DECIPHERING MY MYELOMA LABS

Do you understand your myeloma diagnosis and your myeloma lab results?

This guide attempts to simplify the complex process of understanding your myeloma markers and helps you track your treatment history. Based on the actual lab printouts you receive in the clinic, we've added color-coding to help you identify the most important myeloma markers.

Priority	Secondary	Not as important

Special Thanks to myeloma specialist Dr. Guido Tricot of the University of Iowa, pathologist Dr. Michael Misialek of Newton-Wellesley Hospital, Jen Higbee of Huntsman Cancer Institute, and Barbara Waagen for their contributions to this document.

Please note that the Reference Ranges given are not necessarily consistent between laboratories. Each laboratory is required to establish its own reference ranges. Abnormal results must be flagged as High, Low, or Critical if they fall out of the established reference range.

Each section is linked to a HealthTree University Class. Feel free to click on the links in each section for further information.

Do you have suggestions to make this document better? Send your comments to support@healthtree.org, and we will keep revising this document as we learn more.

INDEX

My Myeloma Summary

Revised-International Staging System (R-ISS)	
Stage I	• Serum albumin ≥3.5 g/dL • Serum beta-2-microglobulin <3.5 mg/L • No high-risk cytogenetics • Normal serum lactate dehydrogenase level
Stage II	• Not fitting Stage I or III
Stage III	• 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
The Revised International Staging System was based on a large sample size of 4,445 newly diagnosed multiple myeloma patients from 11 different clinical trials and was updated in 2015. Myeloma experts already knew that high levels of Beta 2 microglobulin and low albumin levels were indicators of higher risk myeloma. The update occurred as myeloma researchers learned more about high-risk genetic features and high levels of LDH, which have now been added to the staging system.	

Learn more as Dr. Muzaffar Quazilbash of the MD Anderson Cancer Center explains myeloma staging in HealthTree University.

Mayo clinic risk stratification for multiple myeloma (mSMART)	
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), Gain 1q, p53 mutation, R-ISS Stage III, High-risk signature by GEP, or High Plasma Cell S-phase.
	25% of newly diagnosed patients.
	The presence of any two high-risk genetic abnormalities is considered double-hit myeloma; three or more high-risk ganetic abnormalities are triple-hit myeloma.
• Genetic abnormalities by FISH or equivalent method • Trisomies may ameliorate the risk • t(11;14) may be associated with plasma cell leukemia	
mSMART was designed for physicians external to Mayo. The guidelines were explicitly written to be clear, simple, and easy to use. Rafael Fonseca, M.D., Mayo Clinic Cancer Center interim director, hematologist, and multiple myeloma specialist has called the advent of mSMART a staple of Mayo Clinic's engagement with those who treat multiple myeloma and a reference in the myeloma community.	

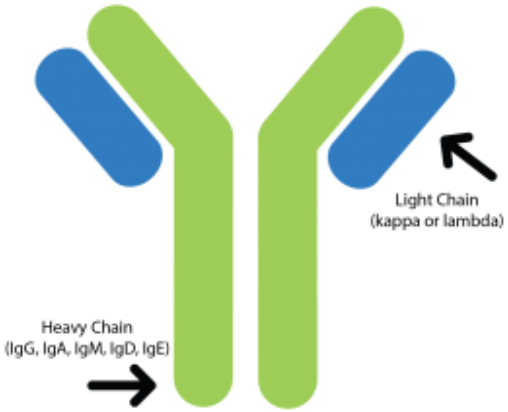
Learn more as Dr. Morie Gertz of the Mayo Clinic (Rochester) explains the mSMART in HealthTree University.

My Myeloma Labs

MONOCLONAL PROTEINS

Multiple myeloma is a blood cancer of white blood cells called plasma cells. Plasma cells come from the bone marrow and produce antibodies (also called immunoglobulins) that fight a wide variety of infections. In myeloma, one of these antibodies grows out of control in the bone marrow, crowding out the other antibodies and other components of the immune system, making too much of one type and reducing the ability for your body to create a broad spectrum of immunoglobulins to fight infections. This is called a monoclonal protein (also called M-protein or M-spike).

Serum protein electrophoresis (SPEP) is a test used to find any abnormal immunoglobulin. Then, another test, such as immunofixation or immunoelectrophoresis, is used to determine the exact type of abnormal antibody (IgG or some other type). This abnormal protein is known by several different names, including monoclonal immunoglobulin, M protein, M spike, and paraprotein.



Antibodies are made up of two parts: heavy chains and light chains. The types of monoclonal proteins are defined by these parts, although sometimes the heavy chain might be missing.

Videos explained by Myeloma specialists about this topic:

- What is the normal structure of an immunoglobulin (antibody)?
- What is a monoclonal protein (or M-spike) and how is it detected?
- What are the different types of myeloma?

SERUM PROTEIN ELECTROPHORESIS (BLOOD TEST)

The SPEP is broken down into five categories: Albumin, Alpha-1, Alpha-2, Beta, and Gamma (see below). In particular, this test can detect the presence of "M protein," another name for the large number of abnormal monoclonal antibodies being produced.

LAB TESTED	REFERENCE RANGE (g/dL)	WHAT IT MEANS
TOTAL PROTEIN	6.0 - 8.3	Measures the total amount of protein in a blood sample.
ALBUMIN	3.75 - 8.3	Albumin proteins keep the blood from leaking out of blood vessels and are important for tissue growth/healing. Low values can indicate malnutrition, kidney or liver disease, inflammation, and protein-losing problems. High values can indicate dehydration.
ALPHA 1	0.19 - 0.46	Low values can indicate severe liver disease, and High values can indicate acute/chronic inflammation.
ALPHA 2	0.48 - 1.05	Low values can indicate malnutrition, severe liver disease, or red blood cell disintegration. High values can indicate kidney disease or acute/chronic inflammation.
BETA	0.48 - 1.0	Beta globulin proteins help carry substances, such as iron, through the bloodstream and help fight infection. Low values can indicate malnutrition or fibrous tissue in the liver, and High values can indicate hypercholesterolemia, iron deficiency anemia, MGUS, or MM.
GAMMA	0.62 - 1.51	These proteins are also called antibodies. They help prevent and fight infection. Low=immune disorder, High/Polyclonal = inflammatory diseases like arthritis, lupus, liver problems, High/Monoclonal = MM, lymphoma, Waldenstrom's macroglobulinemia.
PARAPROTEIN	0 or Negative	Paraproteins form a narrow band or "spike" when they are all the same protein. They are also referred to as "**M proteins**." (M=monoclonal). This is the M-spike number. SPEP and UPEP tell us how much monoclonal protein there is, but not the type.
IMMUNOFIXATION	Negative	Identifies the type of immunoglobulin protein(s) presenting monoclonal bands on a protein electrophoresis pattern; typically, immunofixation determines the presence of a heavy chain (IgG, IgM, IgA) and a light chain (kappa or lambda).
DARATUMUMAB	IgG Kappa	Daratumumab (Darzalex) can influence the results of IFE if a patient has IgG Kappa myeloma and is being evaluated for a complete response. The patient may be in a complete response, but a tiny band of IgG Kappa will show up on the test.

HEALTHTREE UNIVERSITY CLASS

- What is a Serum Protein Electrophoresis (SPEP)?

