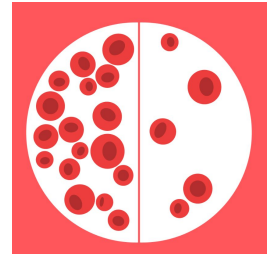
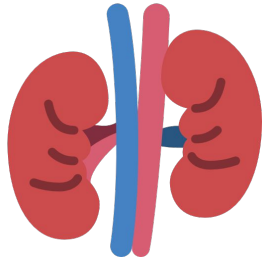




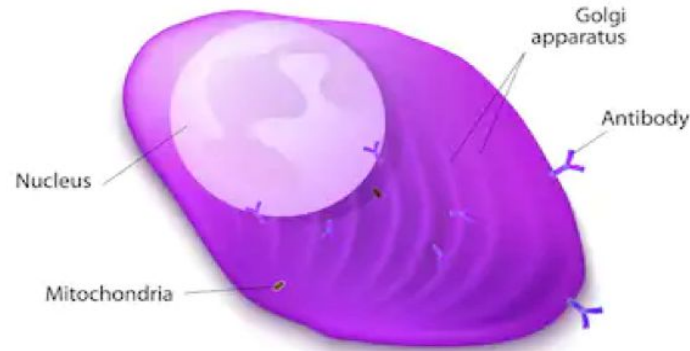
HealthTree Cure Hub
FOR MULTIPLE MYELOMA

Understanding your Myeloma Labs

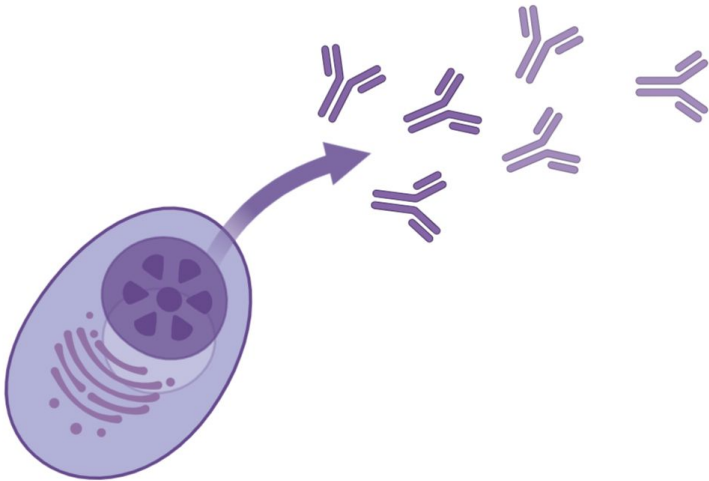
**By monitoring your labs you can prevent
end organ damage and significant disease.**



Multiple Myeloma is a type of cancer of plasma cells



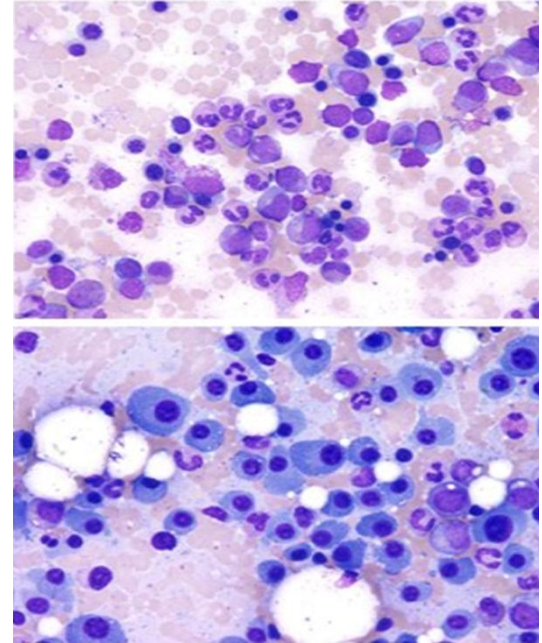
Plasma cells produce proteins called immunoglobulins



- Immunoglobulins are **proteins that attach to foreign substances** entering the body,
 - **Helping fight infections**
- There are many different types and they are specialized for different things.

Multiple Myeloma and Monoclonal Proteins

- Myeloma, secretes abnormal immunoglobulins of only one type that cannot properly fight infections.
- They are called **Monoclonal Proteins**
 - Also called **M-protein**, **M-spike**, and other names.
- **Crowding out** the other antibodies and other components of the immune system.
 - Making too much of one type reduces the ability to create a wide spectrum of immunoglobulins to fight infections.
- As Myeloma cells grow, they start **Crowding out the other Blood cells** in the bone marrow.



