you know that TNF has been called the "friend or foe" cytokine? On one hand, TNF can play a beneficial role in the immune response by promoting inflammation and fighting off infections. On the other hand, excessive TNF production can contribute to chronic inflammation, autoimmune diseases, and even cancer

**Details for nerds**

Gene TNF, or Tumor Necrosis Factor, encodes a pro-inflammatory cytokine that is crucial for immune system regulation, inflammation, cell survival, and apoptosis. TNF is produced by various immune cells, including T cells, monocytes, NK cells, B cells, and dendritic cells, and it has wide-ranging effects on the function and interaction of these cells. In T cells, TNF promotes activation, differentiation, and proliferation, supporting the development of effector and memory T cells. In monocytes, TNF stimulates the production of other pro-inflammatory cytokines and chemokines, driving the recruitment and activation of immune cells at the site of inflammation. TNF also enhances the phagocytic and bactericidal activities of monocytes, contributing to the overall antimicrobial response. In NK cells, TNF supports activation, cytotoxicity, and the production of other cytokines, such as IFN-$\gamma$, which reinforces the immune response against viral infections and tumors. In B cells, TNF contributes to activation, proliferation, and antibody production, playing a role in humoral immunity. TNF also induces the expression of adhesion molecules and chemokines in B cells, promoting their recruitment to inflamed tissues. In dendritic cells, TNF is involved in maturation, antigen presentation, and the expression of co-stimulatory molecules, thereby facilitating T cell activation and the initiation of adaptive immune responses. Overall, the multifaceted functions of TNF in various immune cell types make it an essential mediator of immune responses and a key player in maintaining immunological homeostasis.

**References :** *TNF in the era of immune checkpoint inhibitors : friend or foe ?*. By *Allen Y Chen, Jedd D Wolchok, Anne R Bass* Published on Nat Rev Rheumatol. 2021 Apr ;17(4):213-223. PMID : 33686279 PMCID : PMC8366509 DOI : 10.1038/s41584-021-00584-4 https://pubmed.ncbi.nlm.nih.gov/33686279/

## ANXA1 - Annexin A




### Fun Fact - ANXA1, Annexin A

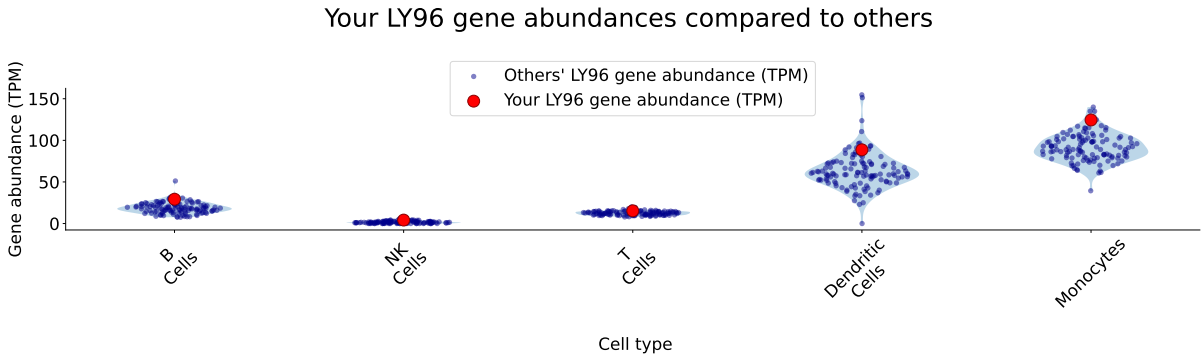
Did you know that ANXA1 is sometimes called the "anti-inflammatory superhero" ? This is because ANXA1 has been shown to have potent anti-inflammatory effects, and it can help to reduce pain, swelling, and tissue damage in many different types of inflammatory diseases