Please note that the Reference Ranges given are not necessarily consistent between laboratories. Each laboratory is required to establish its own reference ranges. Abnormal results must be flagged as High, Low, or Critical if they fall out of the established normal range.

SERUM FREE LIGHT CHAIN TEST

LAB TESTED	REFERENCE RANGE	WHAT IT MEANS
KAPPA FREE LIGHT CHAINS	3.3 - 19.4 mg/L	There are two types of light chains: kappa and lambda. If a patient has kappa myeloma, their doctor will watch for a rise in the kappa numbers. Likewise, the lambda number will be observed if a patient has lambda myeloma. When myeloma progresses, the myeloma cells start to produce more light chains than heavy chains. This can be measured by the Free Light Chain Assay test on a blood specimen. The higher the free light chains, the more aggressive the disease is. Therefore, the serum-free light chain test is a better predictor of outcome than the amount of M-protein in the blood.
LAMBDA FREE LIGHT CHAINS	5.7 - 26.3 mg/L	
KAPPA:LAMBDA RATIO	0.26 to 1.65	This balance of kappa and lambda together is called the kappa/lambda ratio, which can also indicate a change in levels of disease. "The ratio or proportion between the kappa and lambda light chains indicates an excess production of one chain over the other, and therefore can be used to indicate disease progression or remission," said Dr. Christina Gasparetto of Duke University.

HEALTHTREE UNIVERSITY CLASSES

- What is the normal structure of an immunoglobulin (antibody)?
- What are light chains, how are light chains reported, and why?
- How do you measure free light chains?
- Why is knowing your free light chain ratio important?

Please note that the Reference Ranges given are not necessarily consistent between laboratories. Each laboratory is required to establish its own reference ranges. Abnormal results must be flagged as High, Low, or Critical if they fall out of the established normal range.

URINE PROTEIN ELECTROPHORESIS (URINE TEST)

The UPEP is generally performed on a single urine sample. Bence-Jones proteins will be detected if present. A routine urinalysis will not detect Bence-Jones proteins.

LAB TESTED	NORMAL RANGE (mg/day)	WHAT IT MEANS
URINE TOTAL PROTEIN (UPEP)	<229	Measures the total amount of protein in a urine sample of 24 hours.

ALBUMIN IN URINE	33 - 50	Albumin proteins keep the blood from leaking out of blood vessels and are essential for tissue growth/healing. Low values can indicate malnutrition, kidney or liver disease, inflammation, and protein-losing problems. High values can indicate dehydration.
ALBUMIN % URINE	%	
GLOBULIN URINE	50 - 66	The other major protein in the urine, along with albumin.
ALPHA 1 % URINE	%	Low values can indicate severe liver disease. High values can indicate acute/chronic inflammation.
ALPHA 2 % URINE	%	Low values can indicate malnutrition, severe liver disease, or red blood cell disintegration. High values can indicate kidney disease or acute/chronic inflammation.
BETA GLOBULIN % URINE	%	Beta globulin proteins help carry substances, such as iron, through the bloodstream and help fight infection. Low values can indicate malnutrition or fibrous tissue in the liver. High values can indicate hypercholesterolemia, iron-deficient anemia, MGUS orMM
PARAPROTEIN % URINE	0%	The percentage of a monoclonal protein, if present, in the urine.
URINE M-PROTEIN	0 or Negative	This protein is the monoclonal antibody detected in the urine. It is usually called M-Spike. It may be measured in percentage or mg/day.
IMMUNOFIXATION	Negative	This test is generally performed on a 24-hour collection of urine and will measure exact amounts of Bence-Jones proteins present and is used to monitor treatment progress. The higher the level, the more tumor growth.
URINE FREE KAPPA LIGHT CHAINS	<0.9 mg/dL	The serum-free test is tested in the urine. This test can test for free light chains but not whole immunoglobulins. Myeloma can be detected earlier than with UPEP, SPEP, or IFE, but these tests are needed for the complete picture.
URINE FREE LAMBDA LIGHT CHAINS	<0.7 mg/dL	
URINE FREE KAPPA/LAMBDA RATIO	0.7-6.2	

HEALTHTREE UNIVERSITY CLASS

- What is urine protein electrophoresis (UPEP), and is it still used?

Please note that the Reference Ranges given are not necessarily consistent between laboratories. Each laboratory is required to establish its own reference ranges. Abnormal results must be flagged as High, Low, or Critical if they fall out of the established normal range.

IMMUNOGLOBULINS (HEAVY CHAINS BLOOD TEST)

LAB TESTED	NORMAL RANGE (mg/dL)	WHAT IT MEANS
IgG	768 - 1632	This test measures the blood levels of the different antibodies (also called immunoglobulins). There are several different types of antibodies in the blood. Each type of antibody fights a different type of infection. The levels of these immunoglobulins are measured to see if any are abnormally high or low. In multiple myeloma, one type of immunoglobulin has an overgrowth that crowds out the other immunoglobulins. Thus you may be susceptible to certain kinds of infections, like pneumonia. Elevated immunoglobulins that are not related to a person's myeloma can indicate current infection.
IgA	68 - 378	
IgM	60 - 263	
IgD	< or =10	
IgE	< or =214	

HEALTHTREE UNIVERSITY CLASSES

- What does the quantitative immunoglobulin test measure?
- What is hyperviscosity? How is it treated?

Please note that the Reference Ranges given are not necessarily consistent between laboratories. Each laboratory is required to establish its own reference ranges. Abnormal results must be flagged as High, Low, or Critical if they fall out of the established normal range.

BONE MARROW ASPIRATION AND CORE BIOPSY

The bone marrow biopsy tests will show how many cells in the bone marrow are myeloma cells and will also indicate the quality of the specimen that was taken.

LAB TESTED	WHAT IT MEANS
IMMUNOHISTOCHEMISTRY	Part of the biopsy is treated with antibodies that attach to specific molecules on the cell surface, and help to identify different types of cells
PLASMA CELLS ON ASPIRATION	The percentage of plasma cells and their appearance will be reported. This number is important in classifying the type of plasma cell disorder and should be followed overtime.
PLASMA CELLS ON BIOPSY	The percentage of plasma cells and their appearance will be reported. This number is important in classifying the type of plasma cell disorder and should be followed overtime.
CD56 POSITIVE ON IMMUNOFIXATION	Not relevant for the myeloma assessment.
ROULEAUX	Rouleaux are stacks or aggregations of red blood cells (RBCs) that form because of the unique discoid shape of the cells in vertebrates. Conditions that cause rouleaux formation include infections, multiple myeloma, Waldenström's macroglobulinemia, inflammatory and connective tissue disorders.
LEUKOCYTE NUMBER	Not relevant for the myeloma assessment.