Top: Normal Bone Marrow;
Bottom: Multiple Myeloma Bone Marrow

MGUS is a precursor of Myeloma

Diagnosed with the following

Serum monoclonal protein <3 g/dL
Clonal bone marrow plasma cells <10%
Absence of end-organ damage such as hypercalcemia, renal insufficiency, anemia, and bone lesions (CRAB) that can be attributed to the plasma cell proliferative disorder

Smoldering Myeloma is another precursor closer to Myeloma

Diagnosed with the following

Serum monoclonal protein ≥ 3 g/dL, or urinary monoclonal protein ≥ 500 mg per 24 h

Clonal bone marrow plasma cells **10-60%**

Absence of end-organ damage such as hypercalcemia, renal insufficiency, anemia, and bone lesions (**CRAB**) that can be attributed to the plasma cell proliferative disorder, **or amyloidosis**

Multiple Myeloma

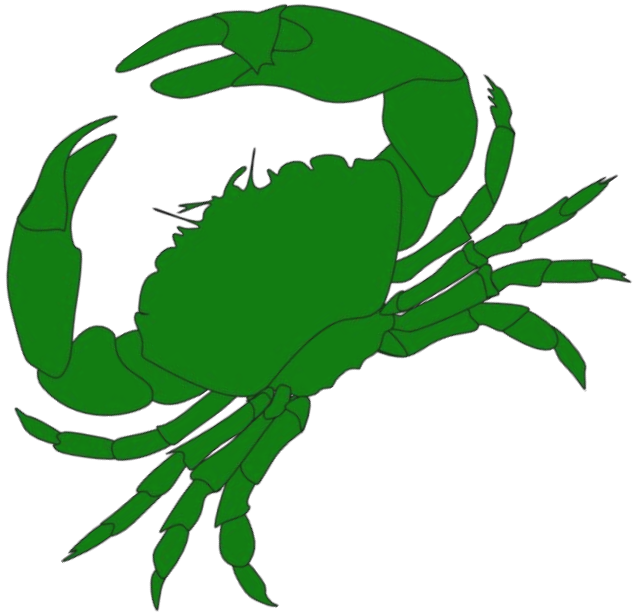
Diagnosed with $\geq 10\%$ plasma cells, and

Presence of end-organ damage such as hypercalcemia, renal insufficiency, anemia, or bone lesions (**CRAB**) that can be attributed to the plasma cell proliferative disorder

Or any of the following:

- **$\geq 60\%$ plasma cells in the bone marrow**
- **Free light chain (FLC) ratio ≥ 100 (with involved FLC level ≥ 100 mg/L)**
- **Extramedullary disease**
- **More than one focal lesion on MRI ≥ 5 mm**

CRAB



- **Calcium:** serum calcium >11 mg/dL
- **Renal insufficiency:** creatinine clearance (eGFR) <40 mL per minute or serum creatinine >2 mg/dL
- **Anemia:** hemoglobin value <10 g/dL
- **Bone lesions:** one or more osteolytic lesions on skeletal radiography, computed tomography (CT), or positron emission tomography-CT (PET-CT)

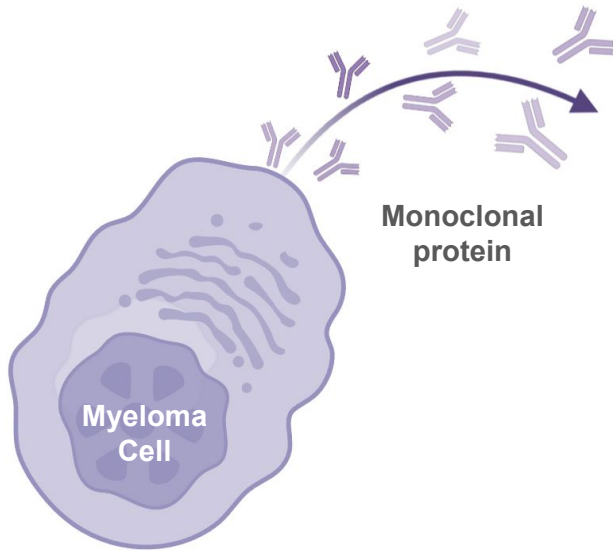
R-ISS Myeloma Staging

- **Measured only at the time of diagnosis of active Multiple Myeloma**
- The experts already knew that **high levels of Beta 2 microglobulin** and **low albumin** levels were indicators of higher risk myeloma. This staging system was updated as myeloma researchers learned more about **high-risk genetic features** and high levels of **LDH**.
- The Revised International Staging System was last updated in **2015**.