**Details for nerds**

Gene ANXA1, or Annexin A1, encodes a calcium-dependent phospholipid-binding protein that plays a vital role in the regulation of immune responses, inflammation, and cellular processes such as apoptosis, proliferation, and migration. ANXA1 exerts its effects on various immune cells, including T cells, monocytes, NK cells, B cells, and dendritic cells, primarily through its anti-inflammatory and immunomodulatory properties. In T cells, ANXA1 can inhibit activation and proliferation, as well as modulate the release of cytokines, thus contributing to the regulation of adaptive immune responses. In monocytes, ANXA1 promotes the resolution of inflammation by stimulating their differentiation into anti-inflammatory macrophages, which then produce anti-inflammatory cytokines such as IL-10 and TGF-$\beta$. ANXA1 also facilitates the clearance of apoptotic neutrophils by monocytes and macrophages, which is a crucial process in resolving inflammation. In NK cells, ANXA1 is involved in the regulation of cytotoxicity and cytokine production, maintaining a balance between pro-inflammatory and anti-inflammatory responses. Although ANXA1 expression in B cells and dendritic cells is not as well-defined, its role in these cells is linked to the overall modulation of immune cell functions through its anti-inflammatory actions. In B cells, ANXA1 may influence activation and antibody production, while in dendritic cells, it may affect maturation, migration, and antigen presentation. Overall, ANXA1 is a critical component in maintaining immune homeostasis and resolving inflammation through its diverse effects on various immune cell types.

**References :** *Annexin-A1 : Therapeutic Potential in Microvascular Disease*. By *Gareth S. D. Purvis, Egle Solito and Christoph Thiemermann* Published on Front Immunol. 2019 ; 10 : 938. PMCID : PMC6502989 PMID : 31114582 DOI : 10.3389/fimmu.2019.00938 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6502989/

## LY96 - Lymphocyte Antigen 96




### Fun Fact - LY96, Lymphocyte Antigen 96

LY96 is like a trusty sidekick to TLR4, another protein in our body. Together, they form a dynamic duo, detecting dangerous bacterial invaders and sounding the alarm for our immune system to fight back.

**Details for nerds**

Gene LY96, or Lymphocyte Antigen 96, encodes a small glycoprotein also known as myeloid differentiation factor 2 (MD-2), which is crucial for the recognition of lipopolysaccharide (LPS) and the activation of innate immune responses. LY96 is predominantly expressed in monocytes, macrophages, and dendritic cells, and functions as a co-receptor with Toll-like receptor 4 (TLR4) for LPS detection. Although LY96 is mainly associated with innate immune cells, it indirectly influences adaptive immune cells, such as T cells, NK cells, and B cells, through the regulation of innate immune responses. In monocytes, macrophages, and dendritic cells, LY96 facilitates the recognition of LPS, leading to the activation of these cells and the release of pro-inflammatory cytokines, such as TNF-$\alpha$, IL-6, and IL-12. This activation, in turn, influences T cells by promoting their activation, differentiation, and cytokine production. In NK cells, LY96 indirectly supports their activation and cytotoxicity through the cytokines released by activated monocytes and macrophages, such as IL-12 and IL-18. Although LY96 does not directly affect B cells, its role in these cells is related to the overall coordination of immune responses, where the cytokines produced by activated monocytes, macrophages, and dendritic cells can influence B cell activation, proliferation, and antibody production. In summary, LY96 plays a pivotal role in the initiation of immune responses by mediating LPS recognition and influencing the function and interaction of various immune cell types, thereby contributing to both innate and adaptive immunity.

**References :** *The structural basis of lipopolysaccharide recognition by the TLR4-MD-2 complex*. By *Beom Seok Park, Dong Hyun Song, Ho Min Kim, Byong-Seok Choi, Hayyoung Lee, Jie-Oh Lee* Published on Nature. 2009 Apr 30 ;458(7242):1191-5. DOI : 10.1038/nature07830 https://pubmed.ncbi.nlm.nih.gov/19252480/