LEUKOCYTE MORPHOLOGY	Not relevant for the myeloma assessment.
CIRCULATING PLASMA CELLS	Circulating plasma cells are generally a poor prognostic factor.
PLATELET NUMBER	Not relevant for the myeloma assessment.
PLATELET MORPHOLOGY	Not relevant for the myeloma assessment.
ASPIRATION DIFFERENTIAL COUNT (300 CELLS)	
ERYTHROIDS	Not relevant for the myeloma assessment.
PLASMA CELLS	Circulating plasma cells are usually a poor prognostic factor.
MYELOBLASTS	Not relevant for the myeloma assessment.
MYELOIDS	Not relevant for the myeloma assessment.
M:E RATIO	Not relevant for the myeloma assessment.
BONE MARROW ASPIRATE OR CORE BIOPSY	
SPECIMEN QUALITY	An indication of how representative the specimen is of the marrow. Look for terms such as “hemodiluted,” which implies blood contamination.
CELLULARITY	A measure of how cellular the marrow is. It will be reported as a percentage. Look for terms normal, hypo or hypercellular.
SPICULES	A measurement of quality. The presence of spicules means the sample is from the marrow with little or no blood contamination.
MYELOID TO ERYTHROID RATIO	A measure of developing white to red cells.
TRILINEAGE HEMATOPOIESIS	Refers to whether there is a normal development of the white cells, red cells, and platelets.
HEMATOPOIETIC MATURATION	
MEGAKARYOCYTE MORPHOLOGY	Appearance of the platelet precursor cells.
PLASMA CELL NUMBER	The percentage will be a significant determinant of classifying the type of disorder. A typical percentage of plasma cells is <5%
PLASMA CELL MORPHOLOGY	Look for terms such as “mature,” “immature,” or “atypical.” “Mature” is generally a better prognostic feature than the others.
CORE BIOPSY SPECIMEN QUALITY	Size of biopsy is important for assessing adequacy. It should be over 1cm.
BONE TRABECULAE	Should be present, which implies the sample is truly representative of the marrow.
CELLULARITY	Reported as a percentage of cells to fat in the marrow. Look for terms like normal, hypo or hypercellular.

BONE MARROW CLOT IMMUNOHISTOCHEMISTRY	
CD138	Stains may be performed to highlight the different cell types present. CD138 is an antibody stain that marks plasma cells and aids in enumeration.

HEALTHTREE UNIVERSITY CLASSES

- Why do a Bone Marrow Biopsy?
- Why are bone marrow biopsies (BMB) used in myeloma, and what tests are run on the BMB samples?
- What are the genetic tests that can be done on a sample of bone marrow? Can liquid biopsies (blood tests) be used to determine myeloma genetics? How often should testing be repeated?

Please note that the Reference Ranges given are not necessarily consistent between laboratories. Each laboratory is required to establish its own reference ranges. Abnormal results must be flagged as High, Low, or Critical if they fall out of the established normal range.

CHEMISTRY PANELS

Chemistry panels are run regularly during and after treatment to check your body's normal functions such as heart, kidney, insulin production, electrolyte levels, etc. Some indicators can also determine the aggressiveness of the myeloma.

LAB TESTED	REFERENCE RANGE	WHAT IT MEANS
TOTAL PROTEIN	6.5-8.6 mg/dL	Total protein in the blood, which includes both albumin and globulin. See special note for albumin.
ALBUMIN SERUM	3.5-4.7 mg/dl	A protein found in the blood. Low levels can be a sign of more advanced myeloma.
CALCIUM SERUM	8.4-10.2 mg/dl	May be higher in people with advanced myeloma because of bone destruction. Higher calcium levels should trigger your doctor to do more testing. High calcium can also cause severe constipation and loss of appetite. It can make patients feel weak, drowsy, and confused. If the calcium level gets high enough, it can cause kidney failure, and one may even lapse into a coma.
PHOSPHORUS SERUM	2.4-4.3 mg/dl	Phosphorus and calcium levels have an inverse relationship.
ANION GAP	17mE/L	The anion gap is a measurement of the relationship between the "electrolytes" (Sodium, Potassium, Chloride and Carbon Dioxide) and the combination of Magnesium and Phosphorus. Decreased levels (below 10 mEq/L) is used as a monitor of multiple myeloma.
GLUCOSE	64-128 mg/dl	Monitors glucose levels and insulin production.
BLOOD UREA NITROGEN (BUN)	6-22 mg/dL	Urea is a waste product excreted by the kidneys. High levels are the first sign of dehydration or possible kidney damage.

CREATININE SERUM	52-1.08 mg/dl	Creatinine is a waste product excreted by the kidneys. Elevated levels indicate poor hydration or possible kidney damage.
CREATININE CLEARANCE	>60 mL/min	Creatinine clearance is the gold standard measurement for kidney function. This measures urine excretion of creatinine against serum creatinine. If serum creatinine is elevated, creatinine clearance is low. As the kidneys start to fail, they lose the ability to dispose of excess salt, fluid, and body waste products, leading to symptoms such as weakness and leg swelling.
URIC ACID SERUM	2.5-7.0 mg/dl	Uric acid levels are watched during treatment. An elevated level can indicate tumor lysis syndrome.
ALKALINE PHOSPHATASE	38-126 IU/l	Alkaline Phosphatase levels are elevated in bone and liver disease.
BETA 2 MICROGLOBULIN, SERUM	1.21-2.70 mcg/mL	Tests for the severity of MM. This is another protein produced by the malignant cells. High levels indicate more aggressive disease. Decrease shows good treatment response. It can also identify kidney damage.
LACTATE DEHYDROGENASE (LDH), SERUM	100 - 253 or 300 - 600 or u/L	LD blood level is a nonspecific marker for the presence of tissue damage somewhere in the body. It cannot be used to identify the underlying cause or location of the cellular damage. LDH levels are elevated in aggressive myeloma and are associated with poor prognosis if there is no explanation for its increase other than myeloma. Each laboratory has a different range for what's normal. Your lab report should show the range that your lab uses for each test. LDH labs with different reference ranges cannot be compared to each other. The normal range is just a guide. Your doctor will look at your results based on your age, health, and other factors. A value that isn't in the normal range may still be normal for you.
SODIUM SERUM	136-144 mEq/l	Sodium, Potassium, Chloride and Carbon Dioxide are also known as "electrolytes" and are all linked to acid/base balance which is a delicate system maintained by lungs and kidneys which eliminate excessive amounts of each one to maintain this critical pH balance. The most important effects are the neurological and cardiac effects of elevated or decreased levels.
POTASSIUM SERUM	3.3-5.0 mEq/l	
CHLORIDE SERUM	98-107 mEq/l	
CARBON DIOXIDE	20-29 mM	A measure of acid-base status.
MAGNESIUM SERUM	1.6-2.3 mEq/l	Magnesium and calcium levels are linked and need to be kept in balance.
BILIRUBIN TOTAL	0.2-1.3 mg/dl	Total Bilirubin includes both direct and indirect bilirubin. Total bilirubin is a byproduct of hemoglobin and/or red cell destruction.
BILIRUBIN, INDIRECT	0.1-1.0 mg/dl	
BILIRUBIN, DIRECT	0-0.4 mg/dl	
SGOT (ALSO KNOWN AS) SERUM GLUTAMIC - OXALOACETIC TRANSAMINASE ASPARTATE	15-40 U/ml	The SGOT test measures an enzyme found in the liver, muscles (including the heart), and red blood cells. It is released into the blood when cells that contain it are damaged. The SGOT level is measured to check the function of your liver, kidneys, heart, pancreas, muscles,

AMINOTRANSFERASE AST AMINOTRANSFERASE		and red blood cells. It is also measured to check on medical treatments that may affect the liver.
SGPT (ALSO KNOWN AS) SERUM GLUTAMIC-PYRUVIC TRANSAMINASE ALANINE AMINO TRANSAMINASE	8-50 U/ml	The SGPT enzyme is present in liver cells. When a cell is damaged, it leaks this enzyme into the blood, where it is measured. It rises dramatically in acute liver damage, such as viral hepatitis or paracetamol (acetaminophen) overdose.