Stage I	<ul style="list-style-type: none">• Serum albumin ≥ 3.5 g/dL,• Serum beta-2-microglobulin < 3.5 mg/L,• No high-risk cytogenetics, and• Normal serum lactate dehydrogenase level
Stage II	<ul style="list-style-type: none">• Not fitting Stage I or III
Stage III	<ul style="list-style-type: none">• Serum beta-2-microglobulin > 5.5 mg/L, and• High-risk cytogenetics [t(4;14), t(14;16), or del(17p)] or elevated serum lactate dehydrogenase level

This staging system is only a **guide** for your doctor on how to treat your myeloma, and does not fully predict the evolution of the disease.

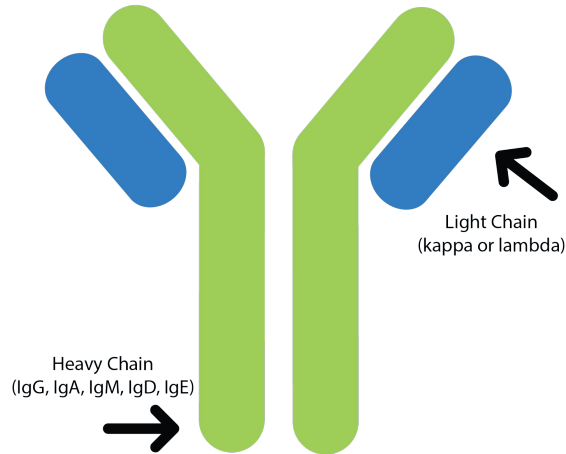
M-Spike Tests



- **Serum/Urine Protein Electrophoresis** (SPEP/UPEP) are tests used to find and quantify abnormal proteins.
 - The abnormal protein produced by the Myeloma, is known by several different names, including **Monoclonal Immunoglobulin, M protein, M spike, paraprotein, and others.**
- **Immunofixation** shows the exact type of the antibody that is abnormal.
- **A normal result** = 0 g/dL or negative.

**When treated with a monoclonal antibody,
like Darzalex, this antibody will be shown
in the electrophoresis and Immunofixation
studies as a little M spike.**

Free Light Chains



- This test measures the free light chains, **Kappa and Lambda**
- It is important to know your **myeloma subtype** in order to monitor the relevant light chain.
- **Kappa reference values:** 3.3 to 19.4 mg/L
- **Lambda reference values:** 5.71 to 26.3 mg/L

Reference values may vary from lab to lab

**About 25% of myeloma patients will have
NEGATIVE SPEP (no M-Spike), but will have
a POSITIVE light chain.**

**Free Light Chains in the blood can help
detect an early progression or relapse.**



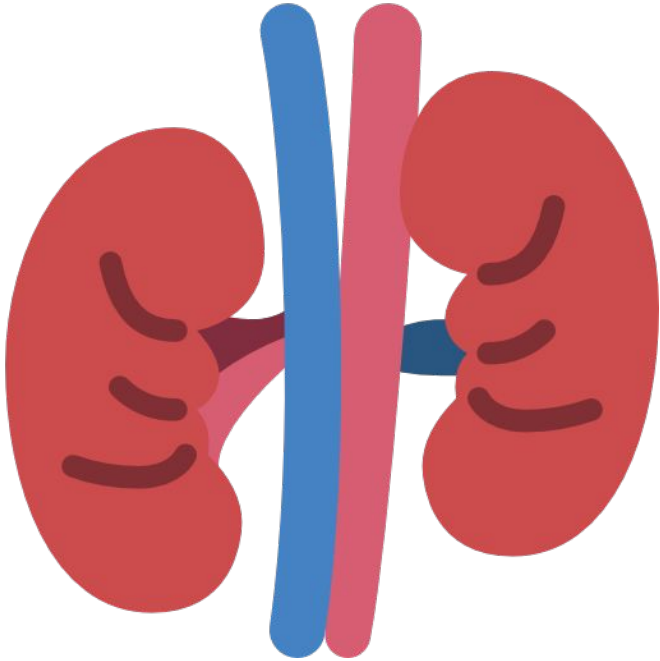
Light Chain Ratio (in Multiple myeloma)



- **The Ratio** is the balance between the kappa and lambda light chains.
- **With a normal creatinine** (< 2 mg / dL): reference values are 0.26 – 1.65.
- **With a elevated creatinine** (≥ 2 mg / dL): reference values are 0.37 – 3.1.