HEALTHTREE UNIVERSITY CLASSES

- What other blood tests are useful if you suspect a myeloma diagnosis?
- What kidney dysfunction is associated with myeloma and why?

MYELOMA CROWD ARTICLES

- Multiple Myeloma Diagnosis
- What are C.R.A.B. Symptoms of Multiple Myeloma
- Myeloma Patients Should Monitor Their Kidney Function Early & Often

Please note that the Reference Ranges given are not necessarily consistent between laboratories. Each laboratory is required to establish its own reference ranges. Abnormal results must be flagged as High, Low, or Critical if they fall out of the established normal range.

COMPLETE BLOOD COUNT (CBC)

Multiple myeloma is a cancer of the plasma cells. These are immune system cells that produce specialized molecules called antibodies to help fight infectious agents. Because most plasma cells live in bone marrow, multiple myeloma tumors are usually, but not always, found in bone. The bone marrow is where blood cells are produced. Because multiple myeloma crowds out bone marrow, it can cause several kinds of blood deficiencies such as : Anemia, a shortage of red blood cells, Thrombocytopenia, a shortage of blood platelets, and Leukopenia, a shortage of white blood cells.

	REFERENCE RANGE	WHAT IT MEANS
WHITE BLOOD CELL COUNT (WBC)	3.2-10.6 k/ul	White blood cells are produced in the bone marrow. White blood cell counts include: Neutrophils (also known as granulocytes), Lymphocytes, Monocytes, Eosinophils, and Basophils. The counts are reported in two ways. First as a percentage of the total WBC count and also as an "absolute" count or an actual number of cells present. When there are too few white cells, Leukopenia lowers resistance to infections and can cause such ailments as pneumonia. High WBC may indicate illness or cancer growth.
RED BLOOD CELL COUNT (RBC)	3.88-5.46 10^{12} /L	Low RBC counts indicate anemia resulting in fatigue and lowered oxygen transport and can result from bleeding or low RBC production in the bone marrow.
HEMOGLOBIN (HGB)	12.1-15.9 g/dL	Hemoglobin is carried in the red blood cells. Anemia causes weakness, reduced ability to exercise, shortness of breath, and

		dizziness. If The hemoglobin is less than 7.5 G/DL, many facilities will transfuse unless the patient is symptomatic. If it is less than 9%, Aranesp injections are sometimes used to stimulate red blood cell production.
HEMATOCRIT (HCT)	34.3-46.6 %	Hematocrit measures the percentage of whole blood volume made up of red blood cells. This measurement depends on the number of red blood cells and the size of red blood cells.
MEAN CORPUSCULAR VOLUME (MCV)	77.8-94 fL	MCV measures the average red blood cell volume
MEAN CORPUSCULAR HGB (MCH)	26.5-32.6 pg	MCH is a measure of the hemoglobin content in the average red cell.
MEAN CORPUSCULAR HGB CONCENTRATION (MCHC)	32.7-36.9	MCHC is the average hemoglobin concentration in a given volume of packed red cells.
RED CELL DISTRIBUTION WIDTH (RDW)	10.8-14.1%	
PLATELET COUNT	150 - 440 k/ul	Platelets are produced in the bone marrow, and their primary function is to induce coagulation at points of injury. When blood platelet counts are low (thrombocytopenia), minor scrapes, cuts, or bruises may cause serious bleeding.
MEAN PLATELET VOLUME	5.9-9.8 fl	Platelets are microscopic cells. This test measures their size and volume.
NEUTROPHIL / GRANULOCYTE ABSOLUTE COUNT (ANC) or (AGC)	1.3-7 k/ul	Neutrophils (granulocytes) are the most numerous of the white blood cells. They are the "soldiers" that fight infections. They engulf infectious particles (bacteria)in your body. Low levels indicate the inability to fight infection.
NEUTROPHIL OR GRANULOCYTE PERCENT	44-76 %	
LYMPHOCYTE ABSOLUTE COUNT	0.8-3.1 k/ul	Lymphocytes are the essential cell type in the body's immune system. There are three major types of lymphocytes: B lymphocytes that produce antibodies; T lymphocytes that have several functions and assist in antibody production; and natural killer (NK) cells that can attack virus-infected cells or tumor cells. Low levels indicate the inability to fight infection.
LYMPHOCYTE PERCENT	14.7-42.6 %	
MONOCYTE ABSOLUTE COUNT	0.2-0.7 k/ul	Monocytes also help to fight infections. When they enter the tissues, they fight infection, ingest dead cells and assist in immune responses.
MONOCYTE PERCENT	4-8.9 %	
EOSINOPHIL ABSOLUTE COUNT	0-0.4 k/ul	Eosinophils are elevated in allergic reactions and help to fight certain parasitic infections.

EOSINOPHIL PERCENT	0-6 %	
BASOPHIL ABSOLUTE COUNT	0-0.1 k/ul	Basophils also participate in allergic reactions.
BASOPHIL PERCENT	0.0-1.7 %	
IMMATURE GRANULOCYTE ABSOLUTE COUNT (MD)	-	Immature neutrophils or granulocytes cells may be released prematurely from the bone marrow.
IRON	60-150 µg/dl	These tests are all related to your body's red cell production status and help the physician monitor your disease because red cells transport iron.
IRON BINDING CAPACITY	35-150 mcg/dL	
IRON SATURATION	14-50%	
FERRITIN	11-336 mcg/L	
FOLATE	>4.0 mcg/L	
TOTAL IRON BINDING CAPACITY (TIBC)	250-400 mcg/dL	
TRANSFERRIN SATURATION		
VITAMIN B12	180-914 ng/L	
THYROID STIMULATING HORMONE (TSH)	0.3-4.2 mIU/L	Can be a contributing factor to anemia.

HEALTHTREE UNIVERSITY CLASSES

- What other blood tests are useful if you suspect a myeloma diagnosis?
- What is plasma cell leukemia?
- Primary PCL vs. secondary PCL

MYELOMA CROWD ARTICLES

- Multiple Myeloma Diagnosis

Please note that the Reference Ranges given are not necessarily consistent between laboratories. Each laboratory is required to establish its own reference ranges. Abnormal results must be flagged as High, Low, or Critical if they fall out of the established normal range.

BLOOD COAGULATION		
	REFERENCE RANGE	WHAT IT MEANS
INTERNATIONAL NORMALIZED RATIO (INR)	3.2-10.6 k/ul	INR is the actual number used for measuring therapeutic Coumadin dosing.
PROTHROMBIN TIME (PT)	12-15.5 seconds	Prothrombin times are used to investigate prolonged bleeding disorders and monitor warfarin (Coumadin) anticoagulant therapy.
PARTIAL THROMBOPLASTIN TIME (APTT)	24-35 seconds	Partial thromboplastin times are used to investigate prolonged bleeding disorders and monitor heparin anticoagulant therapy
Please note that the Reference Ranges given are not necessarily consistent between laboratories. Each laboratory is required to establish its own reference ranges. Abnormal results must be flagged as High, Low, or Critical if they fall out of the established normal range.		

IMMUNOLOGY/ALLERGENS		
	NORMAL RANGE	WHAT IT MEANS
C-REACTIVE PROTEIN	0-0.8 mg/dL	An elevated C-Reactive Protein is an indicator of inflammation in your body. It is an indirect measurement of the size and growth of myeloma tumors.
Please note that the Reference Ranges given are not necessarily consistent between laboratories. Each laboratory is required to establish its own reference ranges. Abnormal results must be flagged as High, Low, or Critical if they fall out of the established normal range.		

TOXICOLOGY / DRUG LEVELS		
LAB TESTED	NORMAL RANGE	WHAT IT MEANS
CYSTATIN C	Varies per age	Cystatin C is a protein encoded by the CST3 gene and is mainly used as a biomarker of kidney function.

PULMONARY FUNCTION TESTS	
These tests check for pulmonary function prior to and between treatments.	
LAB TESTED	WHAT IT MEANS
FVC	FVC - Forced Vital Capacity - after the patient has taken in the deepest possible breath, this is the volume of air that can be forcibly and maximally exhaled out of the lungs until no more can be expired. FVC is usually expressed in units called liters. This PFT value is critically important in the diagnosis of obstructive and restrictive diseases.

FEV1	Forced Expiratory Volume in One Second - this is the volume of air that can be forcibly exhaled from the lungs in the first second of a forced expiratory maneuver. It is expressed as liters. This PFT value is critically important in the diagnosis of obstructive and restrictive diseases.
DLCO / DSBHB	Diffusing capacity of the lungs for carbon monoxide (DLCO).

MY IMAGING TESTS

Imaging tests are critical for a myeloma diagnosis as well as detection of recurring myeloma. It is important to know that not every imaging test will be performed on every patient and many times the imaging tests are alternated.

IMAGING TEST	WHAT IT MEANS
SKELETAL SURVEY / BONE SCAN	This is a traditional X-ray that looks for the number of visible lytic lesions. The number of lytic lesions found can help describe the stage of myeloma.
BONE MARROW CHARACTERISTICS	Sometimes CT or MRI can detect marrow abnormalities, which would be reported as “enhancement.”
WHOLE BODY LOW DOSE COMPUTED TOMOGRAPHY	The more advanced Whole-Body Low Dose Computed Tomography (WBLDCT) is superior in detecting bone defects, and it has prognostic significance. However, it has the disadvantage of a much larger radiation dose than a skeletal survey. Like the skeletal survey, CT displays mostly bone destruction, but it can also be useful for assessing bone stability. The International Myeloma Working Group (IMWG) includes lytic lesions detected by WBLDCT as justification for treatment in myeloma patients, even those who are not otherwise symptomatic.
POSITIVE EMISSION TOMOGRAPHY (PET) SCAN	A PET scan can detect enlarged lymph nodes, liver or spleen, and bone lesions. The test is repeated to measure the size of these and other structures during and after treatment. A report is generated by a radiologist with an interpretation for your physician. PET is helpful for evaluating focal lesions after therapy.
FOCAL/LYTIC LESIONS ON PET	Particular notes of focal/osteolytic lesions progression on PET scans.
COMPUTED TOMOGRAPHY (CT) SCAN	A CT Scan can detect enlarged lymph nodes, liver or spleen, and bone lesions. A CT scan can be used to measure the size of these and other structures during and after treatment. A report is generated by a Radiologist with an interpretation for your physician.
FOCAL/LYTIC LESIONS ON CT	Particular notes of focal/osteolytic lesions progression on CT scans.
PET/CT	When PET and CT are combined, sequential images are acquired and merged into a single superimposed image. This means that the functional imaging of PET can be aligned with the anatomic imaging of CT scanning. Importantly, PET/CT has prognostic significance and is considered a factor in assessing measurable or minimal residual disease status (MRD).
WHOLE BODY DIFFUSION WEIGHTED IMAGING	Diffusion-Weighted Magnetic Resonance Imaging, also known as Whole Body Diffusion-Weighted Imaging (WB DWI), is an advance in imaging that will likely have an increasing role in detecting and quantifying disease as well as guiding therapy. WB DWI is currently the most sensitive technique for bone marrow imaging.

MAGNETIC RESONANCE IMAGING (MRI)	Magnetic Resonance Imaging results are reported by a Radiologist with an interpretation for your physician. This test is used to monitor changes in lesions. MRI scans are helpful in patients with suspected SMM to rule out focal bone marrow lesions that can be seen before true osteolytic disease occurs. Helpful in assessing extramedullary disease, suspected cord compression, or when detailed imaging of a specific symptomatic area is needed.

HEALTHTREE UNIVERSITY CLASSES

- What imaging is used at diagnosis to detect myeloma bone disease?
- How often should imaging be repeated?
- How is myeloma bone disease monitored?
- What are lytic and focal bone lesions and how common are they?
- What is extramedullary disease?
- What is a plasmacytoma?
- Do you need a CT scan or is an MRI enough?

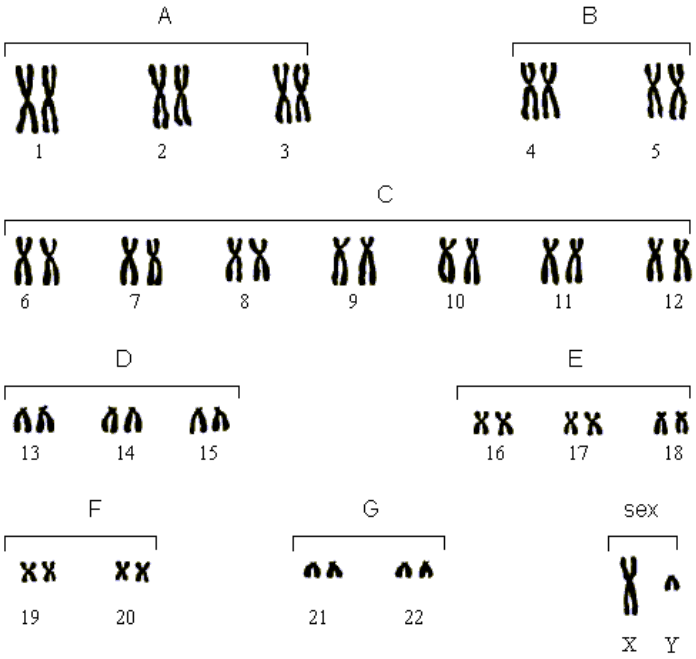
MYELOMA CROWD ARTICLES

- Multiple Myeloma Diagnosis
- Dr. Jens Hillengass from Roswell Park Comprehensive Cancer Center presented Novel Imaging in Multiple Myeloma.
- Myeloma Crowd Round Table with Drs. Jens Hillengass and Ola: Myeloma Imaging

My Myeloma Genetics

In humans, each cell typically contains 23 pairs of chromosomes, for a total of 46. Twenty-two of these pairs, called autosomes, look the same in both males and females. The 23rd pair, the sex chromosomes, differ between males and females.

The 22 pairs are numbered by size (autosomes). The other two chromosomes, X and Y, are the sex chromosomes. A woman will have two X chromosomes, and a man one X and one Y. This picture of the human chromosomes lined up in pairs is called a karyotype. Autosomes are further divided into seven groups: A to G.



Nomenclature

[Total number of chromosomes], [Sex chromosomes], [Chromosomal Alterations] [Number of cells analyzed with that karyotype]

Normal results

46, XX (Female) or 46, XY (Male).