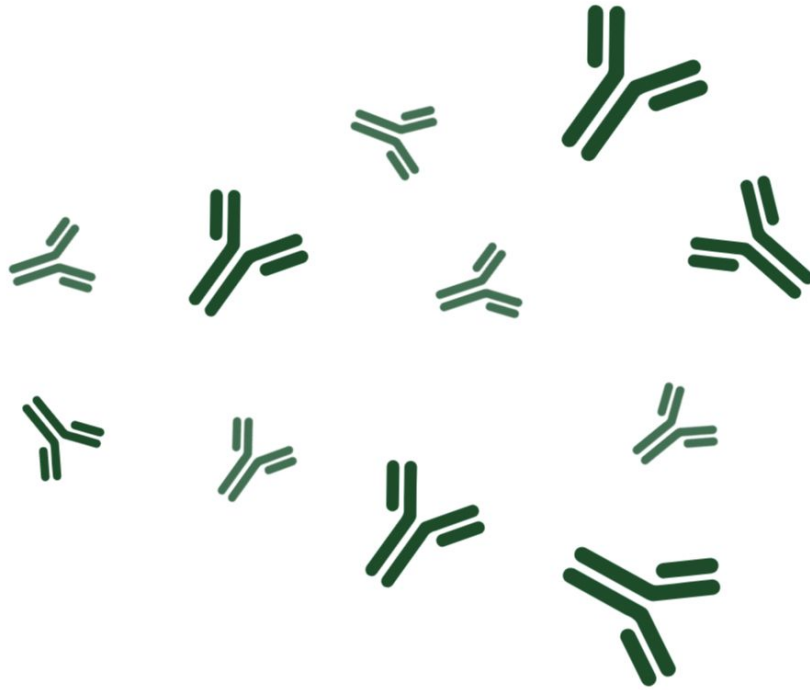
Reference values may vary from lab to lab

Light Chain Ratio (in Multiple myeloma)



- If Kappa/Lambda Ratio is **above 8** or **less than 0.125** it is considered a significant **abnormality** that needs to be investigated.
- People who have **kidney problems** often have **higher levels** of light chains at baseline.

Immunoglobulins (Heavy chains)



Immunoglobulin A

68 - 378

mg/dl ▼

Immunoglobulin G

768 - 1632

mg/dl ▼

Immunoglobulin M

60 - 263

mg/dl ▼

Immunoglobulin D

< or = 10

mg/dl

Immunoglobulin E

< or = 214

mg/dl

Reference values may vary from lab to lab

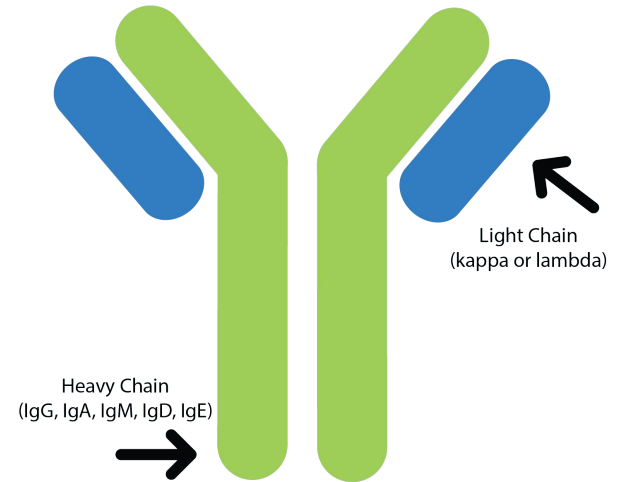
The myeloma subtype

Defined by the M-Spike immunofixation, and the highest results in the free light chain and immunoglobulins testing, composed like this:

Heavy chain (if any) + Light chain + Phase

Examples:

- IgG Kappa MGUS
- Kappa light chain only Smoldering Myeloma
- IgA Lambda Multiple Myeloma



Complete Blood Count

Because multiple myeloma crowds out bone marrow, it can cause several kinds of blood deficiencies such as :



Anemia, a shortage of red blood cells shown on the **Hemoglobin**,



Thrombocytopenia, a shortage of blood **Platelets**,



Leukopenia, a shortage of **White Blood Cells** (leukocytes),

- Neutropenia, a shortage of **Neutrophils**, and
- Lymphopenia, a shortage of **Lymphocytes**.



White Blood Cell count (WBC)

3.2 - 10.6

k/ul



Hemoglobin (HGB)

12.1 - 15.9

g/dl

Platelets

150 - 440

k/ul



Lymphocyte Absolute Count

0.8 - 3.1

k/ul



Absolute Neutrophils Count (ANC)

1.3 - 7

k/ul



Reference values may vary from lab to lab

Comprehensive Metabolic Panel

Chemistry panels are run regularly during and after treatment to check your body's normal functions.

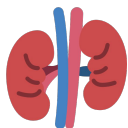


Albumin. One of the most abundant proteins in humans. Diminished by the monoclonal proteins.



High **Calcium.** Caused by bone destruction done by MM,

- It may result in severe constipation and loss of appetite, weakness, drowsiness, and confusion.



Elevated **Serum Creatinine** or Low **eGFR** may indicate poor hydration or possible kidney damage.

Reference values may vary from lab to lab

Albumin

3.5 - 4.7

g/dl ▼

Calcium

8.4 - 10.2

mg/dl ▼

Creatinine (Serum/Blood)

0.52 - 1.08

mg/dl ▼

eGFR (Estimated glomerular filtration rate) / Creatinine Clearance

>60

ml/min

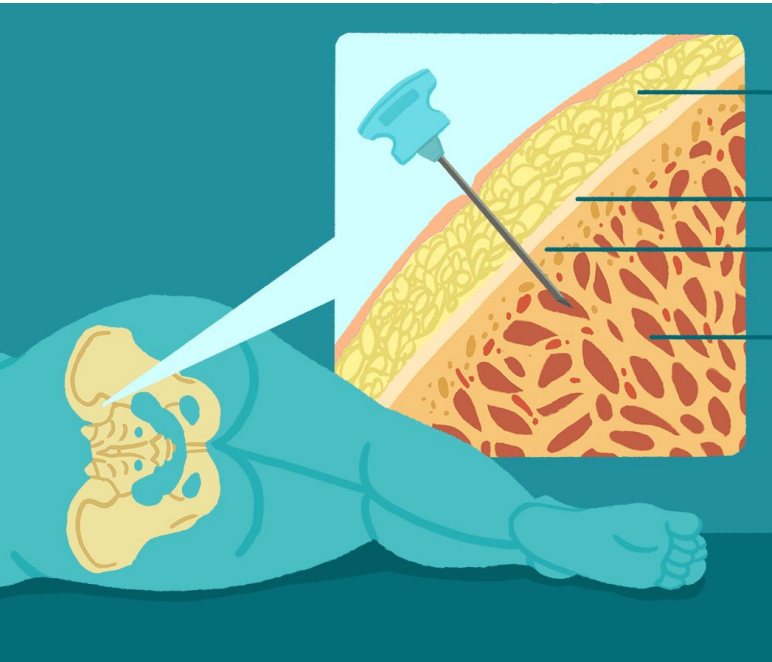
Glucose

64 - 128

mg/dl ▼

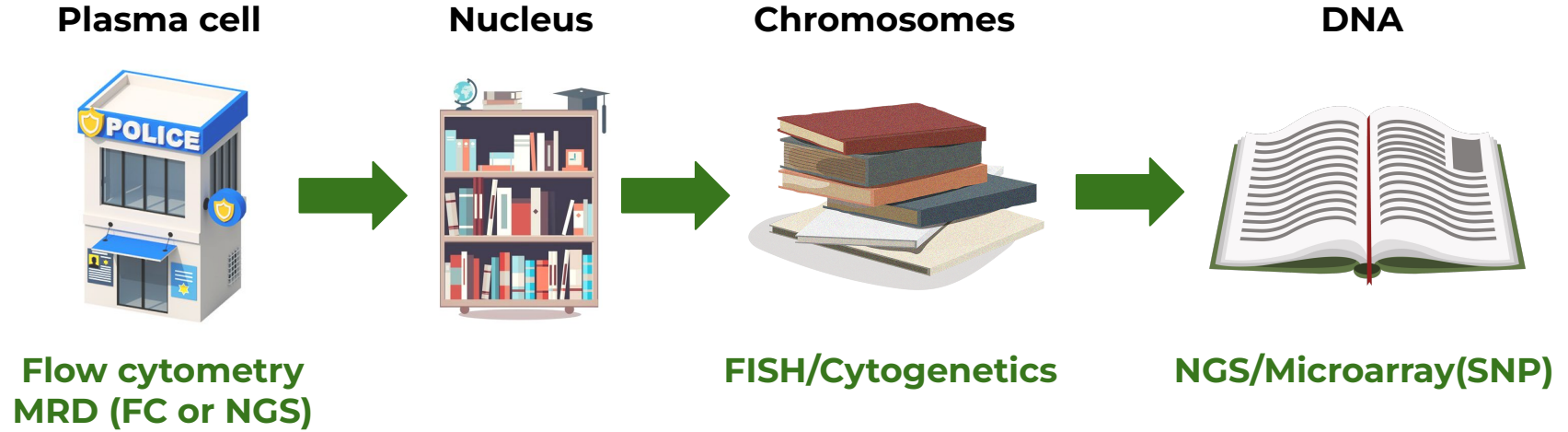


Plasma Cell Percentage



- The percentage in the bone marrow core biopsy will be a major determinant of the classification of the type of disorder.
 - **Normal** = <5%
 - **MGUS** = <10% + Absence of end-organ damage
 - **Smoldering myeloma** = 10-60% + Absence of end-organ damage