Common symbols for alterations used in karyotypes

del (deletion), t (translocation), dup (duplication), + (gain of), - (loss of), p (the short arm of the chromosome), q (long arm of the chromosome), / (Mosaicism, two populations of cells that coexist with different karyotypes).

Example

47, XX,+21, +21, -14, t(2;8)(q21;p13) [8] / 46, XX [12]: Female with 8 of 20 cells presenting a gain of two chromosomes 21, a loss of one chromosome 14, and a balanced translocation between chromosome 2 and chromosome 8, with breaks in 2q21 and 8p13, and a second cell population (12 of 20 cells) with a normal female karyotype.

Learn more as Dr. Brian Van Ness from the University of Minnesota explains Chromosomes and Dr. Leif Bergsagel of the Mayo Clinic (Scottsdale) explains Karyotyping-classical cytogenetics.

If you want to learn more about what genetic tests can be done on a sample of bone marrow, you will find here a quick summary made by three Myeloma specialists at HealthTree University.

COMMON GENETIC ABNORMALITIES IN MYELOMA

YOUR RESULTS	WHAT IT MEANS
Hyperdiploidy 	Normal chromosomes or genes typically come in sets of two (2). In healthy people, the chromosomes of plasma cells are in normal pairs. If three copies exist, it is called a **trisomy**. If four copies exist, it is called a **tetrasomy**, and so on. This is also sometimes called hyperdiploid myeloma (too many chromosomes). Hyperdiploid myeloma is typically less aggressive than hypodiploid myeloma (too few chromosomes). This 2015 paper by French myeloma researchers found that trisomies of chromosome 3 and 5 improved overall survival, even for patients with the 4;14 translocation. In the same paper, it was found that trisomy of chromosome 21 worsened overall survival. In this 2017 article, myeloma researchers studied 227 patients with tetrasomies. The most common tetrasomies were 9, 15 and 11. The median overall survival of patients with one or more tetrasomies was superior compared to patients with trisomies (3 copies of the chromosomes) or patients with neither. If the patients had a high-risk genetic feature (like del17p or t4;14) plus a trisomy or tetrasomy, they had better overall survival than those with high-risk features without tetrasomies, but worse than those with no high-risk features. The most common gene addition in multiple myeloma is **a gain of 1q**. This gain occurs in approximately 40% of myeloma patients. According to a recent study, this gene addition is not considered high-risk if you have three copies of the chromosome. It is only considered high-risk if you have four or more copies of the chromosome. Reference: Rapid Assessment of Hyperdiploidy in Plasma Cell Disorders Using a Novel Multi-Parametric Flow Cytometry Method. Learn more as Dr. Brian Van Ness and Dr. Rafael Fonseca explain hyperdiploid myeloma at HealthTree University.
Hypodiploidy 	Normal chromosomes or genes typically come in sets of two (2). In healthy people, the chromosomes of the plasma cells are in normal pairs. In patients with multiple myeloma, genes of the myeloma cells can become deleted. One or both of the genes in a normal pair can be missing. Common gene deletions in myeloma include deletion of chromosome 13, chromosome 1p, or chromosome 17p. A less common deletion is of chromosome 16.

Translocation 	Normal chromosomes or genes typically come in sets of two (2). In healthy people, the chromosomes of plasma cells are in normal pairs. In patients with multiple myeloma, sometimes the chromosomes can break apart and swap places with parts of another chromosome. This is called a translocation. For example, in a 4;14 translocation, part of chromosome 4 has swapped places with chromosome 14. Common translocations include t(4;14), t(11;14), t(14;16), t(14;20). Less common translocations include t(6;14) and t(12;14). Translocations can be considered standard risk or high risk. Standard risk include t(11;14) and t(6;14). High risk include t(4;14), t(14;16) and t(14;20).
Gene Mutation	A gene mutation is an alteration in the DNA sequence that makes up a gene. The gene is a protein inside a cell that helps the cell function properly by providing instructions. It can be inherited or acquired. The mutation can vary in size to involve a single gene or a group of genes on a chromosome. A mutation can cause the cell to malfunction and disrupt normal development or cause a medical condition.

HEALTHTREE UNIVERSITY CLASS

Learn more as Dr. Gareth Morgan from NYU Langone Health, Dr. Cesar Rodriguez Valdes of Wake Forest Baptist Health, and Dr. Brian Van Ness from the University of Minnesota explain what are the different types of chromosomal mutations (e.g. Translocations, Deletions, Insertions, Amplifications) in HealthTree University.

CYTOGENETICS/FISH

YOUR RESULTS	WHAT IT MEANS
Cytogenetics ❑ Normal ❑ Abnormal **Gene additions** ❑ Gain 1q21 **Hyperdiploid** ❑ Trisomy ❑ Tetrasomy **Hypodiploid** ❑ Near-tetraploid ❑ Pseudodiploid ❑ Hypodiploid **Relevant deletions** ❑ 1p ❑ 13q ❑ 16p ❑ 17p (TP53) **Translocations** ❑ FGFR3/MMSET t(4;14) ❑ CCND1 t(11;14) ❑ CCDN2 C-MAF t(14;16) ❑ CCND2 MAFB t(14;20) ❑ MUM1 t(6;14)	**Metaphase cytogenetics** is a test that puts dividing myeloma cells in culture and identifies abnormalities while the cells are dividing. Because myeloma cells can't grow outside the bone marrow environment, only 30% of patients show abnormalities, which means they have more aggressive disease. For the 70% of patients whose myeloma cells don't show abnormalities during cell division, they have less aggressive disease. The advantage of this test is that it identifies the 30% of patients with more aggressive disease, but is not very informative in 70% of patients with less aggressive disease. **The FISH test** allows you to look at certain "hot spots" or probes on the chromosomes and it allows you to find translocations of genes. The FISH test does not need actively dividing cells. This test is informative for all patients. The limitation is that you can only see what you're looking for, or there are only a certain number of probes. The FISH test evaluates the chromosomes in the normal

Pathway Activation/Inactivation ❑ Rb pathway inactivation (P16/INK4a, P18/INK4c, RB1) ❑ PTEN inactivation ❑ P53 inactivation (17p13) **Other Mutations** ❑ C-MYC abnormalities ❑ RAS mutations (K-RAS and N-RAS)	and myeloma cells in the bone marrow. Some may have too many chromosomes, too few chromosomes or other chromosome abnormalities. This test takes approximately 2-3 weeks. It can be used on regular blood or bone marrow samples. The quality of the specimen and of the test matters greatly.

HEALTHTREE UNIVERSITY CLASS

Learn more as Dr. Gareth Morgan of the NYU Langone Health and Dr. Leif Bergsagel of the Mayo Clinic (Scottsdale) explain FISH testing in HealthTree University.

FLOW CYTOMETRY

YOUR RESULTS	WHAT IT MEANS
❑ Cytoplasmic Kappa ❑ Cytoplasmic Lambda ❑ CD 138 ❑ CD 117 ❑ CD 81 ❑ CD 56 ❑ CD 45 ❑ CD 38 ❑ CD 20 ❑ CD 19	**Flow cytometry** is a test used on both blood samples and bone marrow samples to evaluate for the presence of myeloma cells and can detect low levels of myeloma plasma cells after high-dose therapy and transplantation. It is used as the method of choice to assess minimal residual disease (MRD), it doesn't need a baseline sample, and its sensitivity is 1 in 100,000 cells. It looks in more detail than the immunohistochemistry tests and studies the light chains. This test is used to classify cells according to substances present on their surfaces. 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 sensitivity tests can range from 2 color tests (less sensitive) up to 12 color tests (more sensitive). This test helps to identify "markers" on the cell's surface and may give us targets for the use of monoclonal antibodies

NEXT GENERATION SEQUENCING

YOUR RESULTS	WHAT IT MEANS
❑ ATM ❑ BCAR3 ❑ BRAF ❑ DIS3 ❑ FAM46C ❑ FGFR3 ❑ IDH2 ❑ KRAS ❑ NRAS ❑ TP53	**Next Generation Sequencing (NGS)** examines the individual nucleic acids that make up the DNA, this allows the detection of all types of genomic alterations, and unknow translocation patterns. Usually, a targeted sequencing panel is used to test a select number of frequently mutated genes instead of the entire genome, as this is a cheaper and faster approach. The different mutated sequences will be compared with a normal sequence, the frequency of any given change not seen in a healthy person will be reported and categorized. It is used as a method to

❑ TRAF3	assess minimal residual disease (MRD), it needs a baseline sample for assessment, and its sensitivity is 1 in 1 million cells.

HEALTHTREE UNIVERSITY CLASSES

Learn more as Dr. Leif Bergsagel of the Mayo Clinic (Scottsdale) explains the difference between genetic testing such as FISH and Next Generation Sequencing in HealthTree University. Also you'll find a comparison between MRD by Flow cytometry, and MRD by NGS, explained by Myeloma Specialists in HealthTree University.

MINIMAL RESIDUAL DISEASE (MRD) TESTING

YOUR RESULTS	WHAT IT MEANS
By flow cytometry /100,000 analyzed cells **By NGS** /1 million analyzed cells	**Measurable (or minimal) residual disease (MRD)** refers to the small number of cancer cells that can remain in a patient's body during and after treatment and may eventually cause recurrence of the disease. These residual cells typically cause no physical signs or symptoms and are present at such low levels that more refined and sensitive techniques are required to identify them. Monitoring MRD at various points throughout the course of treatment and remission provides important insight into the status of a patient's disease. **Flow cytometry** is a test used on both blood samples and bone marrow samples to evaluate for the presence of myeloma cells and can detect low levels of myeloma plasma cells after high-dose therapy and transplantation. It is used as the method of choice to assess minimal residual disease (MRD) due to its higher accessibility, it doesn't need a baseline sample, and its sensitivity is 1 in 100,000 cells. **Next Generation Sequencing (NGS)** examines the individual nucleic acids that make up the DNA. This is used as a method to assess minimal residual disease (MRD), it needs a baseline sample for assessment, and it has a higher sensitivity of 1 in 1 million cells. **MRD negativity** does not mean there are no myeloma cells in the bone marrow. It means that there are no myeloma cells in the tested sample. Patients with Sustained MRD Negativity (Remain MRD- for over a year) are more likely to have a longer progression-free survival (PFS) and overall survival(OS). If your institution does not do MRD testing, you can send a bone marrow sample to a lab that does. Mayo Clinic is one of the labs accepted by Medicare.

HEALTHTREE UNIVERSITY CLASSES

Learn more at HealthTree University, where we have a complete chapter dedicated to MRD testing. You can find here the first class in which several faculty doctors explain what MRD is and how useful it is.

GENE EXPRESSION PROFILE

WHAT IT MEANS

You receive a **Prognostic Risk Score** (GEP-70), **Molecular Subtype**, and **Virtual Karyotype** unique to your disease.

The Prognostic Risk score and the Molecular Subtype designations have been clinically shown to predict overall survival, event-free survival, complete response duration, and post-relapse survival.

Risk Score: MyPRS distinguishes between patients with high and low-risk disease.
High-Risk: Poor Prognosis, Probability of 5-year OS 38%
Low Risk: Good Prognosis, Probability of 5 year OS 83%

Molecular Subtype: You receive 1 of 7 molecular subtypes associated with your unique genetic lesions, altered genes and outcome variation.

Virtual Karyotype: Your Cytogenetic (FISH) results checking for high-risk chromosome abnormalities.

HEALTHTREE UNIVERSITY CLASS

Learn more as Dr. Gareth Morgan of the NYU Langone Health and Dr. Brian Van Ness from the University of Minnesota explain Gene Expression Profile (GEP) in HealthTree University.

SINGLE NUCLEOTIDE POLYMORPHISM (SNP) ARRAY

WHAT IT MEANS

Single Nucleotide Polymorphism (SNP) Array is a genetic test currently not used in the clinical setting, that allows you to look for differences between cells, and is typically used as a way to estimate gains and losses of chromosomal material in the whole genome. It can be used for relevant mutations like Gain 1q21, or Deletions 17p/16p/13q/1p.

HEALTHTREE UNIVERSITY CLASS

Learn more as Dr. Leif Bergsagel of the Mayo Clinic (Scottsdale) explains what is a SNP Array in HealthTree University.

SPECIFIC GENETIC ABNORMALITIES IN MYELOMA

YOUR RESULTS	WHAT IT MEANS
Gain 1q 	The addition of 1q or gain of 1q is found in 38-40% of myeloma patients. According to a recent study, this gene addition is not considered high-risk if you have **three copies** of the chromosome. It is only considered high-risk if you have **four copies** of the chromosome. The number of copies of the 1q gain is available on your FISH test. If you can't find your number of copies, ask your doctor if the information is available and include the number of copies in the comments section of the FISH test results in HealthTree. In this study, when Next Generation Sequencing was used for 95 patients with the 1q gain, it was found that the most common additional mutations found in 1q gain patients included TP53 (38%) and KRAS (25%). References: • Nature.com - Prediction of outcome in newly diagnosed myeloma • Blood Journal - Outcome of Multiple Myeloma with Chromosome 1q Gain
	Learn more as Dr. Martin Kaiser from The Institute of Cancer Research (London), and Dr. Cesar Rodriguez Valdes of Wake Forest Baptist Health, explain different aspects of the gain 1q in HealthTree University.
Deletion 1p 	The deletion of 1p occurs in 8.4% of myeloma patients. It is believed that deletion of the short arm of chromosome 1 results in the loss of tumor suppressor genes that are part of P73, a member of the TP53 family. TP53 is the master cancer regulator gene. According to studies, the deletion of 1p is associated with shorter remission and survival in patients undergoing autologous stem cell transplant. Patients with del1p may require more intensive therapy. References: • ScienceDirect - Deletion of the Short Arm of Chromosome 1 (del 1p) is a Strong Predictor of Poor Outcome in Myeloma Patients Undergoing an Autotransplant • NCBI - Mapping of Chromosome 1p Deletions in Myeloma • Blood Journal: Outcome of Multiple Myeloma with Chromosome 1q Gain & 1p Deletion after High-Dose Therapy and Autologous Hematopoietic Stem Cell Transplantation