 - **Multiple myeloma** = >10% + Evidence of end-organ damage, or $\geq 60\%$
- Stains may be performed to highlight the different cell types present (IHC or **Immunohistochemistry**).
 - **CD138** is an antibody stain that marks plasma cells and aids in enumeration.

Bone marrow genetics tests



- A Plasma cell is like a police department,
- it will have a nucleus/bookshelf with all the rulebooks/chromosomes of how the department should behave, we have 46 chromosomes in each cell, and
- the rules written inside them are the DNA.

Bone marrow genetics tests

Chromosomes



FISH/Cytogenetics

DNA



NGS/Microarray(SNP)

- A **Myeloma cell** is a police department that is not working well.
- The **rulebooks or rules may have mistakes** or mutations,
 - there may be rules or parts of books missing duplicated, or with other kinds of aberrant changes.
- These **mutations** may vary from cell to cell and from person to person, and might change over time.
- And they may **help or hinder** the progression of the myeloma.

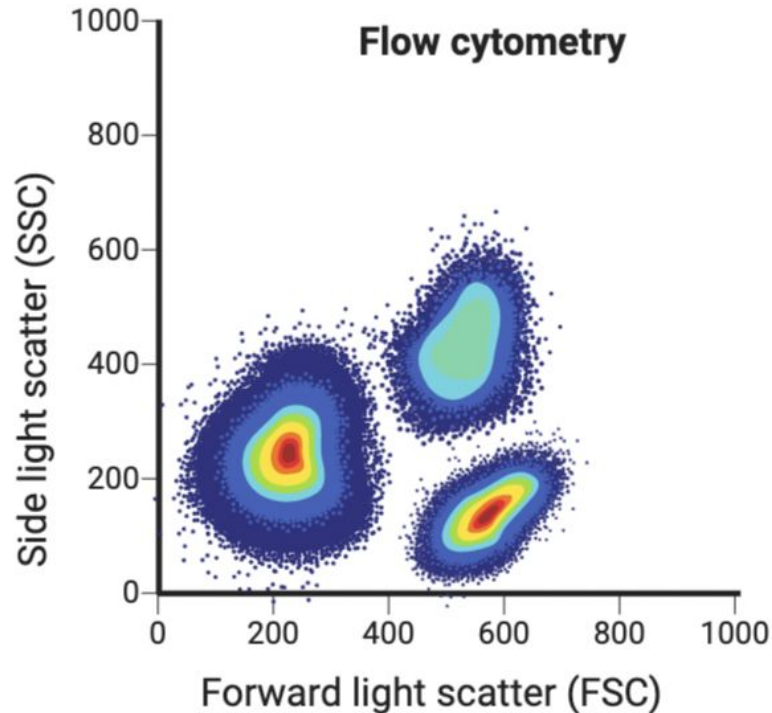
Mayo clinic genetic risk stratification for multiple myeloma (mSMART)

- **Used only in active Multiple Myeloma**
- It was designed for physicians external to Mayo.
- And helps to classify the most common genetic features that can occur in myeloma cells.
- Last updated in **2018**.

Standard Risk	Trisomies, t(11;14) and t(6;14).	
	75% of newly diagnosed patients.	
High risk	Del(17p), t(4;14), t(14;16), t(14;20), Amplification 1q (4 or more copies), p53 mutation , R-ISS Stage III , High-risk signature by GEP, or High Plasma Cell S-phase.	
	25% of newly diagnosed patients.	
	One hit	Only one high-risk factor
	Double hit	Two high-risk factors
	Triple Hit	Three or more high-risk factors

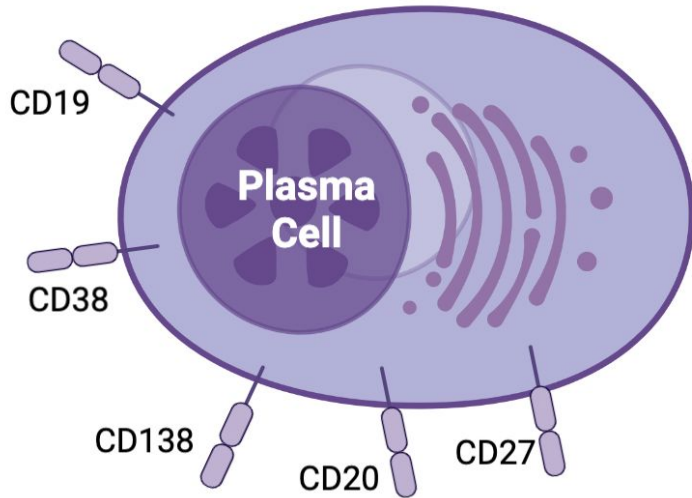
This staging system is only a **guide** for your doctor on how to treat your myeloma, and does not fully predict the evolution of the disease.

Flow Cytometry



- **Flow cytometry** is a test used on both blood samples and bone marrow samples to identify “**markers**” on the cell's surface and may give us targets for the use of immunotherapies, like **monoclonal antibodies**.
- Cells are passed in front of a laser beam which causes them to give off light. Groups of cells can be separated and counted.

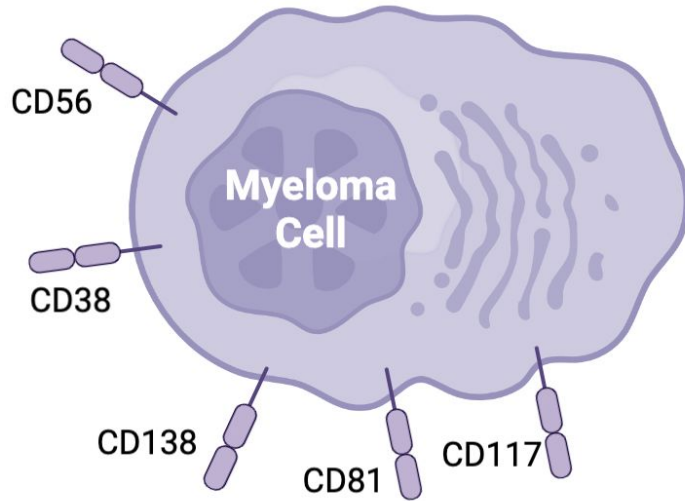
Flow Cytometry in a normal plasma cell



The most common immunophenotype (expected immune markers) of normal **Plasma Cells** may be described as:

- CD38, CD138, CD19, CD20, CD27 predominantly bright **positive**, and
- **Polytypic** cytoplasmic immunoglobulin, this means that they express **both Kappa and Lambda** immunoglobulin.

Flow Cytometry in a myeloma cell



The typical immunophenotype (expected immune markers) of myeloma cells shows several deviations from the normal pattern,

- with some substances that are **expected negative with positive results** (CD56, CD81, CD117, etc.), some others that are expected positive with negative results, and
- **Monoclonal** cytoplasmic immunoglobulin, this means that they express **only Kappa or Lambda** immunoglobulin.

Summary

- ❑ Know what type of myeloma you have.
- ❑ Keep your labs up to date!
- ❑ Monitor your labs (especially the Myeloma Markers).
- ❑ Keep learning! We have multiple resources at [HealthTree University](#).

Thank you!

If you need assistance, contact our team at:

support@healthtree.org

+1 800-709-1113



HealthTree Cure Hub
FOR MULTIPLE MYELOMA