Monosomy 13 	A deletion 13 or monosomy 13 means that the 13 chromosome is missing inside of the multiple myeloma cells. This deletion is commonly found in 59% of myeloma patients. It is not considered a high-risk feature if only found on the FISH test results. It can be considered high risk if it is also found on conventional (also called metaphase) cytogenetics (present in only 17% of patients). The deletion of 13 is commonly found together with the t(4;14) translocation (in 90% of del13 patients). References: • Journal of Clinical Oncology - Clinical utility of the comprehensive approach to detect genetic abnormalities in multiple myeloma • Blood Journal - Treatment of Multiple Myeloma with high-risk cytogenetics: a consensus of the International Myeloma Working Group • Blood Journal - Acquired Chromosomal Abnormalities t(14;16), Del(17p) or Del(13q) after Receiving Chemotherapies Predict the Poor Prognosis of Multiple Myeloma
Deletion 16q 	A deletion 16q occurs in an unknown percentage of myeloma patients. It is considered a higher risk feature. References: • Blood Journal - Gene mapping and expression analysis of 16q loss of heterozygosity identifies WWOX and CYLD as being important in determining clinical outcome in multiple myeloma • Wiley - A molecular diagnostic approach able to detect the recurrent genetic prognostic factors typical of presenting myeloma
Deletion 17p 	A deletion 17p means that one or both of the 17 chromosomes are missing inside of the multiple myeloma cells. This deletion is found in approximately 8-10% of newly diagnosed myeloma patients. The deletion of 17p has an associated gene - TP53. The TP53 gene is the master cancer regulator gene, so when the chromosomes are deleted, myeloma is not regulated normally. Myeloma patients can commonly acquire this gene deletion as their disease progresses. According to Dr. Robert Orlowski, “Some studies suggest that it (del17p) can be as high as 30% and a few even suggest that it may be as high as 50% for patients in the refractory area.” While deletion 17p is typically considered a high-risk feature, it may not be high-risk in all patients. Based on study data, it was found that if only one of the 17p chromosomes were deleted, the myeloma did not behave as high risk. If both of the 17p chromosomes had been deleted, the myeloma behaved as high-risk. This information will not show on your FISH test. You need a Next Generation Sequencing test to find this information. The percentage of del17p cells is important. For example, patients with low percentages of del17p such as 5% will typically be considered lower risk than patients with more than 60% of del17p. Deletion 17p patients may respond better to proteasome inhibitors when used as induction therapy and as maintenance according to recent studies. Other

	treatment approaches may include three or four-drug induction therapies, one or two transplants, and maintenance therapies with double or triple agents as opposed to a single maintenance therapy. References: • Journal Of Clinical Oncology - Mutational Spectrum, Copy Number Changes, and Outcome: Results of a Sequencing Study of Patients With Newly Diagnosed Myeloma • NCBI - The level of deletion 17p and bi-allelic inactivation of TP53 has a significant impact on clinical outcome in multiple myeloma • MyelomaCrowd - Why is del17p in multiple myeloma so aggressive? • Sue Armstrong - p53: The Gene that Cracked the Cancer Code • NCBI - Treatment of multiple myeloma with high-risk cytogenetics: a consensus of the International Myeloma Working Group • nature.com - A high-risk, Double-Hit, group of newly diagnosed myeloma identified by genomic analysis • MyelomaCrowd - ASH 2018: High Risk and "Double Hit" Myeloma • MyelomaCrowd - MCRI Full Show: Overcoming Deletion 17p Using a Specifically Targeted Therapy with Dr. Robert Orlowski, MD, PhD, MD Anderson
	Learn more as Dr. Fotis Asimakopoulos from Moores Cancer Center (UCSD), Dr. Cesar Rodriguez Valdes of Wake Forest Baptist Health, Dr. Donna Reece from Princess Margaret Cancer Centre, and Dr. Leif Bergsagel of the Mayo Clinic (Scottsdale) explain different aspects of deletion 17p in HealthTree University: • What is a 17p deletion? Why is Del of 17p considered high risk? • Can only a percentage of your myeloma cells possess 17p deletion? How is that percentage determined? • What does it mean if you have a mutation in chromosome 17 and a deletion? HowNext-Generation? How does this affect risk? • Will Del17p and other chromosomal abnormalities go away after an auto ASCT? If not why may it not be detected?
Translocation (6;14) 	Approximately 1% of patients have the 6;14 translocation. This means that part of chromosome 6 has swapped places with part of chromosome 14. When this happens, it affects the Cyclin D3 gene or CCND3, which can turn cells into cancer cells. References: NCBI - Cyclin D3 at 6p21 is dysregulated by recurrent chromosomal translocations to immunoglobulin loci in multiple myeloma

Translocation (11;14) 	Approximately 15% of myeloma patients have the 11;14 translocation. This means that part of chromosome 11 has swapped places with part of chromosome 14. It is the most common translocation. It is considered a standard risk feature and can be commonly found in patients of African descent. When this happens, it increases the regulation of Cyclin D1 or CCND1. A helpful therapy that looks particularly promising for this translocation is venetoclax. References: • nature.com - Natural history of t(11;14) multiple myeloma • EHA - Deep And Sustained Response After Venetoclax Therapy In A Patient With Very Advanced Refractory Myeloma With Translocation T(11;14) • ScienceDirect - Clinical Implications of t(11;14) in Patients with Multiple Myeloma Undergoing Autologous Stem Cell Transplantation • Blood Journal - Variable BCL2/BCL2L1 ratio in multiple myeloma with t(11;14)
Translocation (14;16) 	Approximately 3% of patients have the 14;16 translocation. This means that part of chromosome 14 has swapped places with part of chromosome 16. When this happens, it affects the c-MAF gene, which can turn cells into cancer cells. It is generally considered a high-risk feature. References: • Blood Journal - Translocation t(14;16) and multiple myeloma: is it really an independent prognostic factor? • Clinical Lymphoma, Myeloma & Leukemia - Translocation (14;16) Positive Multiple Myeloma: Clinical Features and Survival Outcomes of a High-risk Population
Translocation (14;20) 	Approximately 2% of patients have the 14;20 translocation. This means that part of chromosome 14 has swapped places with part of chromosome 20. When this happens, it affects the MAFB gene, which can turn cells into cancer cells. It is generally considered a high-risk feature. References: • NCBI - The t(14;20) is a poor prognostic factor in myeloma but is associated with long-term stable disease in monoclonal gammopathies of undermined significance. • Wiley - The recurrent translocation t(14;20)(q32;q12) in multiple myeloma results in aberrant expression of MAFB
Translocation (4;14) 	Approximately 12% of patients have the 4;14 translocation. This means that part of chromosome 4 has swapped places with part of chromosome 14. When this happens, it increases the fibroblast growth factor receptor 3 gene (FGFR3) and the multiple myeloma Set domain gene (MMSET). This is considered a high-risk feature. References: • Blood Journal - Lenalidomide Maintenance Significantly Improves Outcomes Compared to Observation Irrespective of Cytogenetic Risk: Results of the Myeloma XI Trial

	• Blood Journal - MMSET I Acts As an Oncoprotein and Regulates GLO1 Expression in T(4;14) Multiple Myeloma Cells
HEALTHTREE UNIVERSITY CLASS	
Learn more as Dr. Fotis Asimakopoulos from Moores Cancer Center (UCSD) explains the importance of **Chromosome 14** and its relation to high-risk myeloma in HealthTree University.	
Learn more about **translocation 4;14** and its relation to high-risk myeloma in Myeloma Crowd.	